

CDC Responds to **ZIKA**



Zika Virus: Information for Clinicians

Updated August 5, 2016



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

This training provides clinicians with information about

- Zika virus epidemiology
- Diagnoses and testing
- Case reporting
- Zika and pregnancy
- Clinical management of Infants
- Sexual transmission
- Preconception guidance
- What to tell patients about Zika
- What to tell patients about mosquito bite protection



ZIKA VIRUS EPIDEMIOLOGY

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Zika virus (Zika)

- Single stranded RNA virus
- Genus *Flavivirus*, family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses
- Primarily transmitted through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*)



Aedes aegypti



Aedes albopictus

Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands.
- Currently outbreaks are occurring in many countries and territories.



Modes of transmission

- Bite from an infected mosquito
- Maternal-fetal
 - Intrauterine
 - Perinatal
- Sexual transmission from an infected person to his or her partners
- Laboratory exposure
- Theoretical: blood transfusion, organ and tissue transplant, fertility treatment, and breast feeding



Example Zika virus incidence and attack rates, Yap 2007

- Infection rate: 73% (95% CI 68–77)
- Symptomatic attack rate among infected: 18% (95% CI 10–27)
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

Note: Rates based on serosurvey on Yap Island, 2007 (population 7,391)



Incubation and viremia

- Incubation period for Zika virus disease is 3–14 days.
- Zika viremia ranges from a few days to 1 week.
- Some infected pregnant women can have evidence of Zika virus in their blood longer than expected.
- Virus remains in semen longer than in blood.



3 - 14 Days



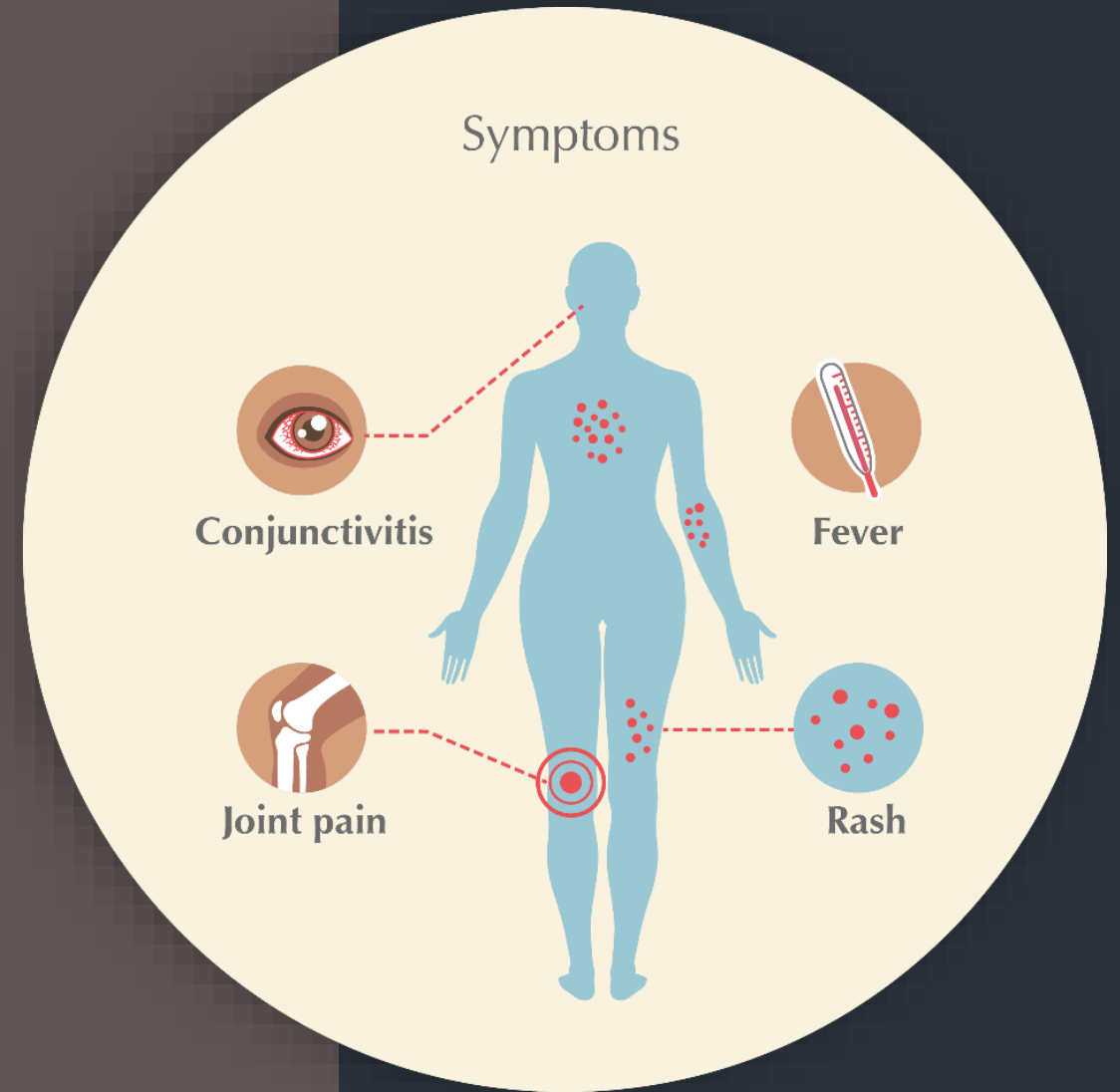
Zika virus clinical disease course and outcomes

- Clinical illness is usually mild.
- Symptoms last several days to a week.
- Severe disease requiring hospitalization is uncommon.
- Fatalities are rare.
- Guillain-Barré syndrome (GBS) reported in patients following suspected Zika virus infection.
 - Relationship to Zika virus infection is not known.



Symptoms

- Many infections asymptomatic.
- Most common symptoms
 - Acute onset of fever
 - Maculopapular rash
 - Joint pain
 - Conjunctivitis
- Other symptoms include muscle pain and headache.



