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

Clinician Outreach and Communication Activity (COCA) Webinar

July 27, 2017

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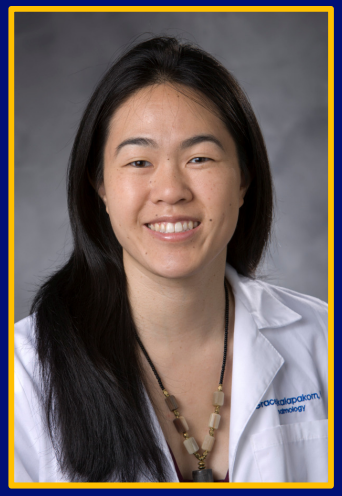
Senior Medical Officer, Office of Infectious Diseases
National Center for Emerging & Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

TODAY'S THIRD PRESENTER



Sasapin Grace Prakalapakorn, MD, MPH
Assistant Professor of Ophthalmology and Pediatrics
Duke Ophthalmology
Duke University School of Medicine

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  - Click the Q&A button in the webinar
  - Type your question in the Q&A box
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CDC'S Response to **Zika**

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

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

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

July 27, 2017

Topics to be covered

- Updated interim guidance for pregnant women
  - Emerging data and current state of epidemic
  - Updated recommendations for testing and interpretation of results
- Pregnancy outcomes after maternal Zika virus exposure
  - Zika Pregnancy and Infant Registries
  - Findings from the Zika Pregnancy and Infant Registries and implications
- Pediatric ophthalmologic findings among infants following congenital Zika virus infection
  - Ocular findings among infants with congenital Zika virus infection
  - CDC guidance for ophthalmologic screening for infants with possible congenital infection

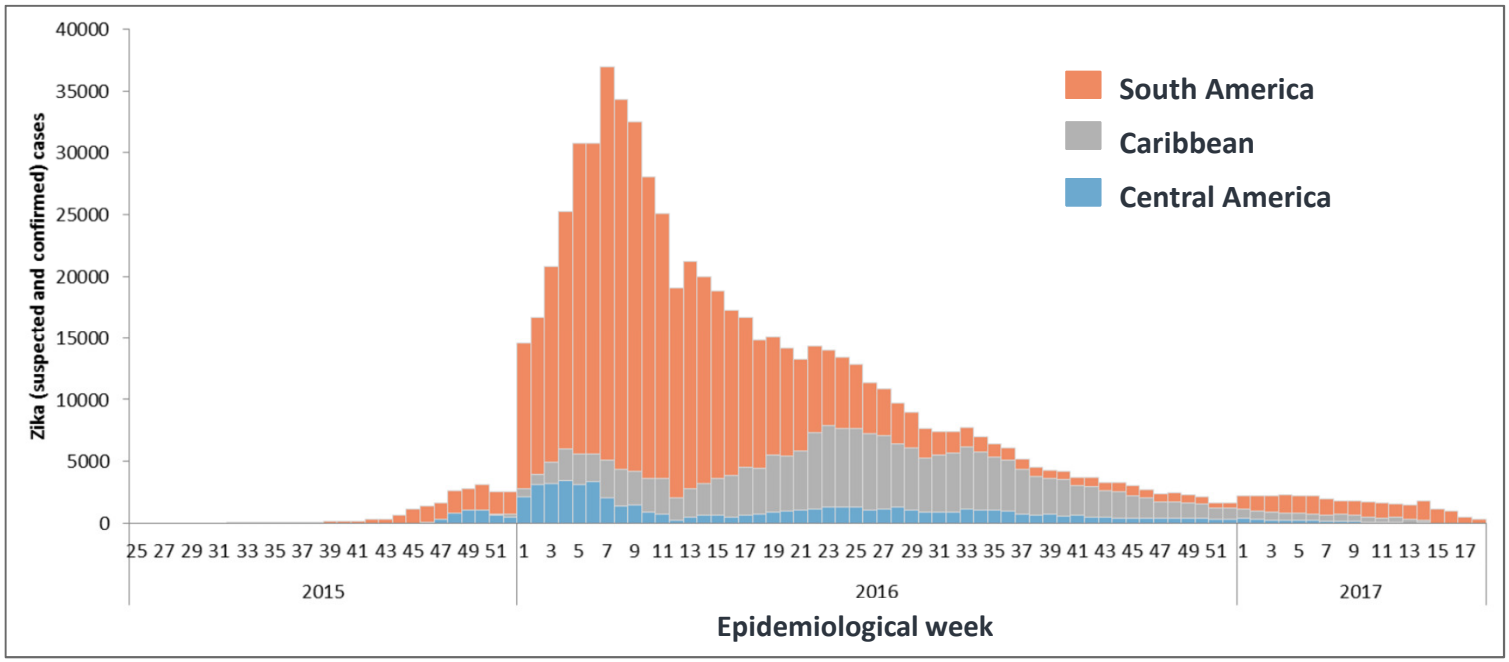
Emerging Data and Current State of Epidemic

Big Picture: Emerging Data and Implications for Zika Testing

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

Declining Trends in Reported Zika Cases in the Americas

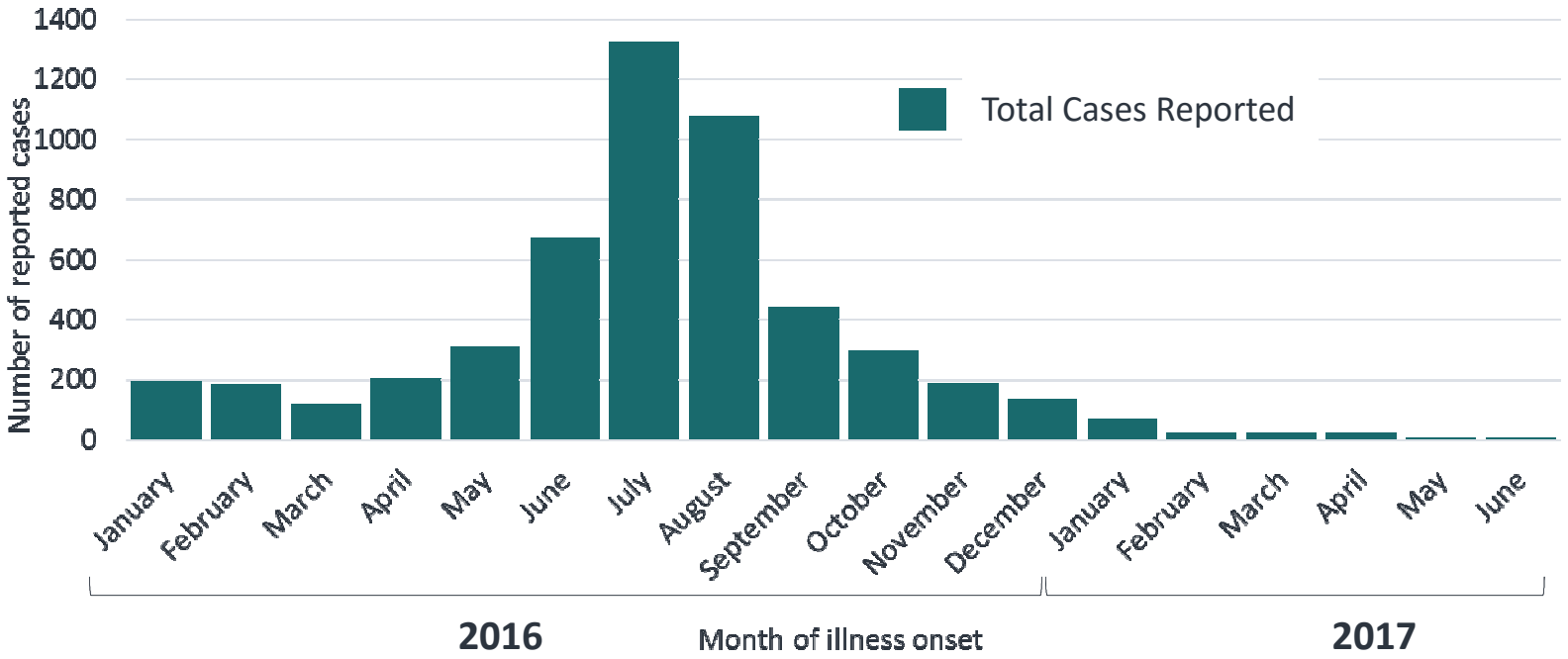
Confirmed and suspected Zika virus in the Americas, 2015–2017 (as of May 25, 2017)



PAHO Regional Zika Epidemiological Update (May 25, 2017):
http://www.paho.org/hq/index.php?option=com_content&view=article&id=11599&Itemid=41691&lang=en

Declining Trends in Reported Zika Virus Disease Cases in the US

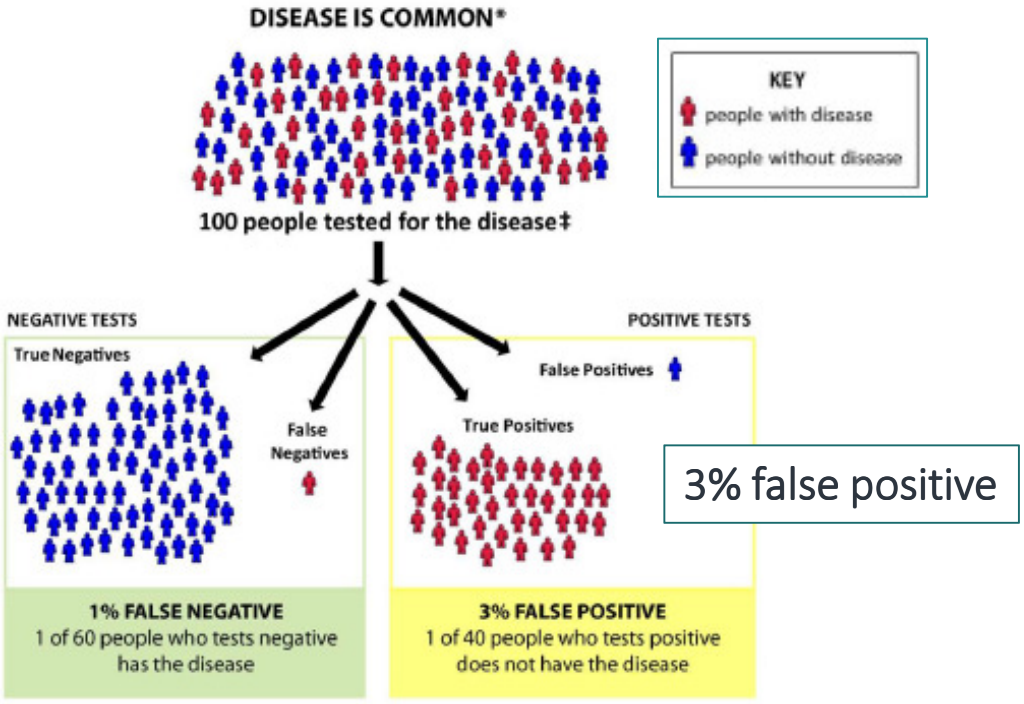
Laboratory-confirmed Zika virus disease cases in US states and Washington, DC, 2016–2017 (as of July 5, 2017)



Hypothetical Example of Disease Prevalence and Implications for Test Performance : Disease is Common

Example 1: Disease is common

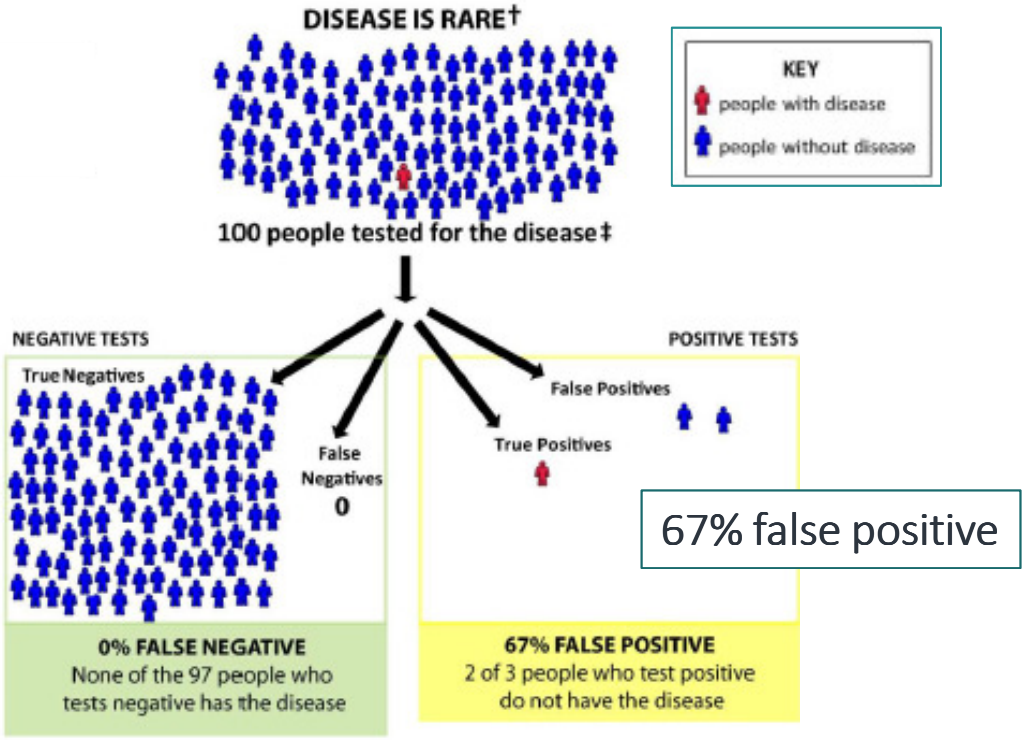
- 40 out of 100 patients in this area have the disease
- Test specificity: 98% (high)
- Test sensitivity: 98% (high)