Reported clinical symptoms among confirmed Zika virus disease cases

Symptoms	N (n=31)	%
Macular or papular rash	28	90%
Subjective fever	20	65%
Arthralgia	20	65%
Conjunctivitis	17	55%
Myalgia	15	48%
Headache	14	45%
Retro-orbital pain	12	39%
Edema	6	19%
Vomiting	3	10%

Yap Island, 2007

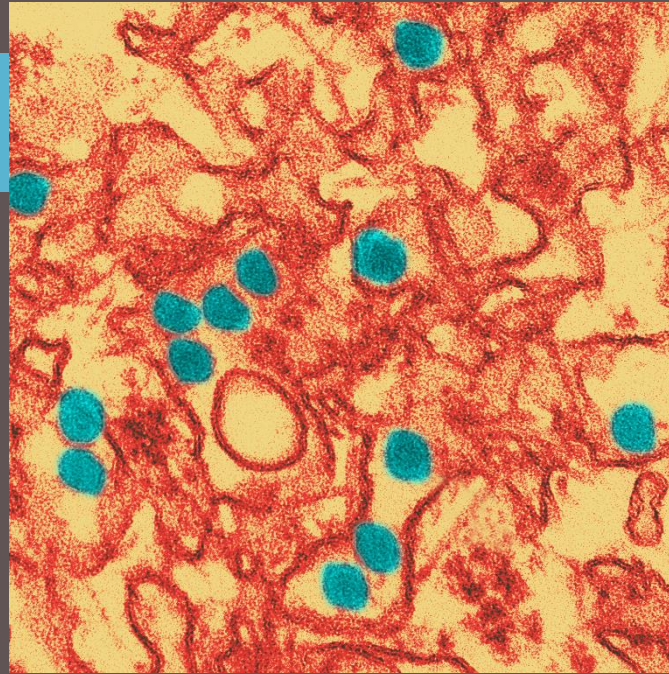
Duffy M. N Engl J Med 2009

Clinical features: Zika virus compared to dengue and chikungunya

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-

Rabe, Ingrid MBChB, MMed “Zika Virus- What Clinicians Need to Know?” (presentation, Clinician Outreach and Communication Activity (COCA) Call, Atlanta, GA, January 26 2016)

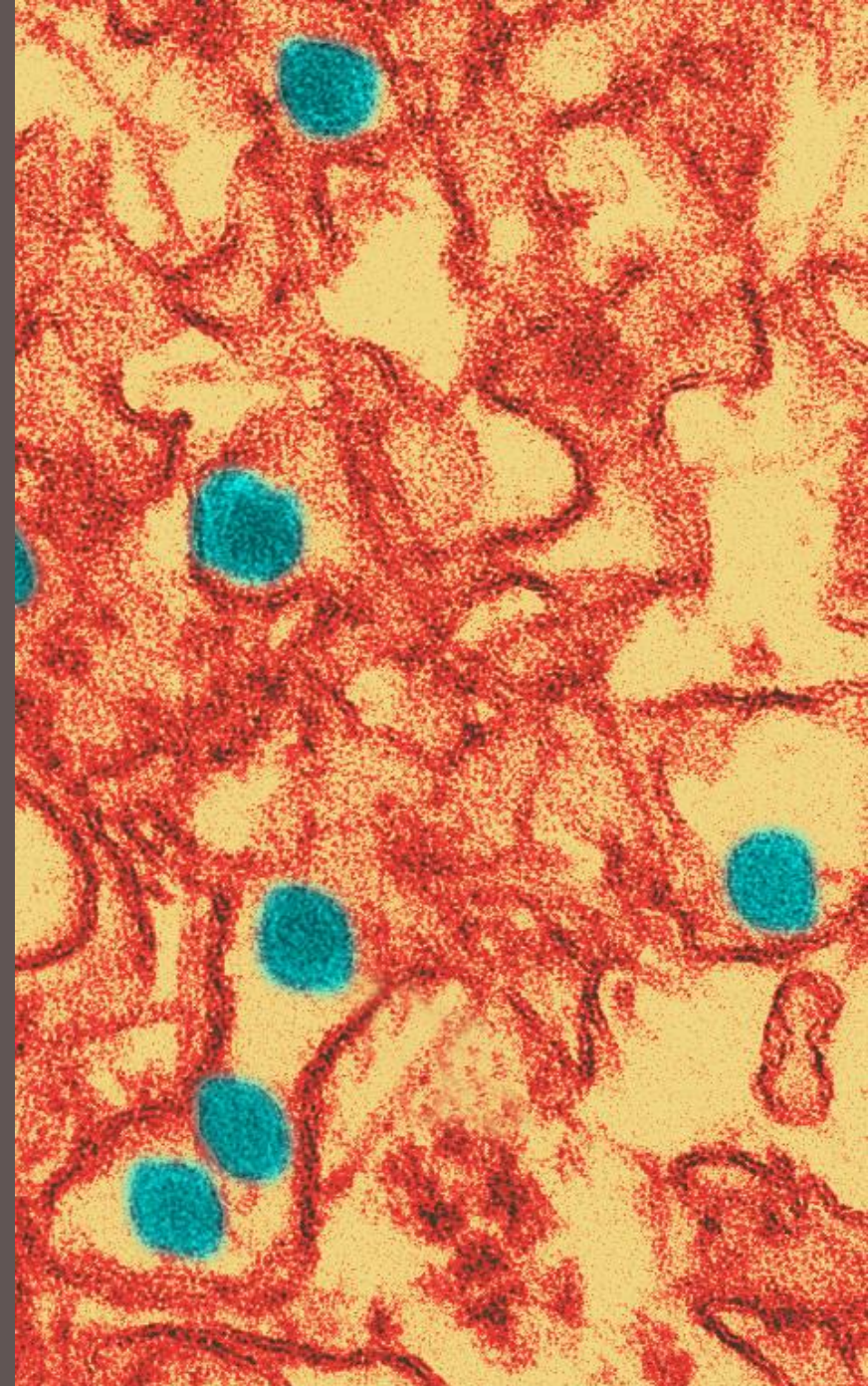
DIAGNOSES AND TESTING FOR ZIKA



Differential diagnosis

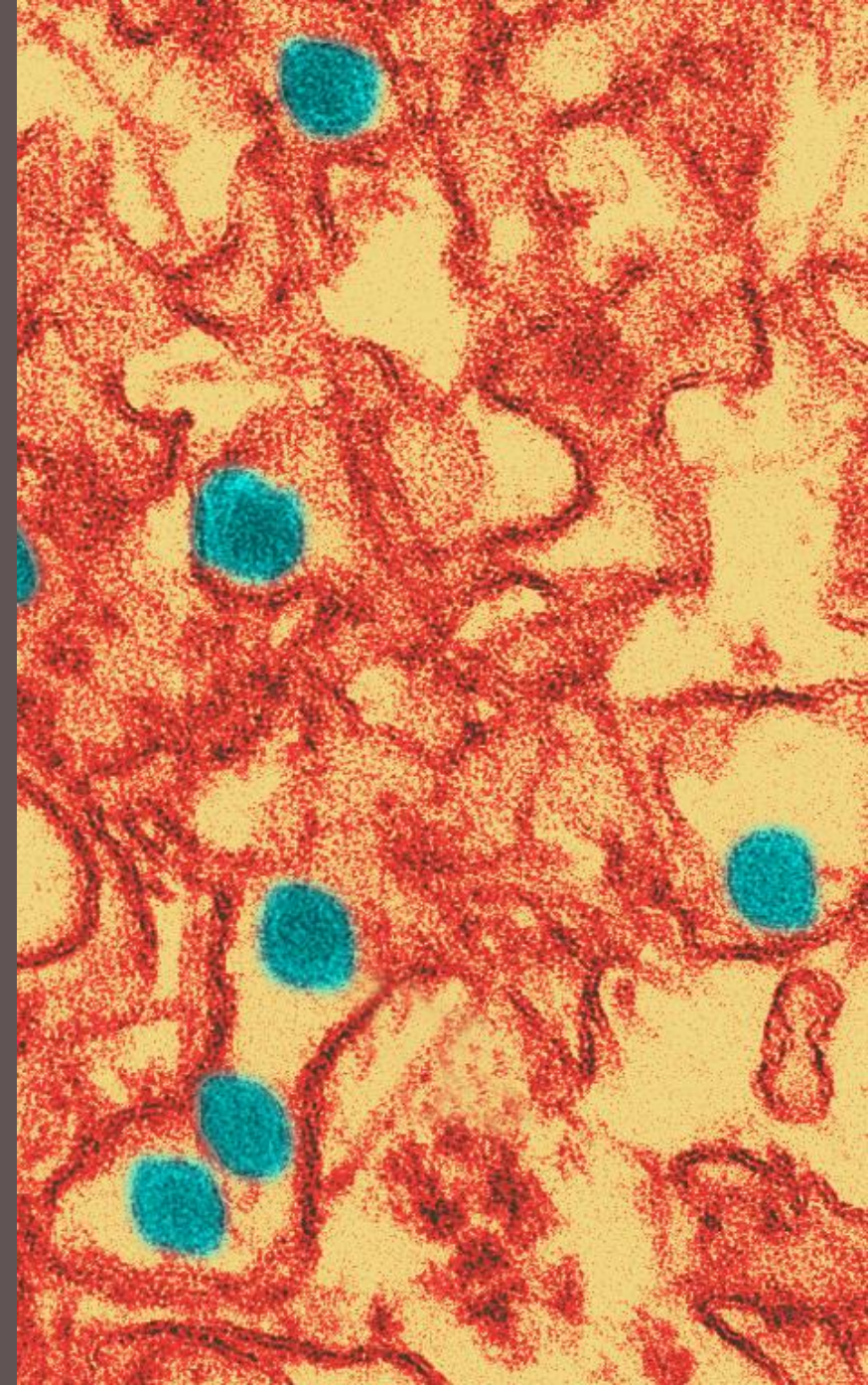
Based on typical clinical features, the differential diagnosis for Zika virus infection is broad. Considerations include

- Dengue
- Chikungunya
- Leptospirosis
- Malaria
- Rickettsia
- Group A Streptococcus
- Rubella
- Measles
- Parvovirus
- Enterovirus
- Adenovirus
- Other alphaviruses (e.g., Mayaro, Ross River, Barmah Forest, O'nyong-nyong, and Sindbis viruses)