Hypothetical Example of Disease Prevalence and Implications for Test Performance : Disease is Rare

Example 2: Disease is rare

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



Prolonged Zika Virus IgM

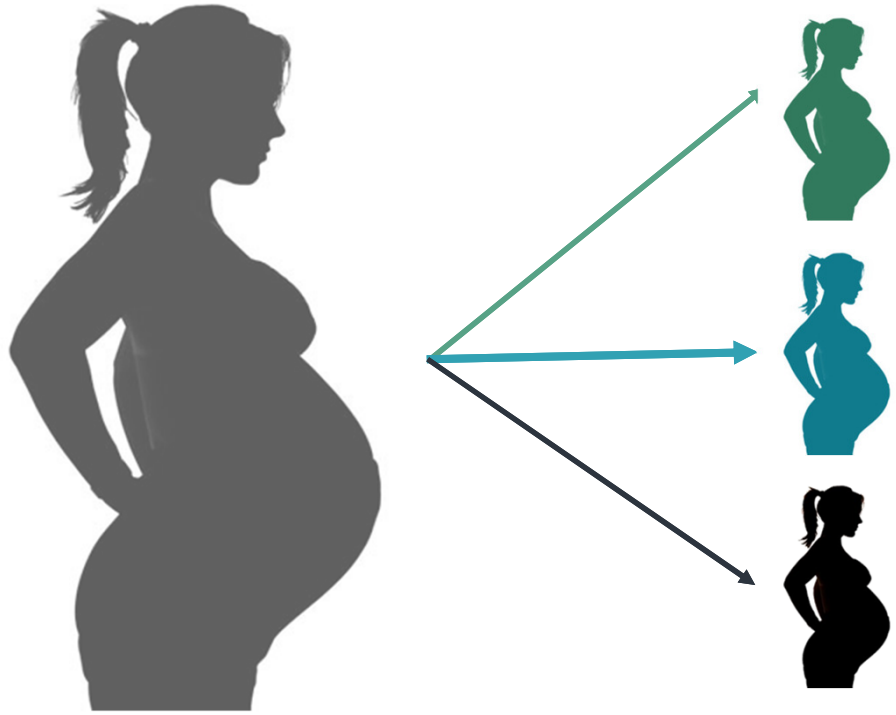
- Zika virus IgM can persist beyond 12 weeks in a subset of infected people

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

CDC HAN-00402: https://emergency.cdc.gov/han/han00402.asp

Pregnant woman with possible exposure to Zika virus before current pregnancy

A positive Zika IgM antibody test result could mean….



Zika virus infection during current pregnancy, meaning pregnancy is likely at risk from Zika

Zika virus infection before current pregnancy, meaning pregnancy is likely not at risk from Zika

False positive result, meaning pregnancy is likely not at risk from Zika

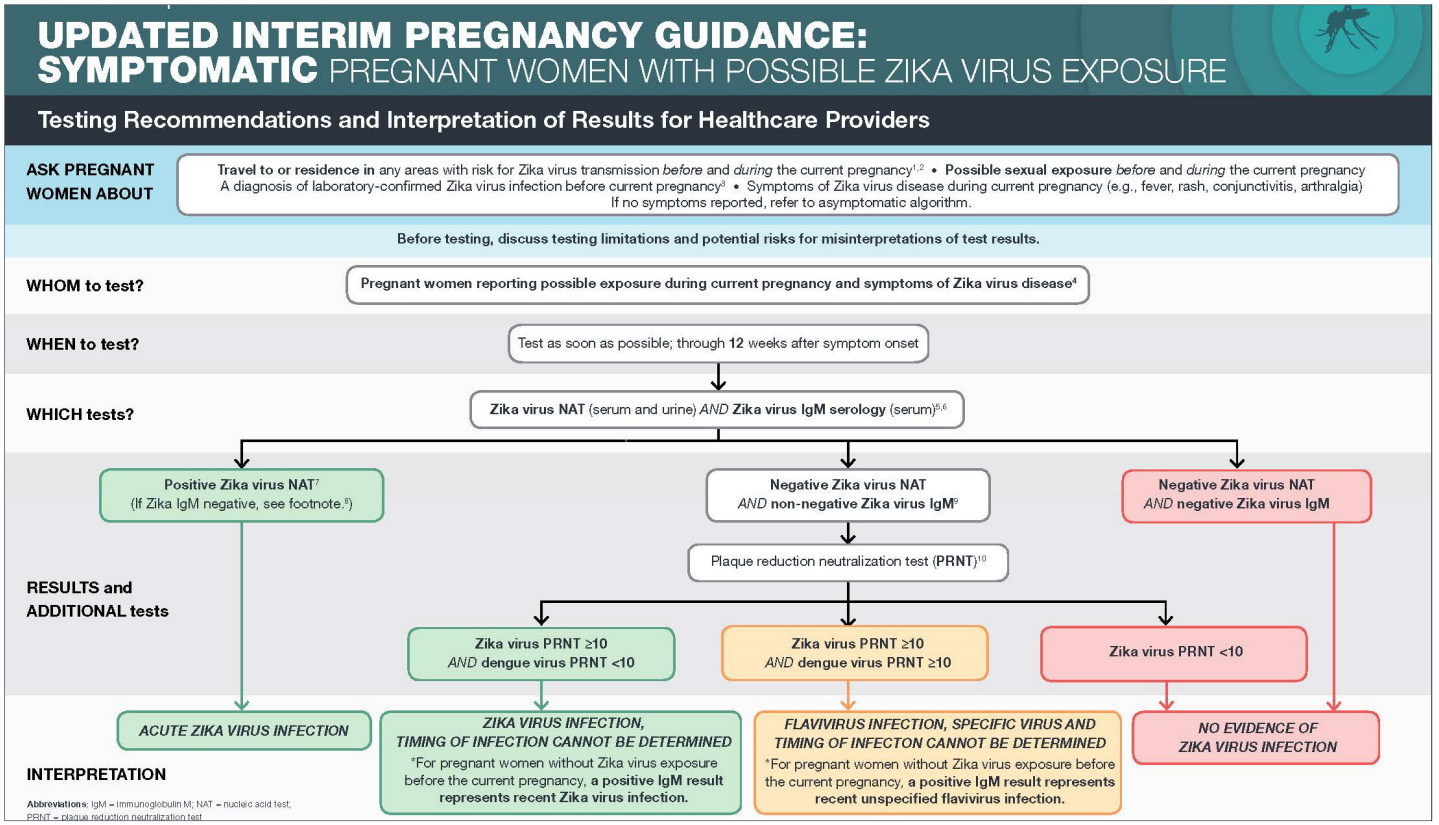
Updated Guidance

Updated Guidance: Emphasis on Shared Decision-Making Model

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

- Clinical judgment is imperative
  - Decisions about testing should be informed by factors such as
    - Length of possible exposure
    - Type or location of travel
    - Intensity of Zika transmission
    - Presence of symptoms
    - Prevention measures
    - Preferences or concerns
    - Jurisdictional recommendations

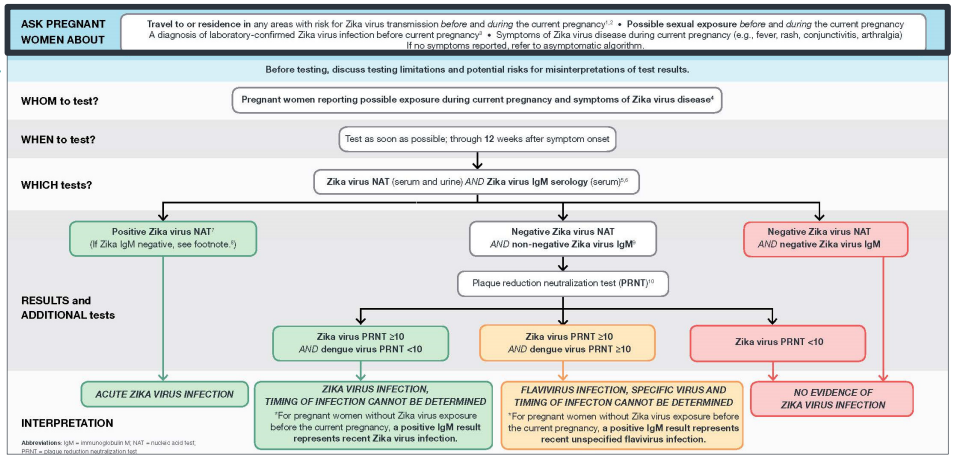
Symptomatic Pregnant Women with Possible Zika virus Exposure



Updated Guidance: Ask Pregnant Women

ASK PREGNANT WOMEN about

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

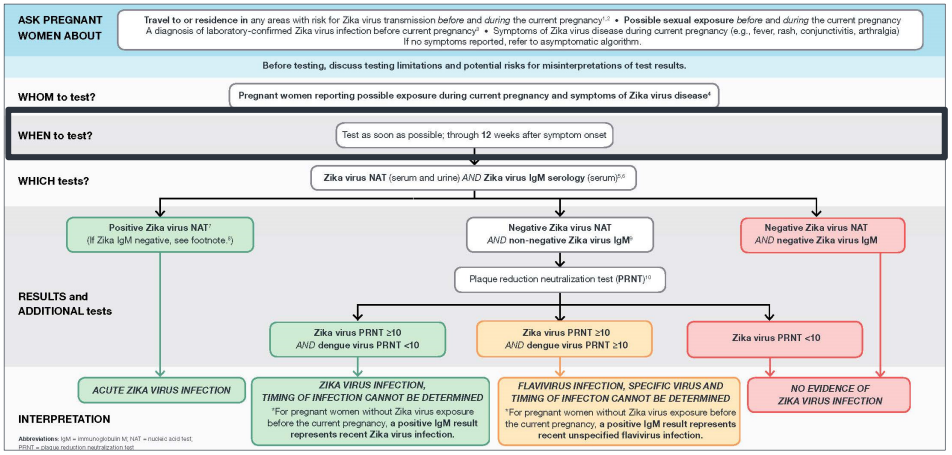


If no symptoms reported, refer to asymptomatic algorithm.

Updated Guidance: When to Test Symptomatic Pregnant Women

WHEN to test?

Test as soon as possible; through 12 weeks after symptom onset



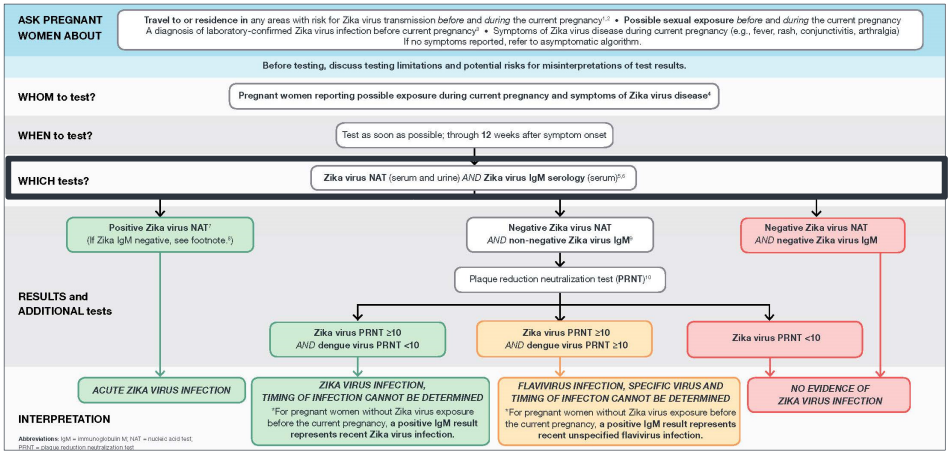
Updated Guidance: Which Tests for Symptomatic Pregnant Women

WHICH tests?

Zika virus NAT* (serum and urine)

AND

Zika virus IgM serology (serum)



NAT = nucleic acid testing

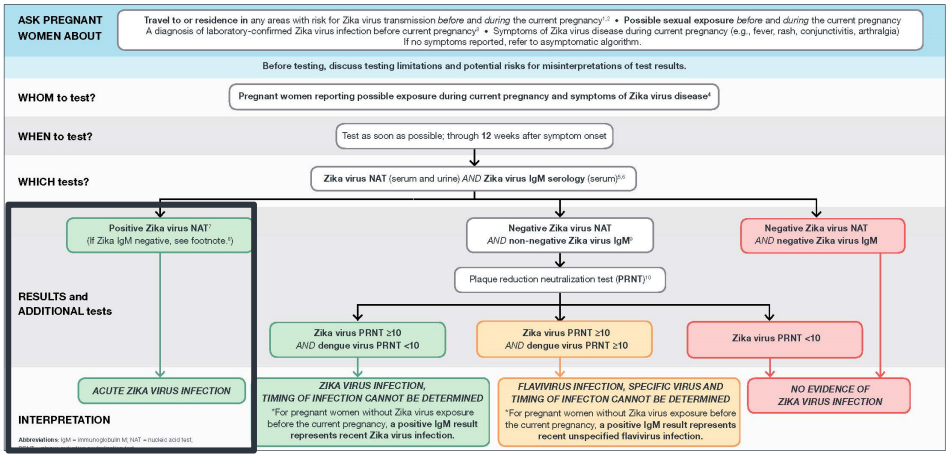
Updated Guidance: Test Results for Symptomatic Pregnant Women

RESULTS & INTERPRETATION

Positive Zika virus NAT on serum and urine specimens

↓

ACUTE ZIKA VIRUS INFECTION



Interpretation of Results of Nucleic Acid and Antibody Testing for Suspected Zika Virus Infection

TABLE 1. Interpretation of results of nucleic acid and antibody testing for suspected Zika virus infection^,†,§,¶,**,††,§§ — United States, 2017

Zika NAT (serum)	Zika NAT (urine)	Zika virus and dengue virus IgM	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result (either assay)	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive (either assay)	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative on both assays	Not indicated	Not indicated	Suggests acute Zika virus infection *Repeat testing on original urine specimen.* *+ If repeat NAT result is positive, interpret as evidence of acute Zika virus infection.* *+ If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after onset or possible exposure or specimen collection date.* *+ If repeat IgM antibody result is positive, interpret as evidence of acute Zika virus infection.* *+ If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection.*
Positive	Negative or not performed	Positive (either assay)	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative on both assays	Not indicated	Not indicated	Suggests acute Zika virus infection *Repeat testing on original urine specimen.* *+ If repeat NAT result is positive, interpret as evidence of acute Zika virus infection.* *+ If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after onset or possible exposure or specimen collection date.* *+ If repeat IgM antibody result is positive, interpret as evidence of acute Zika virus infection.* *+ If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection.*
Negative	Negative or not performed	Any non-negative result (either assay)	≥10	<10	Zika virus infection; timing of infection cannot be determined. *+ For patients with no Zika virus exposure prior to the current pregnancy, a positive IgM result represents Zika virus infection during pregnancy.*
Negative	Negative or not performed	Any non-negative result (either assay)	<10	Any result	No evidence of Zika virus infection
Negative	Negative or not performed	Any non-negative result (either assay)	≥10	≥10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined. *+ For patients with no Zika virus exposure prior to the current pregnancy, a positive IgM result represents unspecified flavivirus infection during pregnancy.*
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended in certain area of residence (i.e. Puerto Rico)		Presumptive Zika virus infection; timing of infection cannot be determined.
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended in certain area of residence (i.e. Puerto Rico)		Presumptive flavivirus infection; timing of infection cannot be determined.
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended in certain area of residence (i.e. Puerto Rico)		Insufficient information for interpretation. Consider repeat testing.
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended in certain area of residence (i.e. Puerto Rico)		No laboratory evidence of Zika virus infection

Oduyebo et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus — United States, July 2017. https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w

Updated Guidance: Test Results for Symptomatic Pregnant Women

RESULTS & INTERPRETATION

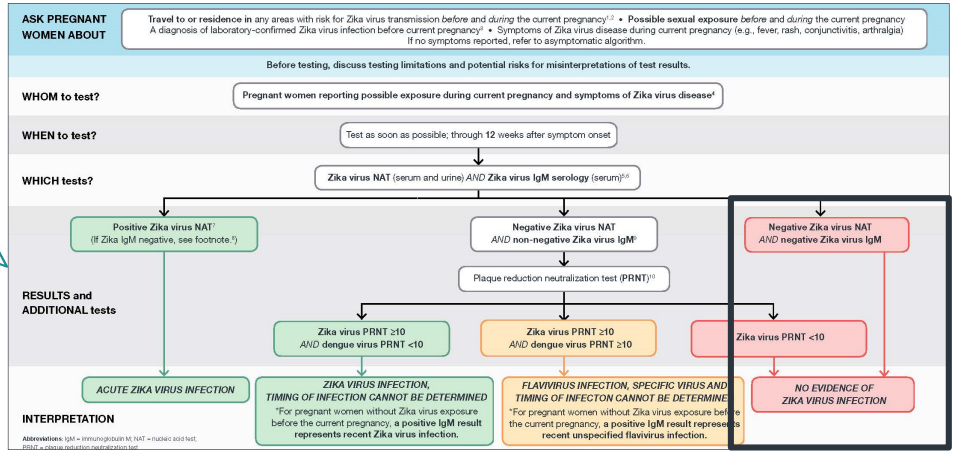
Negative Zika virus NAT

AND

Negative Zika virus IgM

↓

NO EVIDENCE OF ZIKA VIRUS INFECTION



Updated Guidance: Symptomatic Pregnant Women -- PRNT

RESULTS & ADDITIONAL TESTS

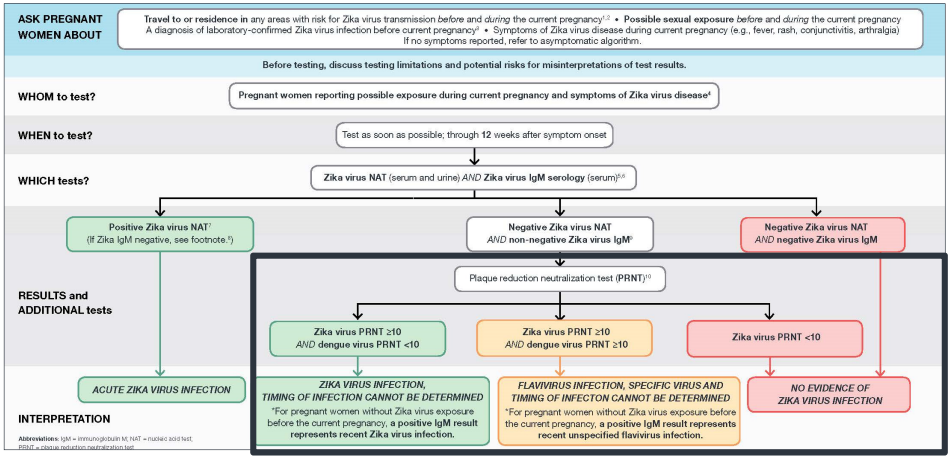
Negative Zika virus NAT

AND

Non-negative* Zika IgM

↓

Plaque reduction neutralization test (PRNT)



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

Updated Guidance: Symptomatic Pregnant Women

RESULTS & INTERPRETATION

Zika virus PRNT ≥10

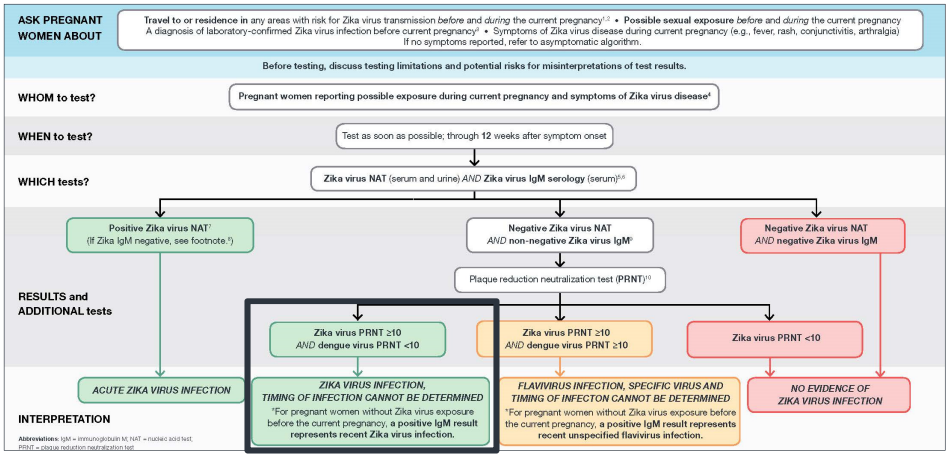
AND

dengue virus PRNT<10

↓

ZIKA VIRUS INFECTION, TIMING OF INFECTION CANNOT BE DETERMINED

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



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

Updated Guidance: Symptomatic Pregnant Women

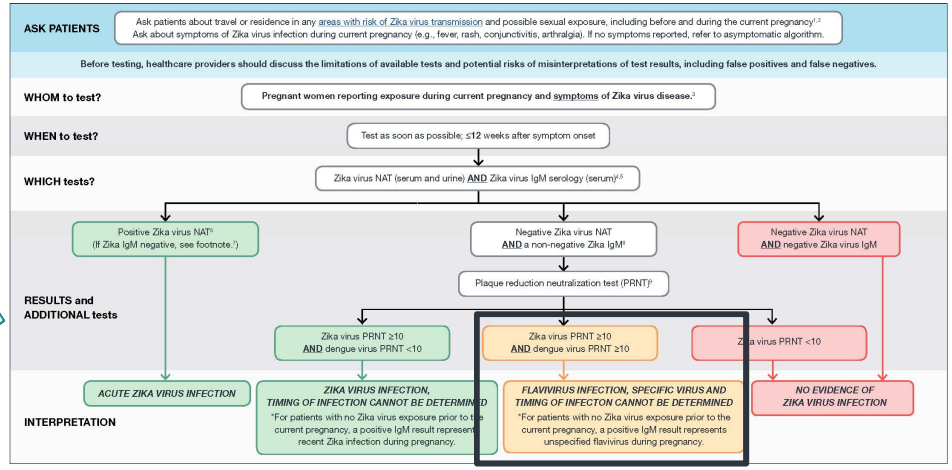
RESULTS & INTERPRETATION

Zika virus PRNT ≥10 **AND** dengue virus PRNT ≥10

↓

FLAVIVIRUS INFECTION, SPECIFIC VIRUS AND TIMING OF INFECTON CANNOT BE DETERMINED

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



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

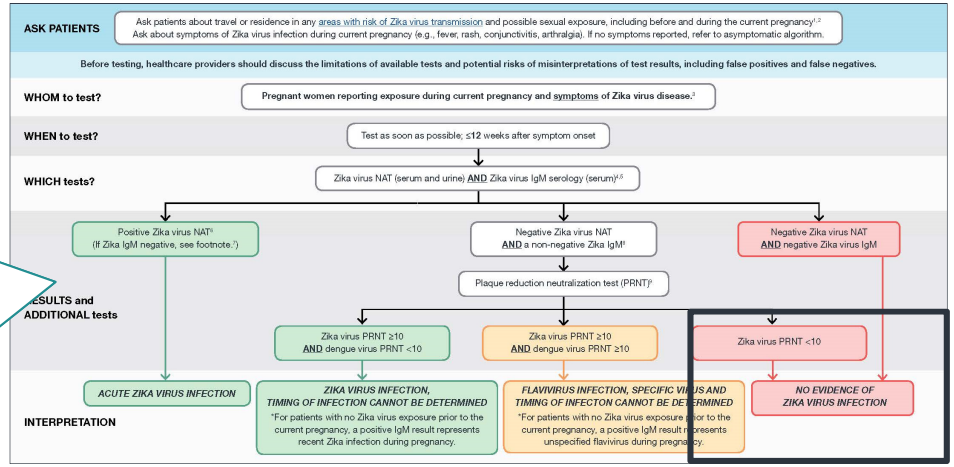
Updated Guidance: Symptomatic Pregnant Women