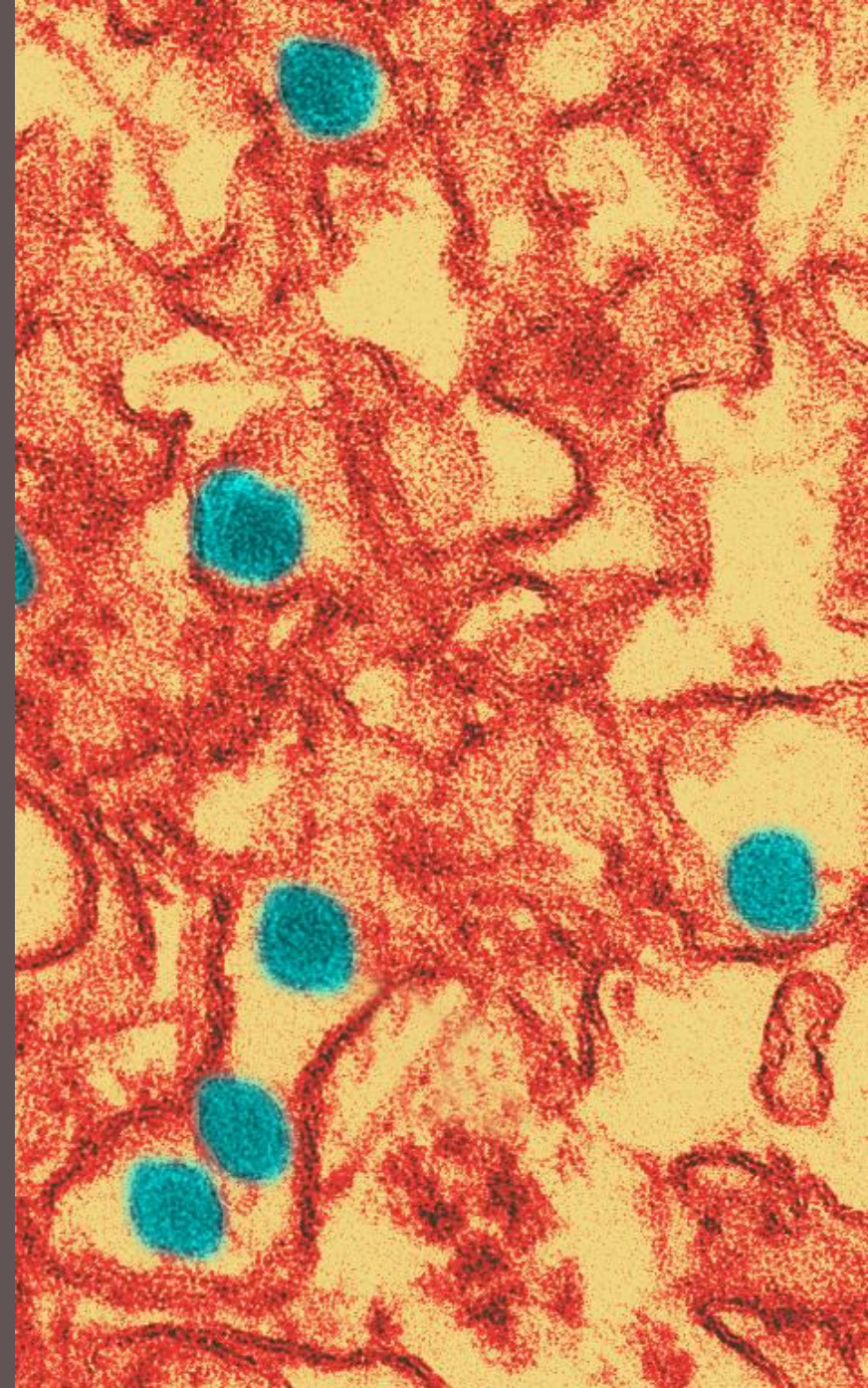
Diagnostic testing for Zika virus

- During first two weeks after the start of illness, Zika virus infection can often be diagnosed by performing real-time reverse transcriptase polymerase chain reaction (rRT-PCR) on serum and urine.
- Serology for IgM and neutralizing antibodies in serum collected up to 12 weeks after illness onset
- Plaque reduction neutralization test (PRNT) for presence of virus-specific neutralizing antibodies in paired serum samples
- Immunohistochemical (IHC) staining for viral antigens or RT-PCR on fixed tissues



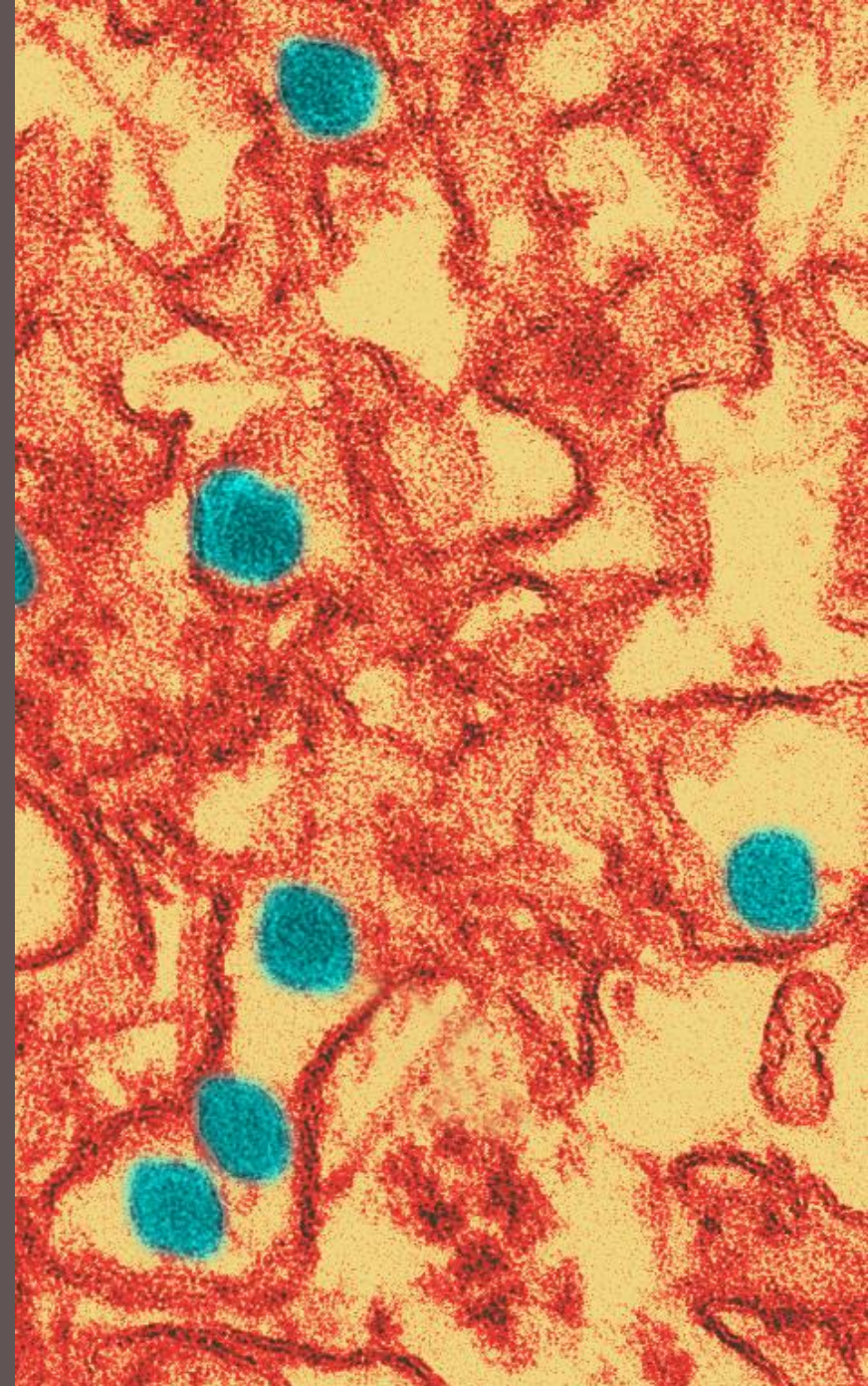
Serology cross-reactions with other flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related *flaviviruses* (e.g., dengue and yellow fever viruses).
- As viremia decreases over time, a negative rRT-PCR collected after symptom onset does not preclude Zika; in this case, serologic testing should be performed.
- Neutralizing antibody testing may discriminate between cross-reacting antibodies in primary *flavivirus* infections.
- Difficult to distinguish infecting virus in people previously infected with or vaccinated against a related *flavivirus*