RESULTS & INTERPRETATION

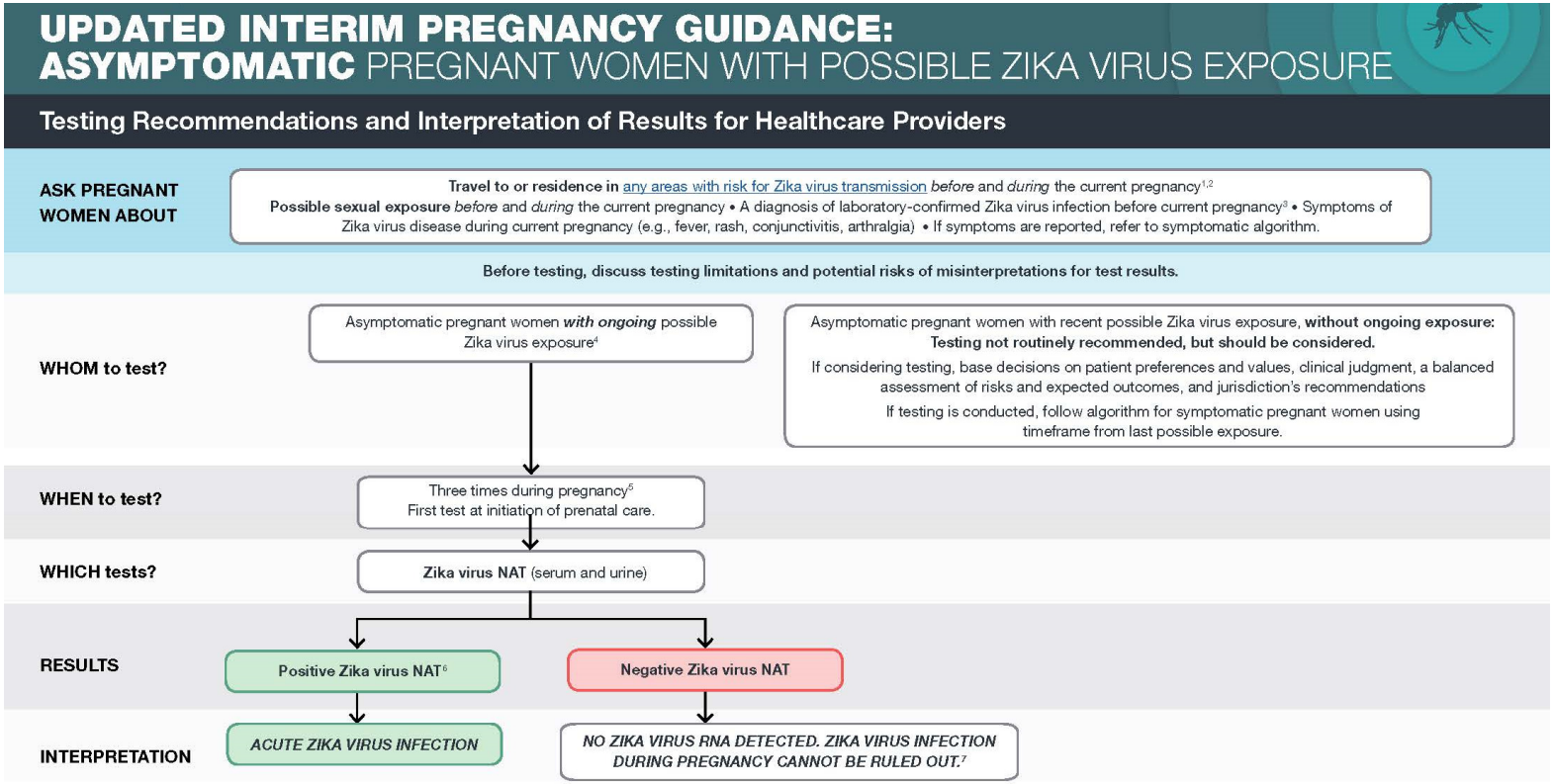
Zika virus PRNT <10

↓

NO EVIDENCE OF ZIKA VIRUS INFECTION



Asymptomatic Pregnant Women with Possible Zika Virus Exposure

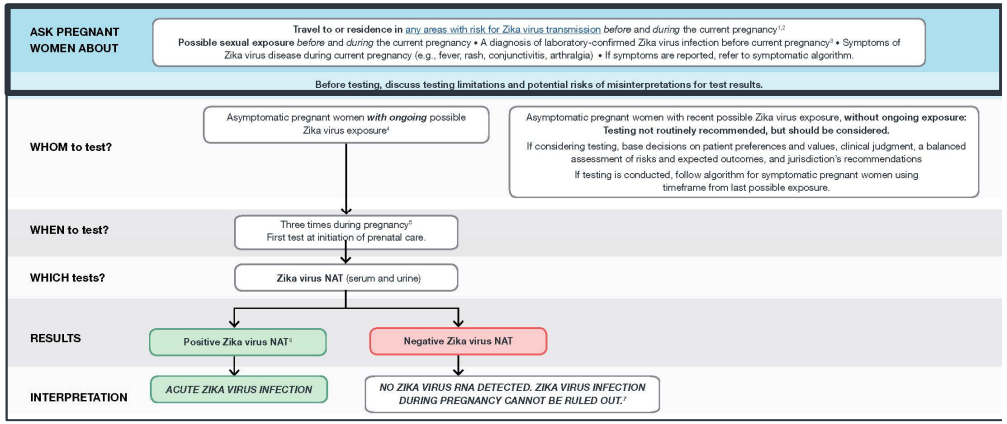


Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

ASK PREGNANT WOMEN about

- Possible Zika exposure before and during current pregnancy
- Diagnosis of laboratory-confirmed Zika virus infection before pregnancy
- Presence of symptoms during current pregnancy

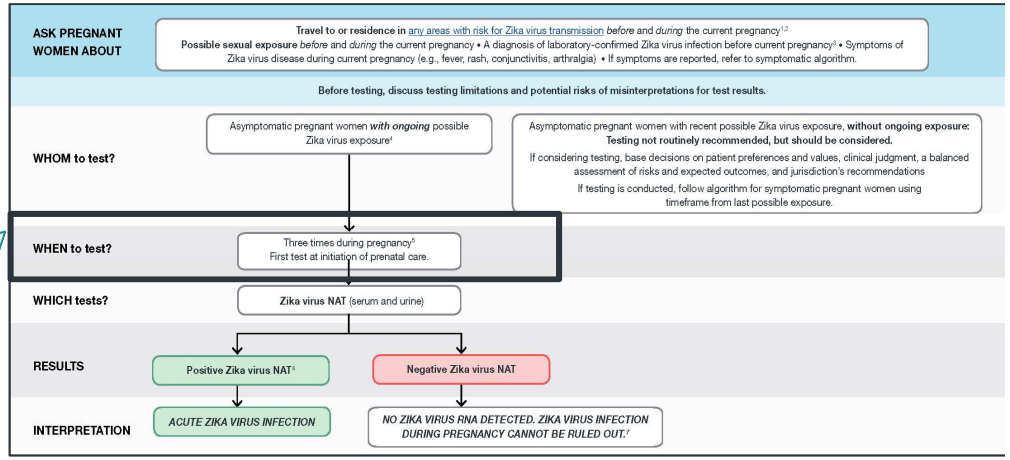
COUNSEL PATIENTS on Zika testing



If symptoms are reported, refer to symptomatic algorithm.

Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

WHEN to test? WHICH tests?
Test with Zika virus NAT on serum and urine three times during pregnancy



Updated Guidance: Asymptomatic Pregnant Women with Ongoing Possible Exposure

REFER TO TABLE 1 FOR INTERPRETATION

TABLE 1. Interpretation of results of nucleic acid and antibody testing for suspected Zika virus infection*, †, §, ¶, **, ††, §§ — United States, 2017

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Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended in certain area of residence (i.e Puerto Rico)		Presumptive Zika virus infection; timing of infection cannot be determined.
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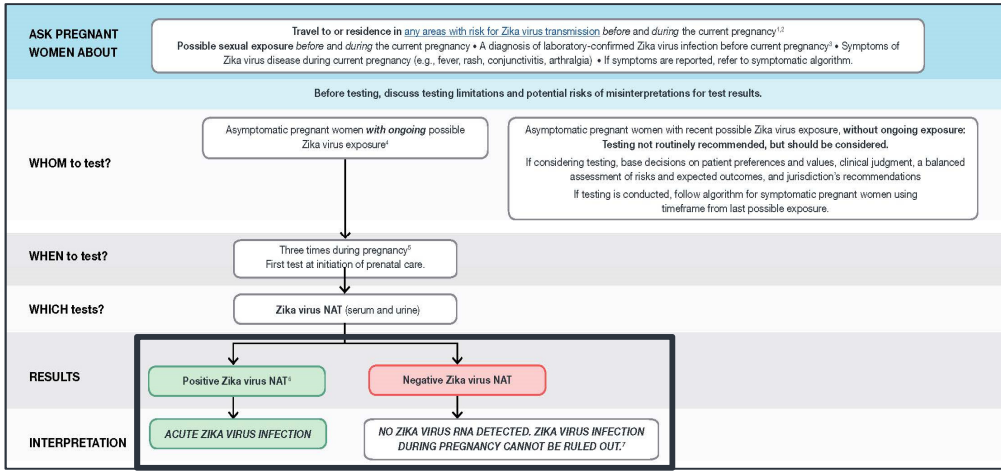
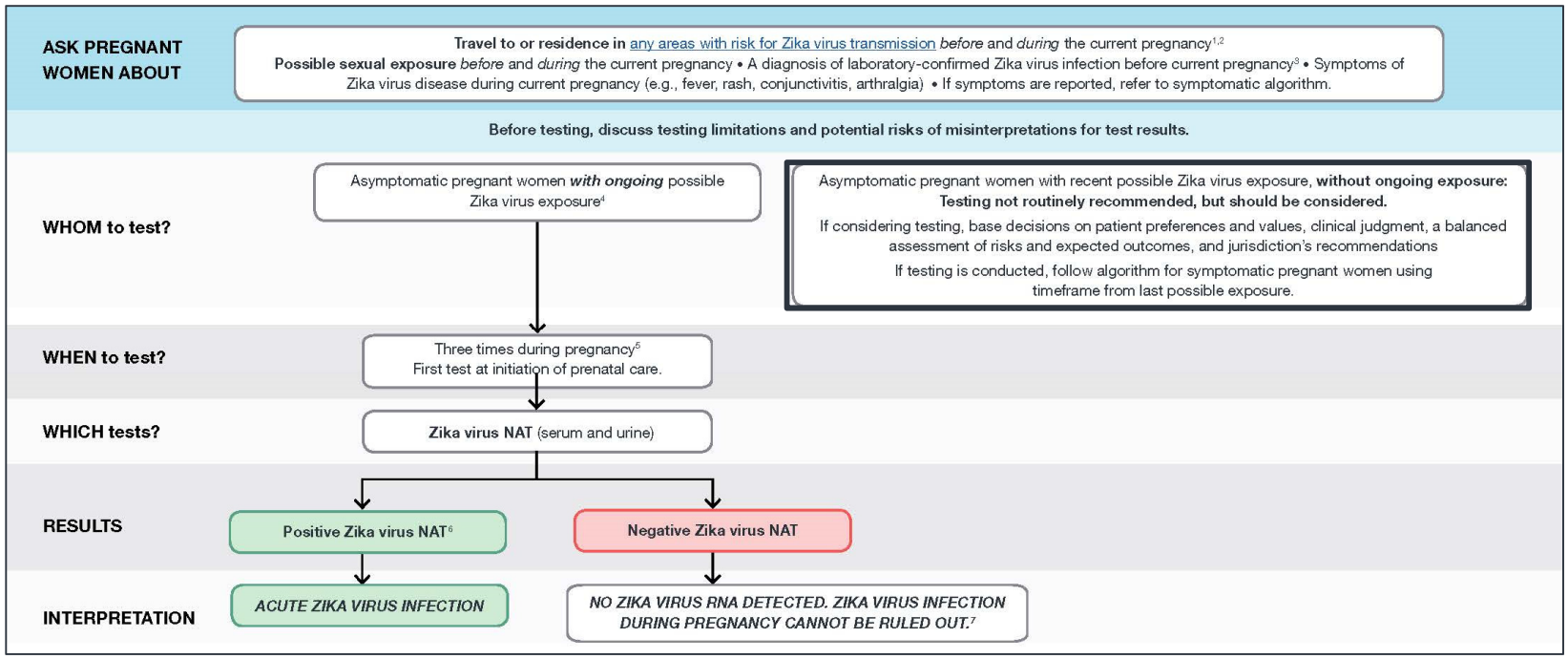
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended in certain area of residence (i.e Puerto Rico)		No laboratory evidence of Zika virus infection