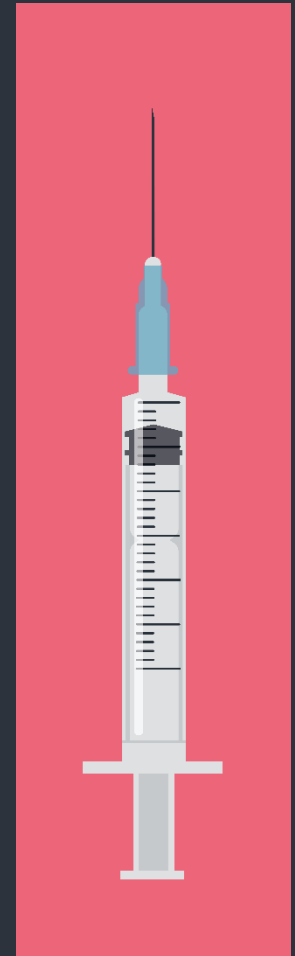
Laboratories for diagnostic testing

- Testing performed at CDC, select commercial labs, and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states.
- Healthcare providers should work with their state health department to facilitate diagnostic testing and report results.



Recommendations

- CDC recommends Zika virus testing for
 - Symptomatic people who live in or recently traveled to an area with active Zika transmission, and
 - People who have had unprotected sex with someone confirmed to have Zika virus infection or who lives in or traveled to an area with active Zika transmission.
- All pregnant women in the US should be assessed for possible Zika exposure at each prenatal care visit.



Recommendations continued...

- Pregnant women with possible Zika exposure and signs or symptoms consistent with Zika virus disease should be tested based on time of evaluation relative to symptom onset in accordance with [CDC guidance](#).
- Pregnant women with ongoing risk of possible Zika virus exposure and who do not report symptoms of Zika virus disease should be tested in the first and second trimester of pregnancy in accordance with CDC guidance.



REPORTING ZIKA CASES

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Reporting cases

- Zika virus disease is a nationally notifiable condition. Report all confirmed cases to your state health department.



Zika pregnancy registry

- CDC established the [US Zika Pregnancy Registry](#) to collect information and learn more about pregnant women in the US with Zika and their infants.
- Data collected will be used to update recommendations for clinical care, plan for services for pregnant women and families affected by Zika, and improve prevention of Zika infection during pregnancy.
- CDC maintains a 24/7 consultation service for health officials and healthcare providers caring for pregnant women. To contact the service, call 770-488-7100 or email ZIKAMCH@cdc.gov
- CDC also established a similar system, the [Zika Active Pregnancy Surveillance System](#), in Puerto Rico.



ZIKA AND PREGNANCY

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Zika and pregnancy outcomes

- Zika virus can pass from a pregnant woman to her fetus during pregnancy or around the time of birth.
- Zika infection in pregnancy is a cause of microcephaly and other severe brain defects. Other problems include
 - Eye defects, hearing loss, impaired growth, and fetal loss.



Zika and pregnancy

- Scientists are studying the full range of other potential health problems caused by Zika virus infection during pregnancy.
- No reports of infants getting Zika through breastfeeding
- No evidence that previous infection will affect future pregnancies

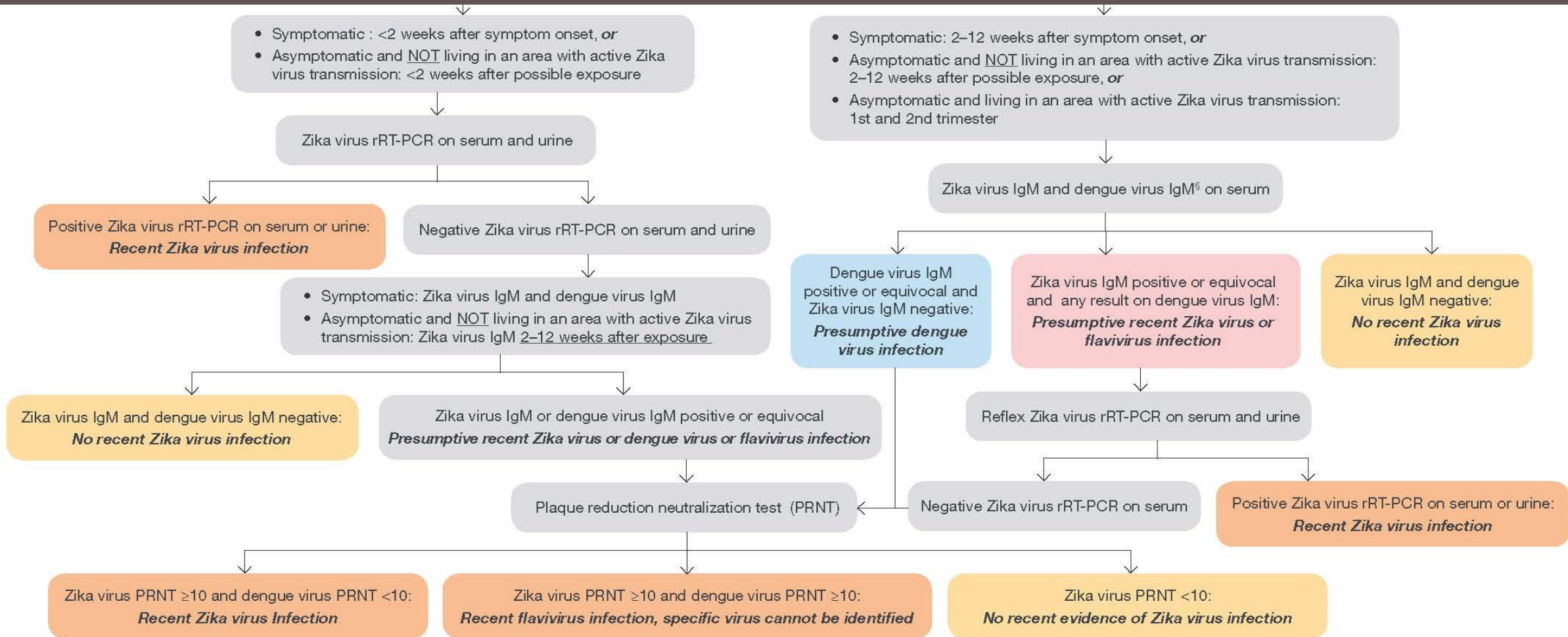


Who to test for Zika during pregnancy

- All pregnant women should be assessed for Zika 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 or other barrier method to prevent infection with a partner who lives in or traveled to an area with active Zika transmission



Testing guidance: Pregnant women with possible Zika exposure



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription-polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported whereas a pregnant woman is considered asymptomatic if symptoms are NOT reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus Immunoglobulin M (IgM), and plaque reduction neutralization test (PRNT) on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (<http://www.cdc.gov/zika/laboratories/lab-guidance.html>). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue IgM antibody testing is recommended only for symptomatic pregnant women.

¶ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (<http://wwwnc.cdc.gov/travel/notices/>), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission).

Clinical management of a pregnant woman with suspected Zika virus infection

Interpretation of Laboratory Results*	Prenatal Management	Postnatal Management
<u>Recent Zika virus infection</u>	<ul style="list-style-type: none"> Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth[†] Decisions regarding amniocentesis should be individualized for each clinical circumstance[§] 	<p>LIVE BIRTHS:</p> <ul style="list-style-type: none"> Cord blood and infant serum should be tested for Zika virus rRT-PCR, Zika IgM, and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta is recommended.[¶] <p>FETAL LOSSES:</p> <ul style="list-style-type: none"> Zika virus rRT-PCR and IHC staining of fetal tissues is recommended.[¶]
<u>Recent flavivirus infection; specific virus cannot be identified</u>		
<u>Presumptive recent Zika virus infection**</u>	<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>LIVE BIRTHS:</p> <ul style="list-style-type: none"> Cord blood and infant serum should be tested for Zika virus rRT-PCR, Zika IgM, and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta should be considered.[¶] <p>FETAL LOSSES:</p> <ul style="list-style-type: none"> Zika virus rRT-PCR and IHC staining of fetal tissues should be considered.[¶]
<u>Presumptive recent flavivirus infection**</u>		
<u>Recent dengue virus infection</u>	<ul style="list-style-type: none"> Clinical management in accordance with existing guidelines (http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf). 	
<u>No evidence of Zika virus or dengue virus infection</u>	<ul style="list-style-type: none"> Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.[†] <ul style="list-style-type: none"> Fetal abnormalities present: repeat Zika virus rRT-PCR and IgM test; base clinical management on corresponding laboratory results. Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman. 	