Updated Guidance: Asymptomatic Pregnant Women with Recent Possible Exposure, but without Ongoing Possible Exposure

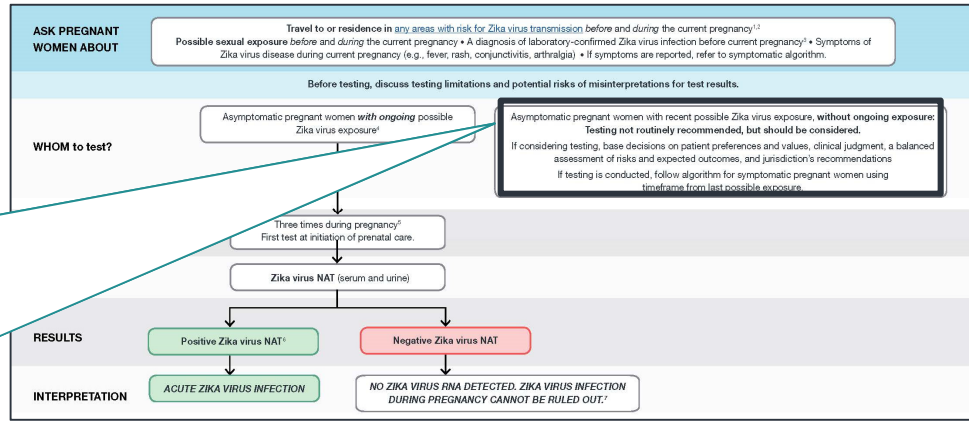


Updated Guidance: Asymptomatic Pregnant Women with Recent Possible Exposure, but without Ongoing Possible Exposure

WHOM to test

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

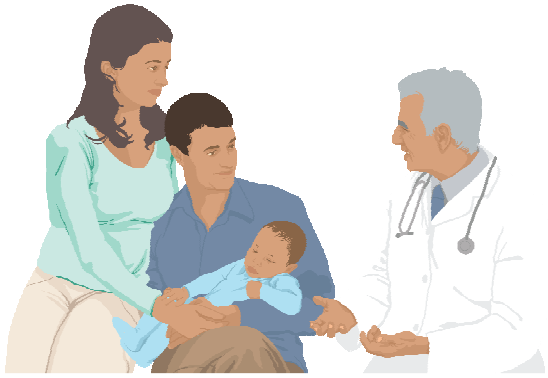
- A shared decision-making model based on patient preferences and values
  - Clinical judgment
- A balanced assessment of risks and expected outcomes
- Jurisdiction's recommendations



If testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure.

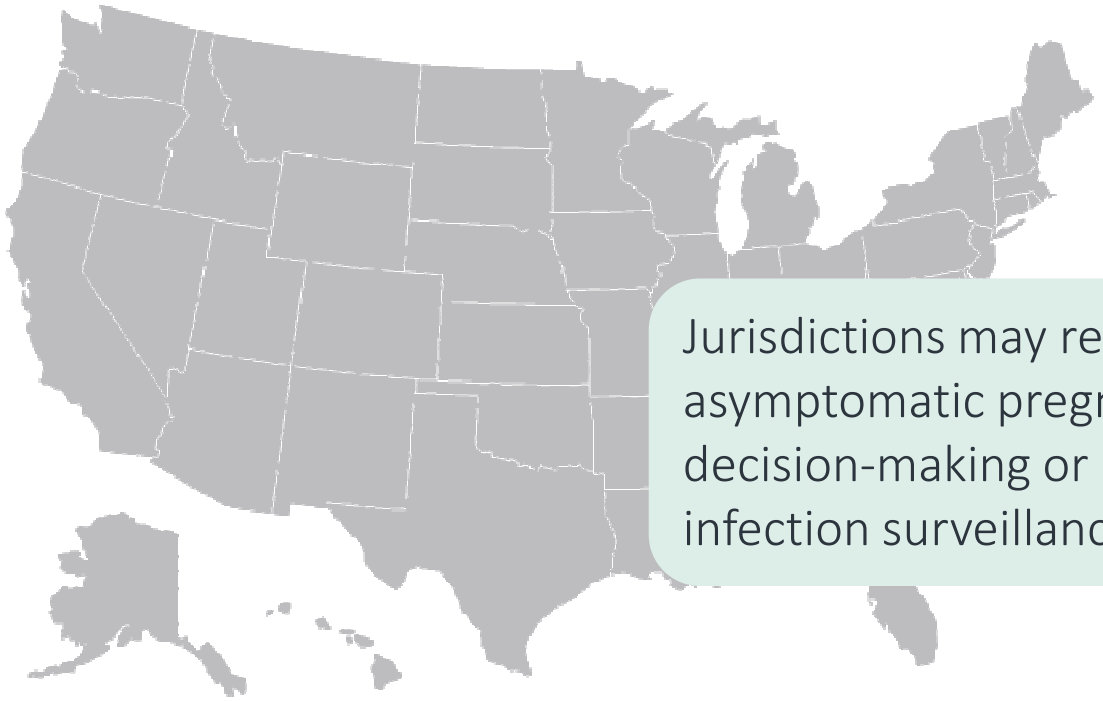
Initial Evaluation Of Infants Whose Mothers Had Possible Zika Virus Exposure During Pregnancy But Were Not Tested

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



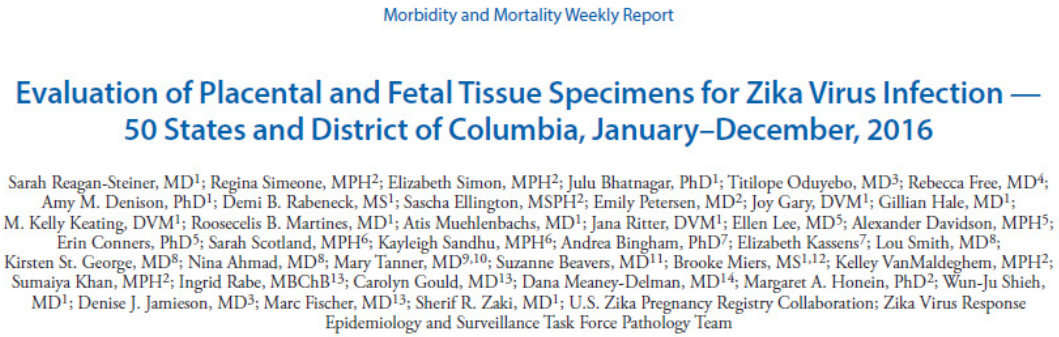
https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-testing.html

Updated Guidance: Asymptomatic Pregnant Women with Possible Zika Virus Exposure



Jurisdictions may recommend testing of asymptomatic pregnant women for clinical decision-making or as part of Zika virus infection surveillance.

Updated Guidance: Testing of Placental and Fetal Tissues



Morbidity and Mortality Weekly Report

Evaluation of Placental and Fetal Tissue Specimens for Zika Virus Infection — 50 States and District of Columbia, January–December, 2016

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Updated Guidance

Testing of placental tissues not routinely recommended for asymptomatic women without ongoing possible exposure when infant or fetus does not have Zika-associated birth defects

Recommendations to Prevent Zika Virus Infection Have not Changed

Do Not Travel	• Pregnant women should **not** travel to areas with risk for Zika virus transmission
Prevent Mosquito Bites	• If a pregnant woman lives in or travels to an area with risk for Zika virus transmission, she should take steps to prevent mosquito bites
Prevent Sexual Transmission	• Take steps to prevent sexual transmission of Zika from a partner who lives in or traveled to an area with risk for Zika virus transmission

Clinical Tools for Implementing Guidance

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

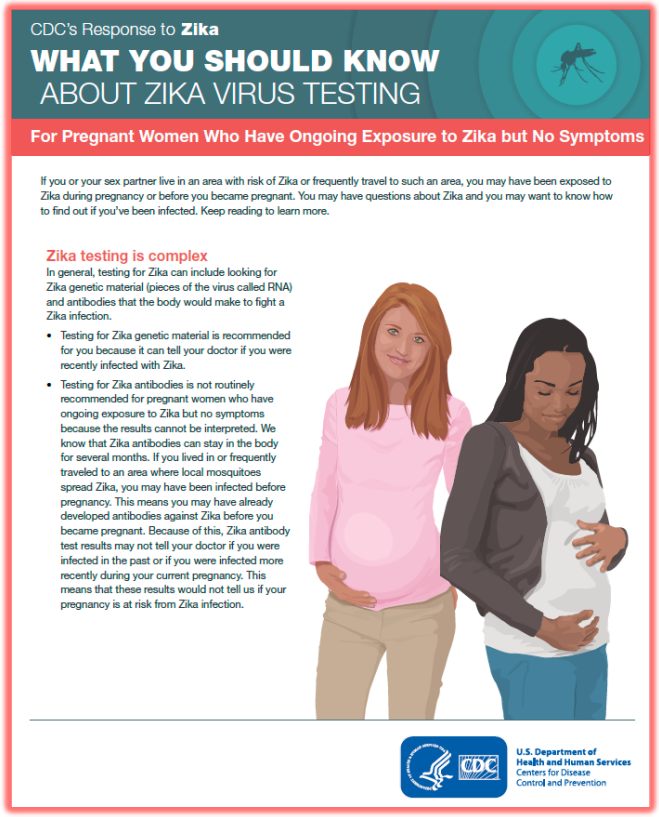
COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS
FOR ASYMPTOMATIC PREGNANT WOMEN WHO WERE RECENTLY EXPOSED TO ZIKA
BUT DO NOT HAVE OI

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

This guide describes recommendations for conducting pretesting counseling for symptomatic pregnant women with possible recent exposure (they or their sex partner live in or recently traveled to an area with risk of Zika). Symptoms of Zika include red eyes, fever, joint pain, rash, muscle pain, and headache. CDC recommends testing for pregnant women with symptoms of Zika.This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on why you will be testing them for Zika and a brief overview of what to expect	*Use one of the two following sentences to begin the discussion:* 1. You may be at risk for having Zika since you or your sex partner recently traveled to *(replace "recently traveled to" with "live in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace "have had" with "during your pregnancy you previously had" as appropriate)* symptoms of Zika. OR/AND 2. You may be at risk of having Zika because you recently had sex without a condom with a person who traveled to *(replace "traveled to" with "lives in" as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace "have had" with "during your pregnancy you previously developed" as appropriate)* symptoms of Zika. Since you were exposed to Zika and are experiencing symptoms *(replace "are experiencing" with "during your pregnancy you previously experienced" as appropriate)*, I think it is best to move forward with testing you for Zika. Before we begin, I would like to tell you what to expect throughout this process.
Patients should be informed that a combination of Zika tests will be required before a final result is determined	You will need a combination of tests to determine whether or not you have Zika. Finding out if you have Zika can require up to three different kinds of tests because the result of one test may require more testing to find out if you recently had a Zika infection. The tests we use to detect Zika can detect other similar viruses often found in the same areas with risk of Zika. Sometimes even after several tests, we may not know which type of virus you were infected with. Each test result is important, because it may help me decide how best to care for you during pregnancy. I want to be sure we take all of the necessary steps to make sure your results are accurate. Each test can take different amounts of time to receive results, which I know can be frustrating. As your healthcare provider I am here to answer any questions you may have. • Reassure the patient that this method of testing is normal • Consider providing the fact sheet *What You Should Know About Zika Virus Testing for Pregnant Women with Symptoms of Zika.*
Let the patient know that you will be ordering two tests; one to look for Zika RNA and one to look for Zika antibodies. Define these terms as they may be unfamiliar	I am going to start the testing process by ordering two tests: • The first test looks for pieces of Zika virus, known as RNA. RNA can be found in blood and urine. • The second test looks for Zika antibodies, which are proteins that your body makes to fight off a Zika infection. Zika test results can be difficult to interpret. If you've had exposure to Zika virus or another similar virus before this pregnancy, it's possible that you've been infected before, and this could affect today's test results.



CDC's Response to **Zika**

WHAT YOU SHOULD KNOW
ABOUT ZIKA VIRUS TESTING

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

If you or your sex partner live in an area with risk of Zika or frequently travel to such an area, you may have been exposed to Zika during pregnancy or before you became pregnant. You may have questions about Zika and you may want to know how to find out if you've been infected. Keep reading to learn more.

Zika testing is complex

In general, testing for Zika can include looking for Zika genetic material (pieces of the virus called RNA) and antibodies that the body would make to fight a Zika infection.