**CLINICAL MANAGEMENT OF INFANTS
WITH CONFIRMED OR POSSIBLE ZIKA
INFECTION**

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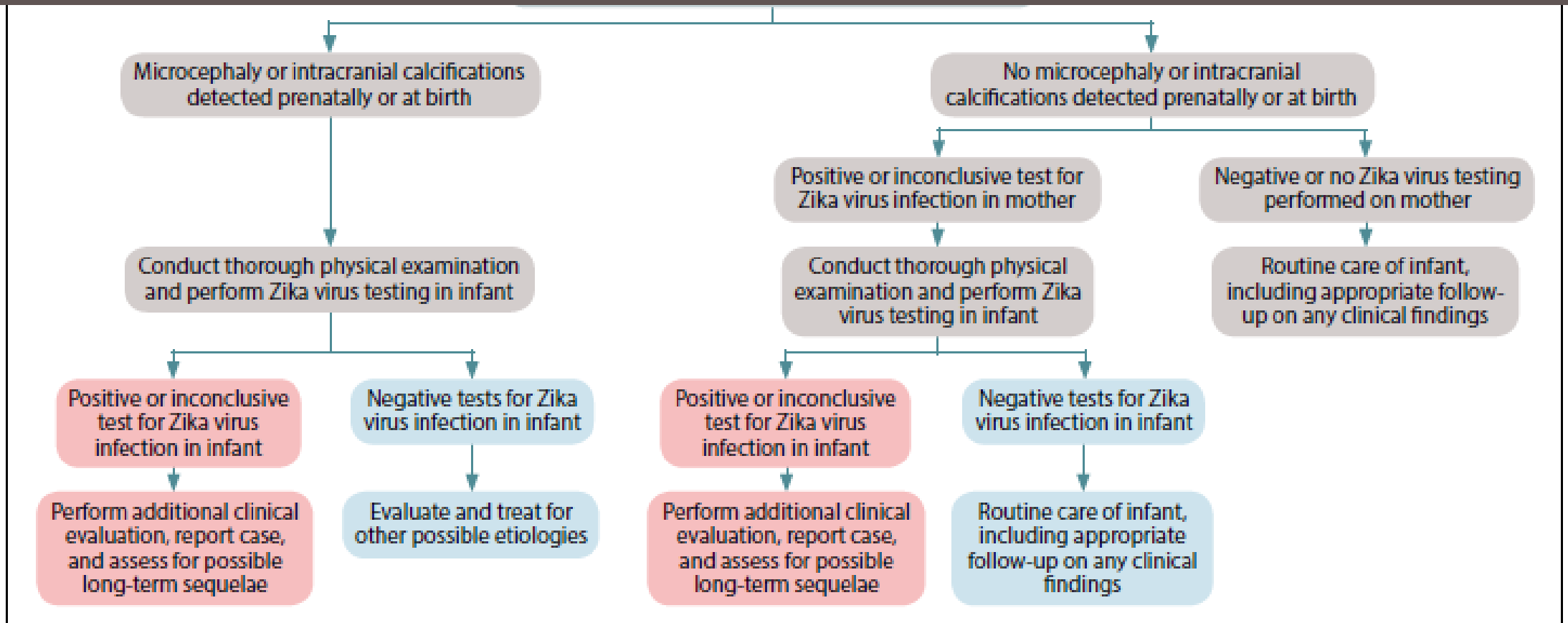
Infants with confirmed or possible Zika infection

Doctors have found problems among fetuses and infants infected with Zika virus before birth, including

- Microcephaly
- Miscarriage
- Stillbirth
- Absent or poorly developed brain structures
- Defects of the eye
- Hearing deficits
- Impaired growth



Testing guidance for infants of women with possible exposure to Zika during pregnancy



*Areas with Zika virus transmission are listed on CDC's website at <http://wwwnc.cdc.gov/travel/notices>.

†Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex based on standard growth curves, not explained by other etiologies.

§Laboratory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical specimen; or 2) positive Zika virus Immunoglobulin M (IgM) with confirmatory neutralizing antibody titers that are ≥ 4 -fold higher than dengue virus neutralizing antibody titers in serum or cerebrospinal fluid. Testing is considered inconclusive if Zika virus neutralizing antibody titers are < 4 -fold higher than dengue virus neutralizing antibody titers.

More information on laboratory testing for Zika virus infection is available at <http://www.cdc.gov/zika/state-labs/index.html>.

Evaluation for all infants with positive or inconclusive Zika virus test results

- Physical examination, measurement of head circumference, and assessment of gestational age
- Evaluation neurologic abnormalities, dysmorphic features, enlarged liver or spleen, and rash/other skin lesions
- Cranial ultrasound
- Ophthalmologic evaluation before hospital discharge or within 1 month after birth
- Evaluation of hearing by evoked otoacoustic emissions testing or auditory brainstem response testing before hospital discharge or within 1 month after birth
- Consultation with appropriate specialist for any abnormal findings



Additional evaluation for infants who have microcephaly or other findings consistent with congenital Zika virus infection

- Consultation with clinical geneticist or dysmorphologist and pediatric neurologist
- Testing for other congenital infections; consider consultation with pediatric infectious disease specialist
- Complete blood count, platelet count, and liver function and enzyme tests
- Genetic or other teratogenic causes should be considered if additional anomalies are identified.



Long term follow up for infants with positive or inconclusive Zika virus test results

- Additional hearing screen at 6 months of age and audiology follow up of abnormal newborn hearing screening
- Continued evaluation of developmental characteristics and milestones, as well as head circumference, through 1st year of life
- Consultation with appropriate medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy) if any abnormalities are noted and as concerns arise



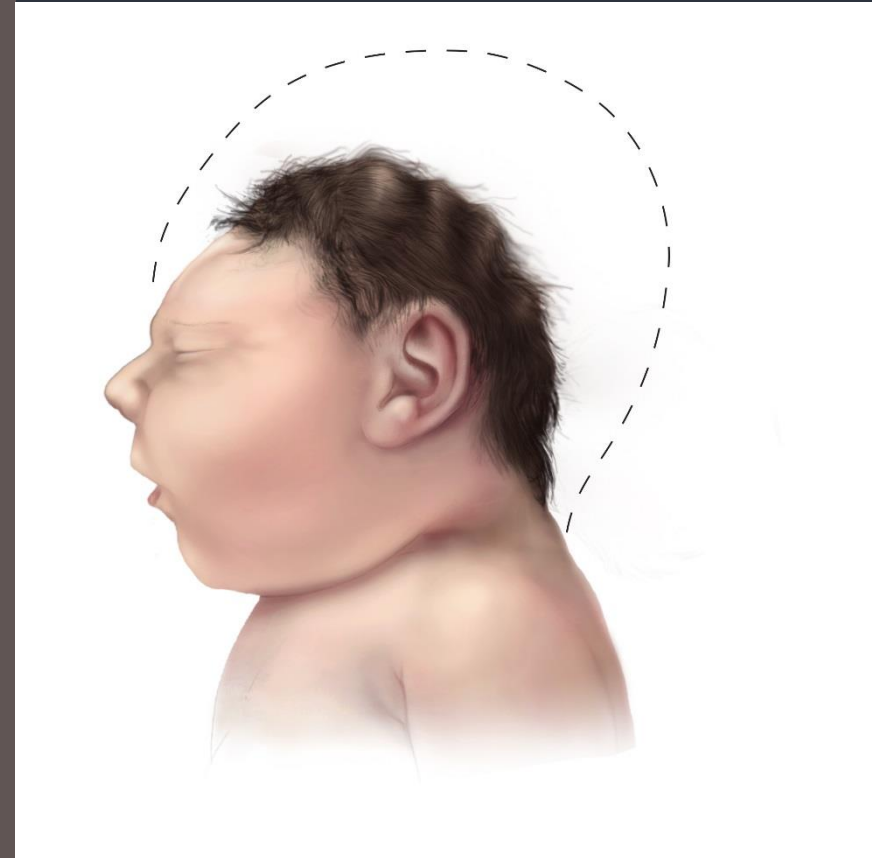
Case definition of microcephaly

Definite congenital microcephaly for live births

- Head circumference (HC) at birth is less than the 3rd percentile for gestational age and sex.
- If HC at birth is not available, HC less than the 3rd percentile for age and sex within the first 6 weeks of life

Definite congenital microcephaly for still births and early termination

- HC at delivery is less than the 3rd percentile for gestational age and sex.