- Testing for Zika genetic material is recommended for you because it can tell your doctor if you were recently infected with Zika.
- Testing for Zika antibodies is not routinely recommended for pregnant women who have ongoing exposure to Zika but no symptoms because the results cannot be interpreted. We know that Zika antibodies can stay in the body for several months. If you lived in or frequently traveled to an area where local mosquitoes spread Zika, you may have been infected before pregnancy. This means you may have already developed antibodies against Zika before you became pregnant. Because of this, Zika antibody test results may not tell your doctor if you were infected in the past or if you were infected more recently during your current pregnancy. This means that these results would not tell us if your pregnancy is at risk from Zika infection.

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

Sharing Up-to-Date Information

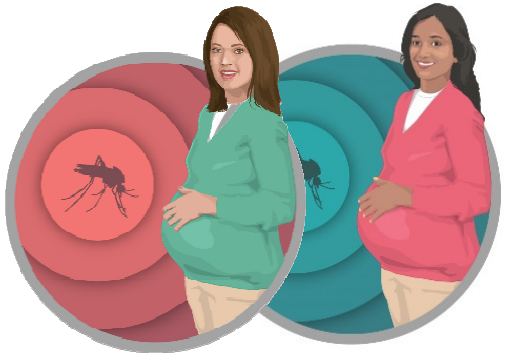
- Providing updated clinical guidance
- Responding to your inquiries:
  - Email: ZikaMCH@cdc.gov
  - Zika Pregnancy Hotline: 770-488-7100
  - CDC-INFO: (800-232-4636)

http://www.cdc.gov/zika

CDC'S Response to **Zika**

Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — US Territories, January 1, 2016–April 25, 2017

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



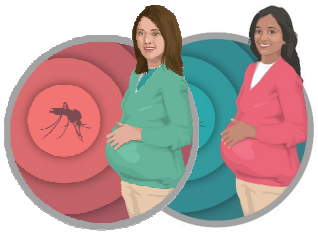
Dana Meaney-Delman, MD, MPH
Co-Lead, Pregnancy and Birth Defects Task Force
Centers for Disease Control and Prevention

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

Zika Pregnancy and Infant Registries: US Zika Pregnancy Registry and Zika Active Pregnancy Surveillance System (ZAPSS)

Purpose of registries

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

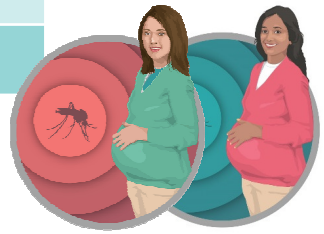


Zika Pregnancy and Infant Registries: Who is Included

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

Zika Pregnancy and Infant Registries: A Comparison

Registry Feature	US Zika Pregnancy Registry	Zika Active Pregnancy Surveillance System
Location	50 States and District of Columbia, US territories and Freely Associated States excluding Puerto Rico	Puerto Rico
Maternal Eligibility	Pregnant women with laboratory evidence of Zika	Pregnant women with laboratory evidence of Zika
Infant Follow-Up	Through 1st year of life	Through 3rd year of life



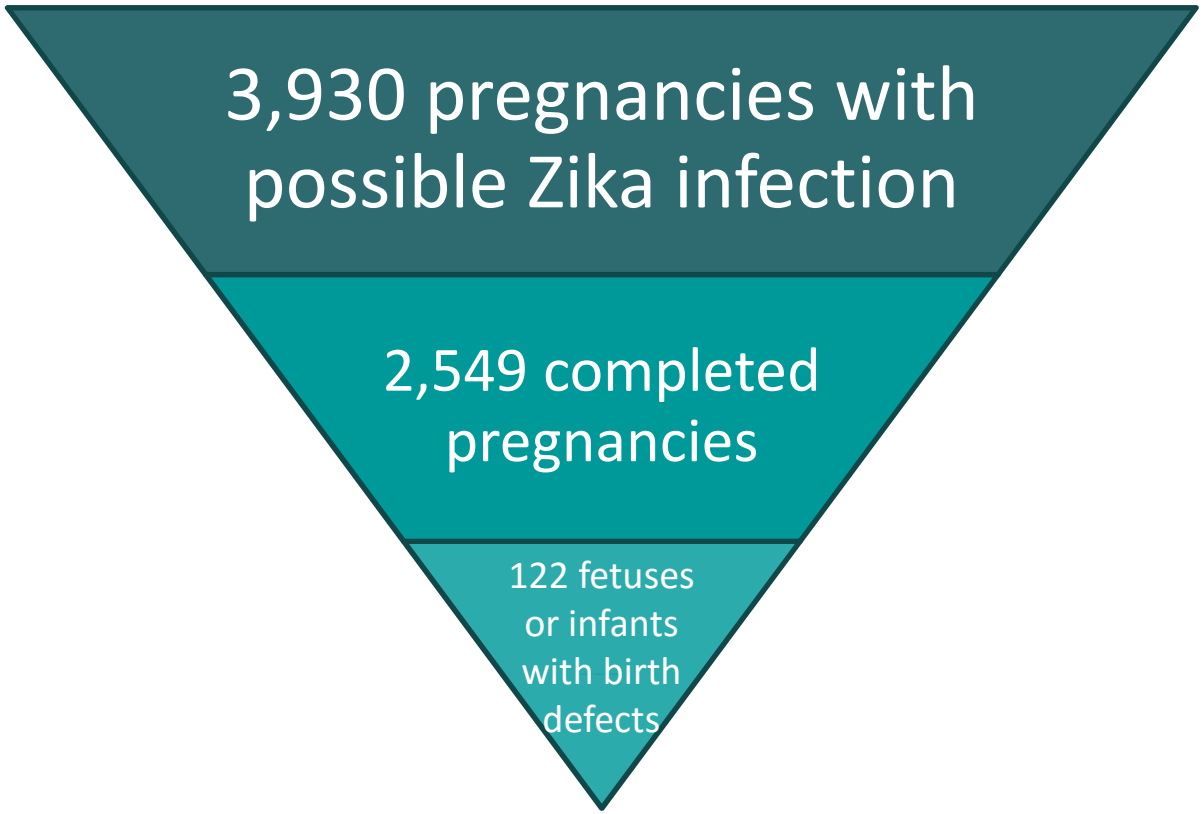
Pregnancy Outcomes Following Zika Virus Infection during Pregnancy in US Territories

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report

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

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

Zika-Related Pregnancy Outcomes in US Territories



Results from Zika Pregnancy and Infant Registries

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

1. Reynolds MR, Jones AM, Petersen EE, et al. Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016. MMWR Morb Mortal Wkly Rep 2017;66:366-373. DOI: http://dx.doi.org/10.15585/mmwr.mm6613e1.
2. Shapiro-Mendoza CK, Rice ME, Galang RR, et al. Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — U.S. Territories, January 1, 2016–April 25, 2017. MMWR Morb Mortal Wkly Rep 2017;66:615-621. DOI: http://dx.doi.org/10.15585/mmwr.mm6623e1

Impact of Third Trimester Infections

- 34% of 3rd trimester infections were symptomatic
- Among mothers diagnosed with infection in the 3rd trimester, 4% had an infant or fetus with Zika virus-associated birth defects

Birth defects observed among pregnancies with symptom onset or positive laboratory testing during any trimester

Infant Follow-up in US Territories

Recommended infant screening and testing reported to Zika pregnancy and infant registries	Live-born infants with birth defects %	Live-born infants without birth defects %	Total %
Infant Zika virus testing	55%	59%	59%
Postnatal neuroimaging	59%	52%	52%
Hearing screening	91%	78%	79%

Public Health Implications

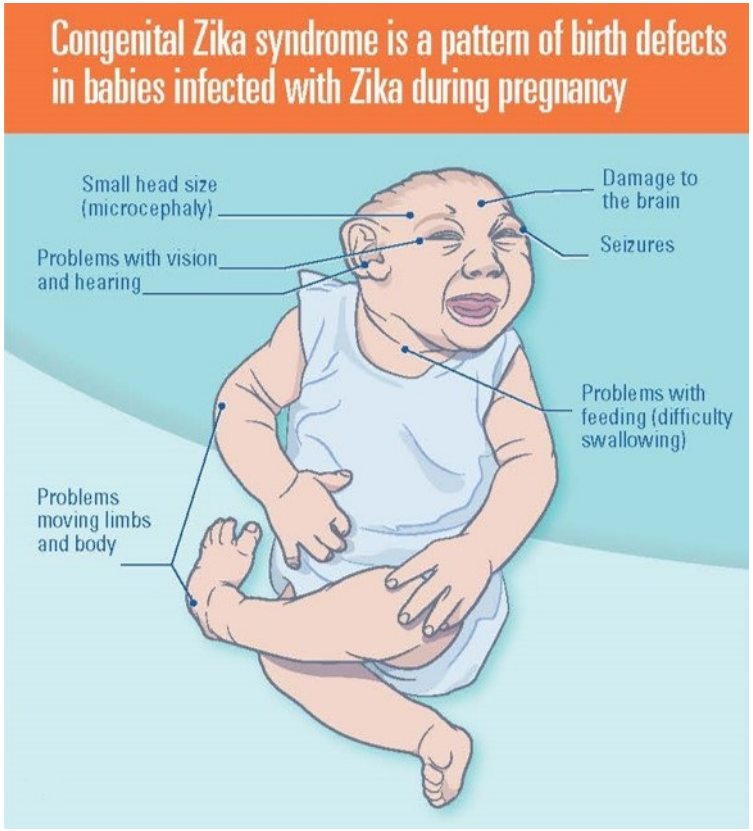
- Highest proportion of Zika-associated birth defects among those with Zika virus infection during first and early second trimester of pregnancy
  - More data are needed to explore whether women infected in the third trimester are at risk for:
    - having a baby with birth defects
    - other adverse pregnancy outcomes
- Identification and follow-up care of infants can facilitate timely and appropriate clinical intervention services and assessment of future needs
- Monitoring of affected pregnancies and continued follow-up care for infant is critical to elucidating the impact of congenital Zika virus infection

What You Can Do to Help

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

Summary

- Zika virus infection diagnosed during any trimester of pregnancy poses a risk to the fetus
- The absence or presence of symptoms in patients with confirmed Zika virus infection does not appear to affect the risk of birth defects
- Healthcare providers can educate patients, follow CDC recommendations for screening and testing, support infants and families, and report to the Zika pregnancy and infant registries



CDC'S Response to **Zika**

Zika Virus Infection:
Pediatric Ophthalmologic Findings

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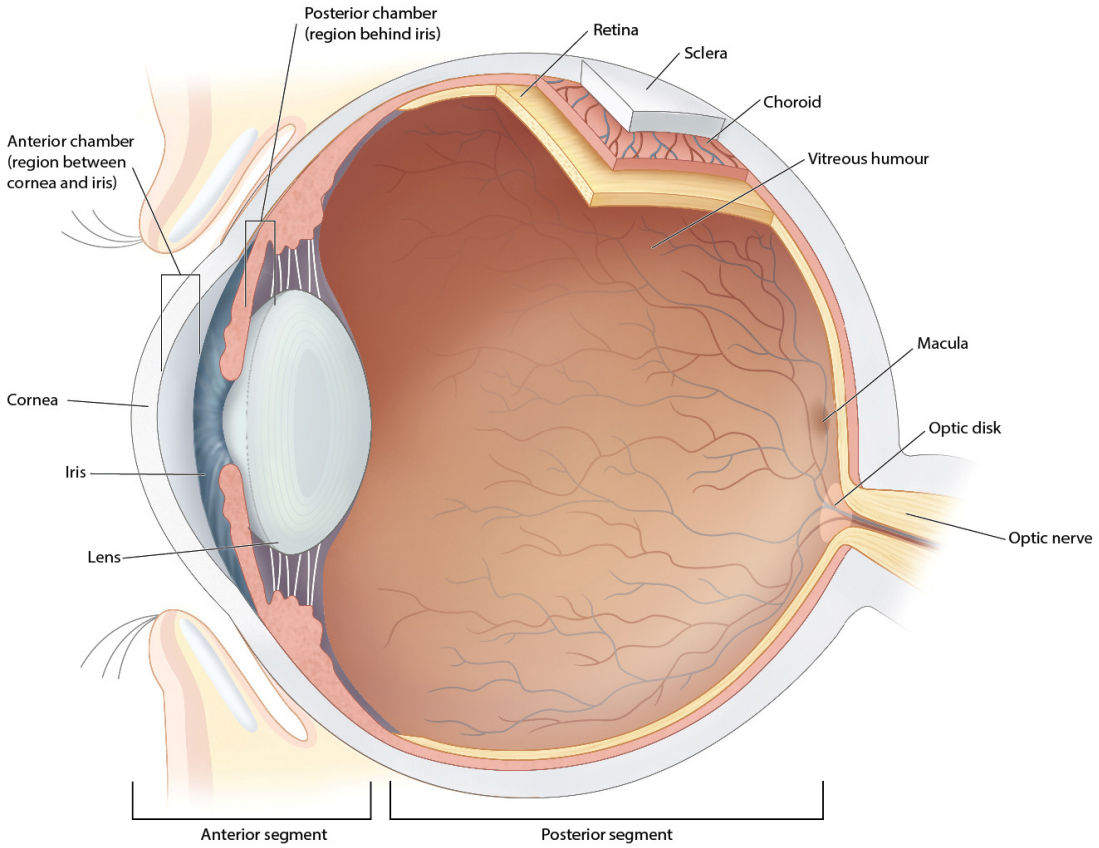
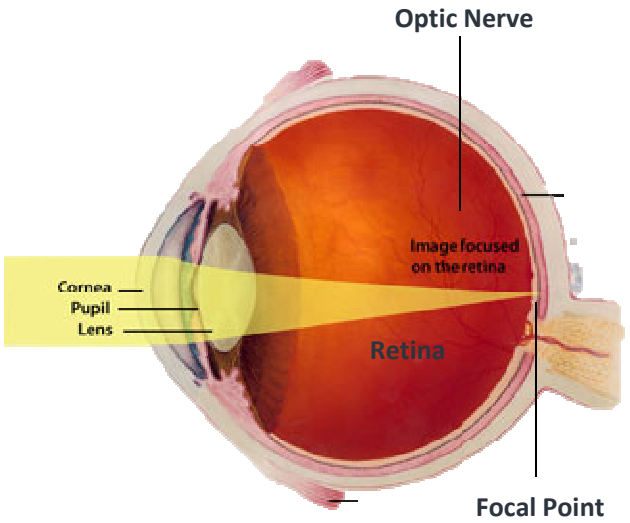
Assistant Professor of Ophthalmology and Pediatrics
Duke University

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

Ophthalmology 101

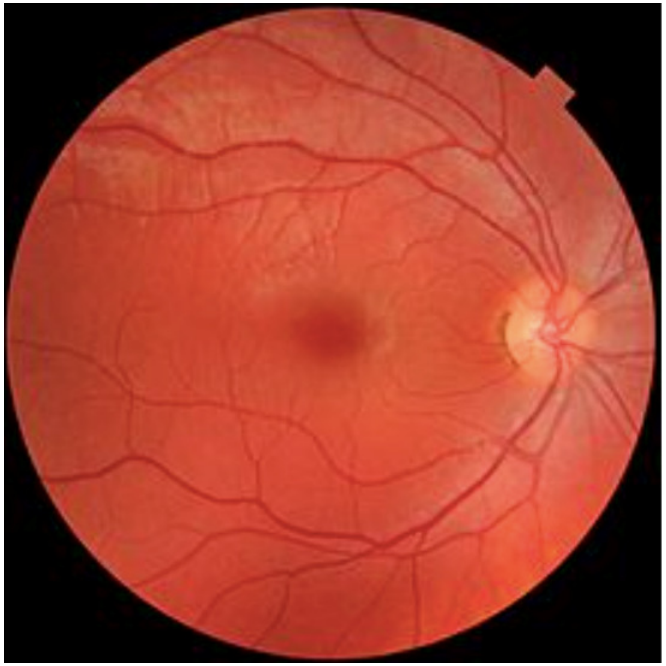
Ocular Anatomy





National Eye Institute

Normal Retina



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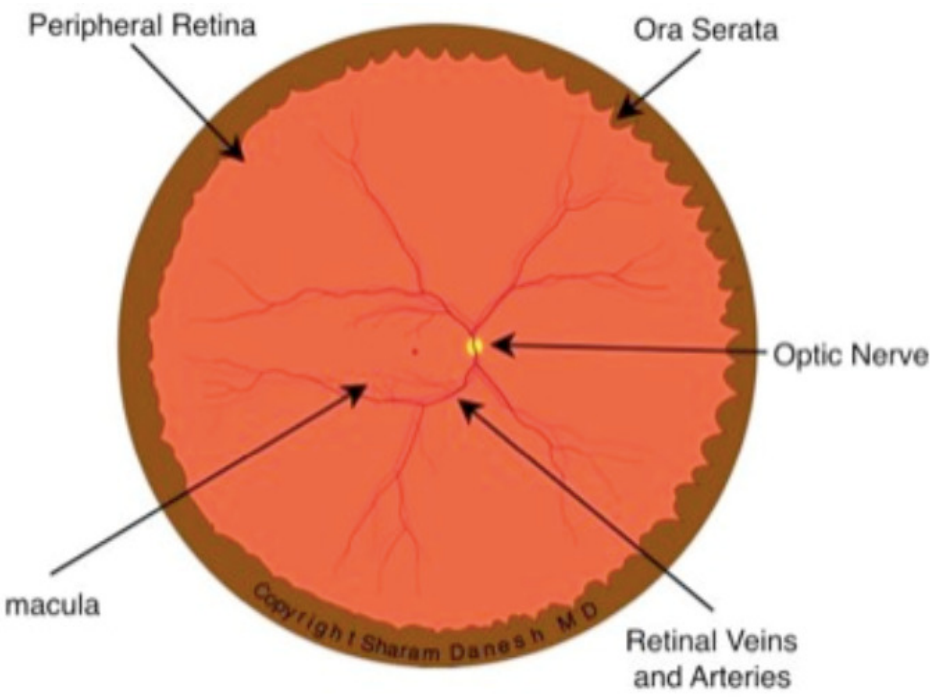
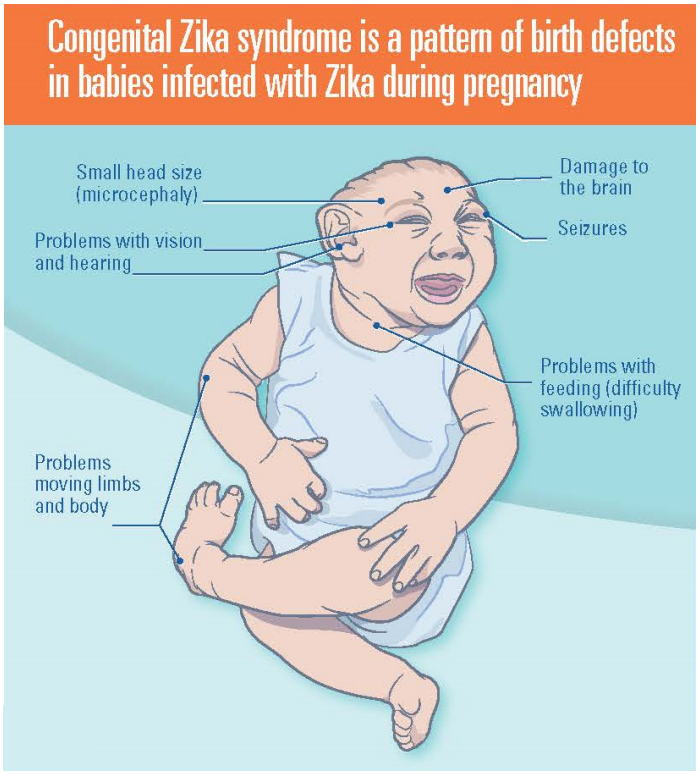


Arizona Eye Institute

Ocular Findings in Congenital Zika Infection

Ocular Findings Associated with Congenital Zika Virus Infection

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



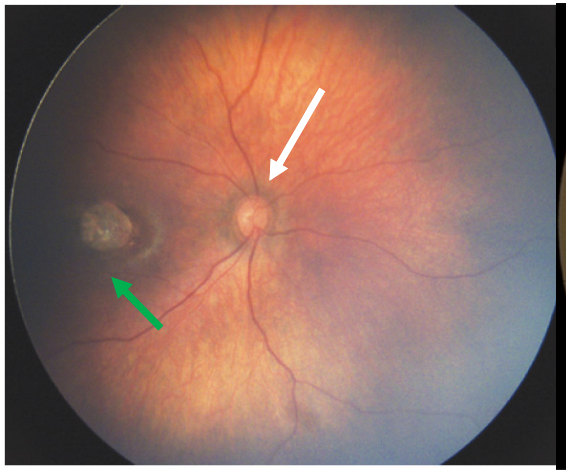
Macular and Optic Nerve Findings

Commonly reported macular findings

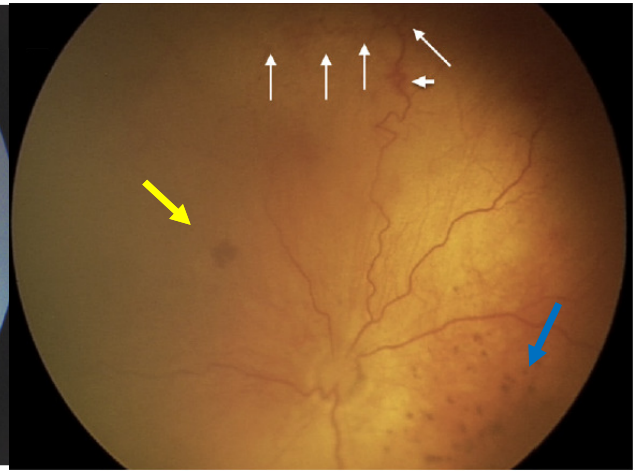
- Macular mottling
- Chorioretinal atrophy

Commonly reported optic nerve findings

- Hypoplasia
- Increased cup to disk ratio
- Pallor



Macular mottling, chorioretinal atrophy, and optic nerve hypoplasia



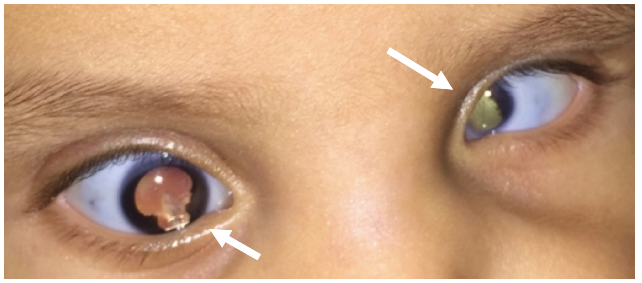
Subretinal hemorrhages, vascular tortuosity, abnormal vessel termination, and focal area of dilation

Ventura CV, et al. Ophthalmological findings in infants with microcephaly and presumable intra-uterus Zika virus infection. Arq Bras Oftalmol. 2016 Feb;79(1):1-3.
Miranda HA, et al. Expanded Spectrum of Congenital Ocular Findings in Microcephaly with Presumed Zika Infection. Ophthalmology. 2016 Aug;123(8):1788-94..

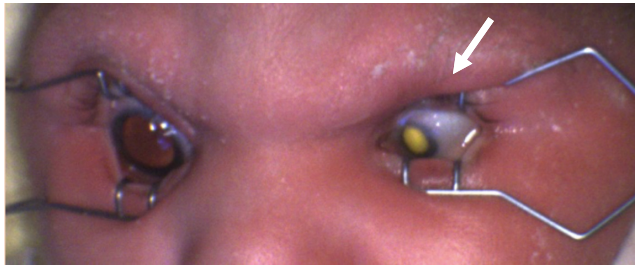
Other Ocular Findings

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

Congenital Glaucoma



Iris colobomas

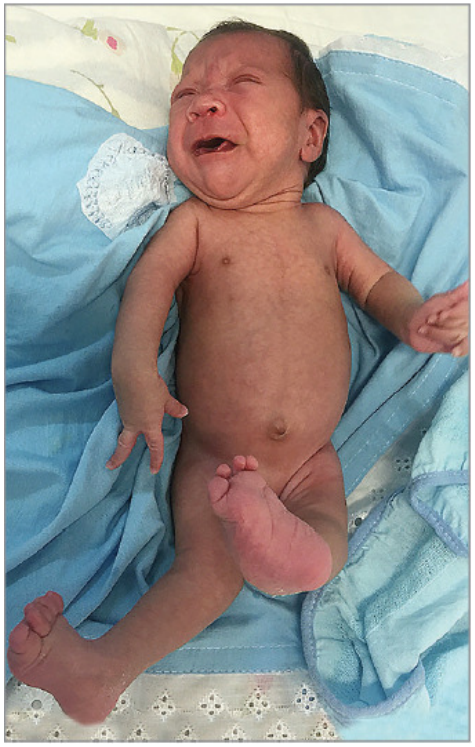


Microphthalmia

de Paula Freitas, et al. Anterior-Segment Ocular Findings and Microphthalmia in Congenital Zika Syndrome. Ophthalmology. 2017 Jul. [Epub ahead of print]
Yepez JB, et al. Ophthalmic Manifestations of Congenital Zika Syndrome in Colombia and Venezuela. JAMA Ophthalmol. 2017 May 1;135(5):440-445

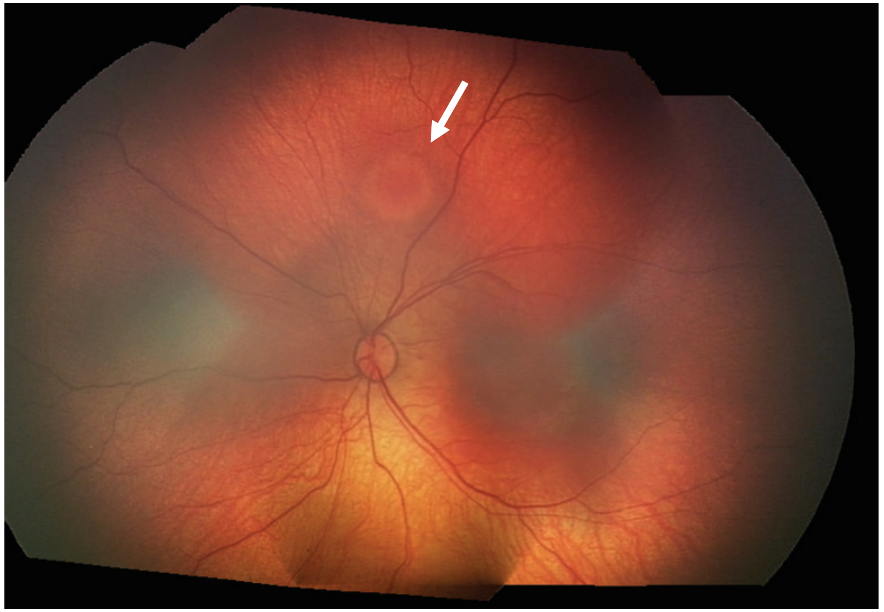
Risk Factors for Ocular Findings

- Smaller head circumference
- Microcephaly
- Other CNS abnormalities
- Earlier trimester infection in pregnancy
- Arthrogryposis

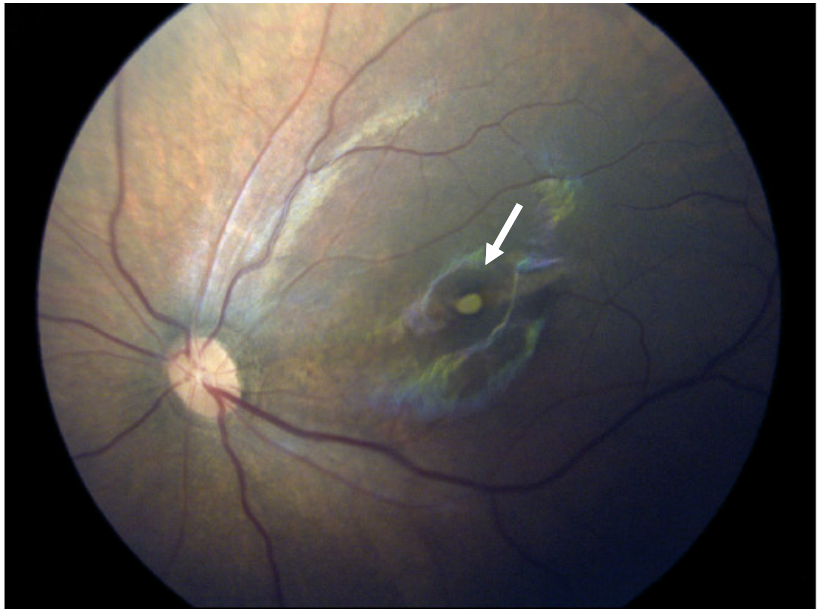


Ventura CV, et al. Risk Factors Associated With the Ophthalmoscopic Findings Identified in Infants With Presumed Zika Virus Congenital Infection. JAMA Ophthalmol. 2016 Aug 1;134(8):912-8.
Zin AA, et al. Screening Criteria for Ophthalmic Manifestations of Congenital Zika Virus Infection. JAMA Pediatr. 2017 Jul 17. [Epub ahead of print]
Moore CA, Staples JE, Dobyns WB, et al. Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. JAMA Pediatr 2017;171:288-95.

Infants with Possible Zika Virus Infection WITHOUT Microcephaly



Hypopigmented retinal lesion



Chorioretinal atrophy

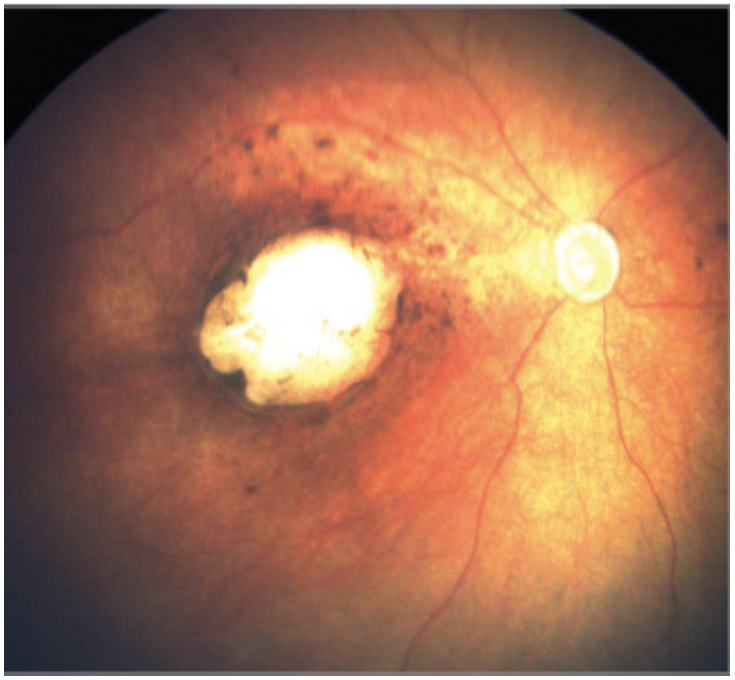
-Ventura CV, et al. Zika: neurological and ocular findings in infant without microcephaly. Lancet. 2016 Jun 18;387(10037):2502.

-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. 2017;317(1):59-68.

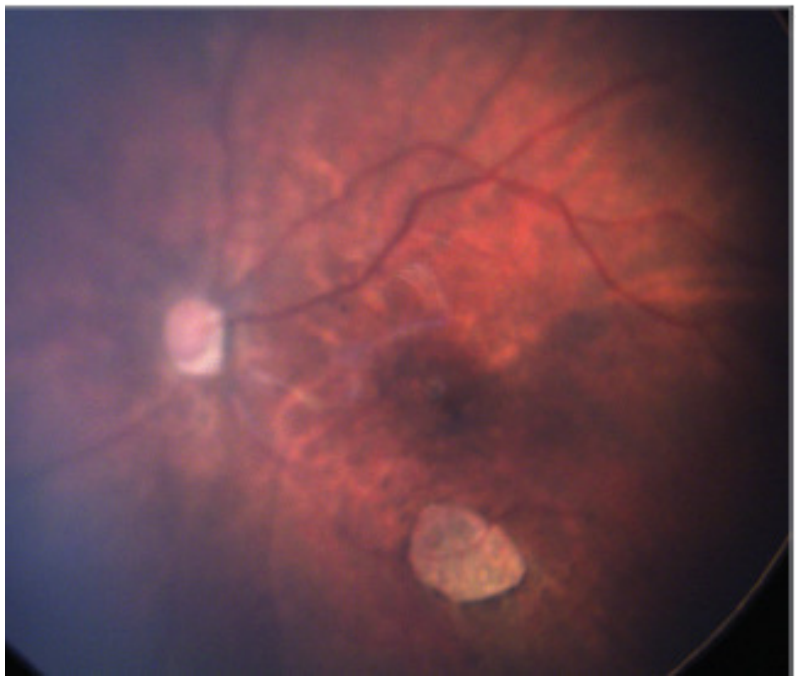
-Ventura CV, et al. First Travel-Associated Congenital Zika Syndrome in the US: Ocular and Neurological Findings in the Absence of Microcephaly. Ophthalmic Surg Lasers Imaging Retina. 2016 Oct 1;47(10):952-955.

-de Paula Freitas, et al. Anterior-Segment Ocular Findings and Microphthalmia in Congenital Zika Syndrome. Ophthalmology. 2017 Jul. [Epub ahead of print

Eye findings in Infants Without CNS Abnormalities



Optic nerve hypoplasia, chorioretinal atrophy, and macular mottling



Optic nerve hypoplasia and chorioretinal atrophy

Zin AA, et al. Screening Criteria for Ophthalmic Manifestations of Congenital Zika Virus Infection. JAMA Pediatr. 2017 Jul 17. [Epub ahead of print]

Eye Findings in Congenital Infections

	Zika	Toxoplasmosis	Rubella	CMV	Herpes Simplex	Syphilis
Conjunctivitis					+	
Keratitis					+	+
Macular Mottling	+ focal pigmentary clumping		+ granular (Salt-and-pepper retinopathy)			+ granular (Salt-and-pepper retinopathy)
Chorioretinal Atrophy	+	+				
Optic Nerve abnormalities	Hypoplasia, cupping, pallor		pallor	pallor		
Cataract	+		+	+	+	
Microphthalmia	+		+	+		
Iris Coloboma	+					
Active inflammation:		+	+	+	+	+

CDC Recommendations: Ophthalmic screening

Who should be referred for screening and when?

- **Before hospital discharge:**
  - Infant whose mother has risk factors for maternal Zika virus infection (travel to or residence in an area with risk of Zika or sex with a partner who traveled to or resided in such an area)

  AND
  - Maternal test results are not available

  AND
  - There is a concern about infant follow-up care
- **Before 1 month of age:**
  - All infants with laboratory evidence of congenital Zika virus infection

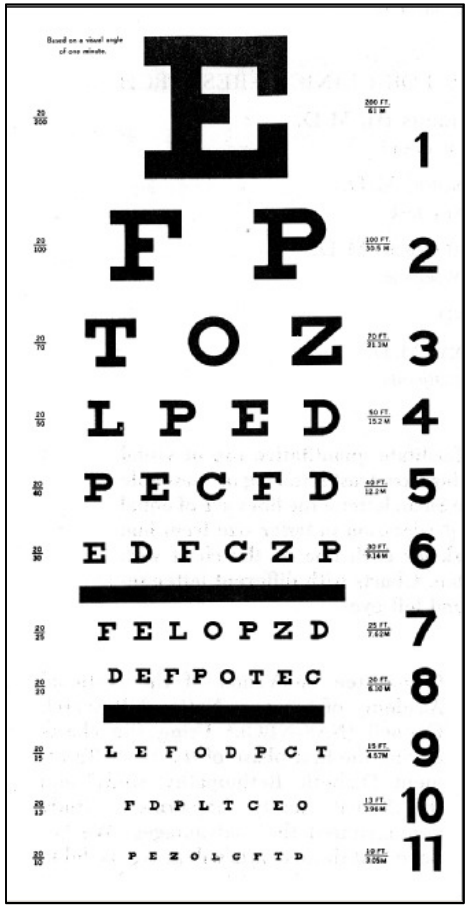
  OR
  - Abnormal findings consistent with CZS
- **Follow up should occur**
  - If the ophthalmologic examination within the first month of age is normal
  - Another complete examination at 3 months of age

Russell K, Oliver SE, Lewis L, et al. Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016. MMWR Morb Mortal Wkly Rep 2016;65:870–878.

Screening should include

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

- Resources for children with vision impairment or loss
  - Low vision specialist
  - Early intervention



National Eye Institute

How can primary care providers help?

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

Russell K, Oliver SE, Lewis L, et al. Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016. MMWR Morb Mortal Wkly Rep 2016;65:870–878.

Summary

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

Thank you!

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

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Today's webinar will be archived

When: A few days after the live call

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

Where: On the COCA Call webpage

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

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Thank you for joining!

Centers for Disease Control and Prevention
Atlanta, Georgia
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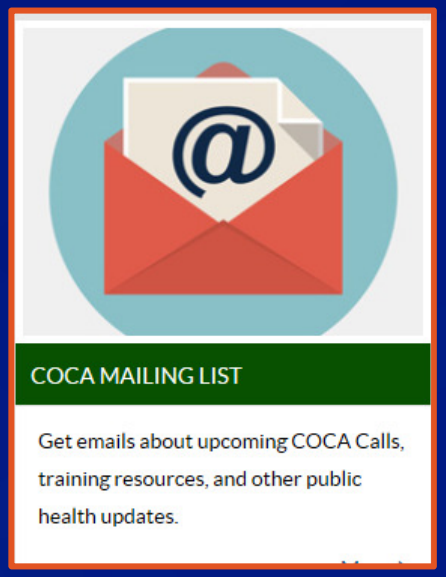

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