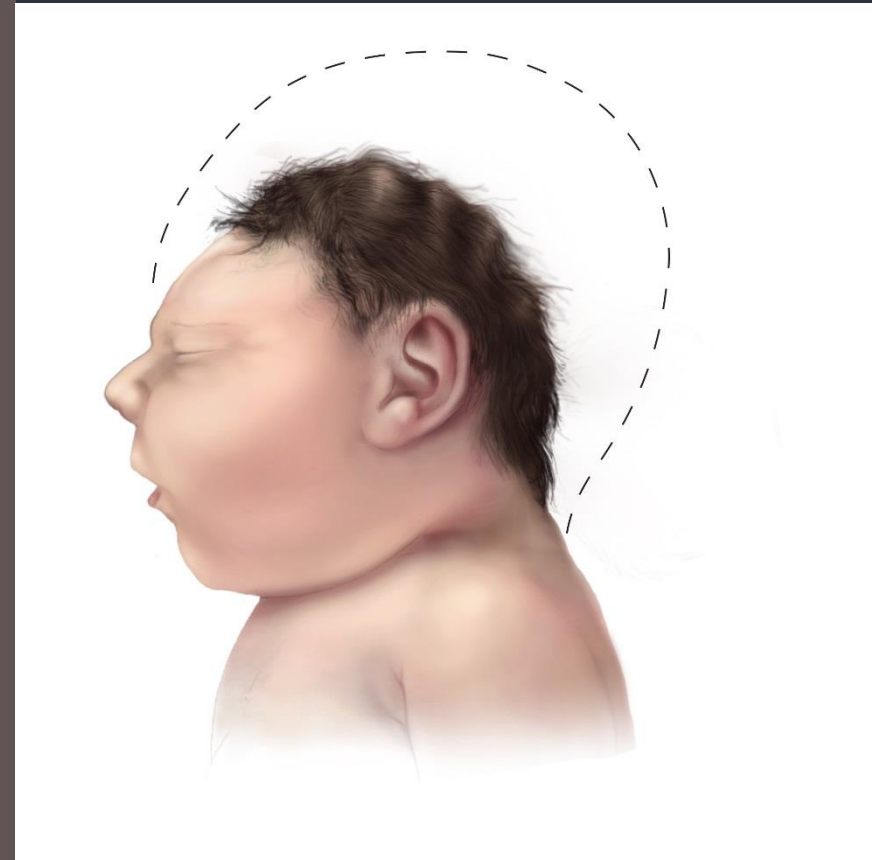
Definitions for *possible* congenital microcephaly

Possible congenital microcephaly for live births

- If earlier HC is not available, HC less than 3rd percentile for age and sex beyond 6 weeks of life.

Possible microcephaly for all birth outcomes

- Microcephaly diagnosed or suspected on prenatal ultrasound in the absence of available HC measurements.



Measuring head circumference for microcephaly



- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
 - Broadest part of the forehead above eyebrow
 - Above the ears
 - Most prominent part of the back of the head

- Take the measurement three times and select the largest measurement to the nearest 0.1 cm
- Optimal measurement at 24-36 hours after birth when molding of the head has subsided

SEXUAL TRANSMISSION

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About sexual transmission

- Zika virus can be passed through sex, even if the infected person does not have symptoms at the time.
- Sex includes vaginal, anal, and oral sex, and the sharing of sex toys.
- Condoms and other barriers* can reduce the chance of getting Zika from sex.
- Not having sex can eliminate the risk of getting Zika from sex.

* Barriers include male and female condoms and dental dams.



What we do not know about sexual transmission

- We do not know how often people with Zika who never develop symptoms pass Zika through sex.
- We do not know if sexual transmission of Zika virus poses a different risk of birth defects than mosquito-borne transmission.



Preventing or reducing the chance of sexual transmission for couples who are pregnant

- Not having sex can eliminate the risk of getting Zika from sex.
- Condoms can reduce the chance of getting Zika from sex.
- Pregnant couples with a partner who lives in or recently traveled to an area with Zika should use condoms (or other barriers to prevent infection) correctly every time they have sex or not have sex during pregnancy.



Non-pregnant couples with a partner who traveled to an area with Zika

- For non-pregnant couples with a partner who has **recently traveled** to an area with Zika
 - At least 8 weeks after a Zika diagnosis or start of symptoms if the traveling partner is female or if the traveling partner (male or female) has no symptoms.
 - At least 6 months after a Zika diagnosis or start of symptoms if the traveling partner is male. This long extended period is because Zika stays in semen longer than in other body fluids.



Non-pregnant couples with a partner who lives in an area with Zika

- Couples living in an area with Zika can use condoms or not have sex as long as there is Zika in the area. If either partner develops symptoms of Zika or has concerns, they should talk to a healthcare provider.



PRECONCEPTION GUIDANCE

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Couples interested in conceiving who DO NOT reside in an area with active Zika virus transmission

- For Women with possible exposure to Zika virus
 - Discuss signs and symptoms and potential adverse outcomes associated with Zika
 - If Zika virus disease diagnosed or symptoms develop, wait at least 8 weeks after symptom onset to attempt conception.
 - If NO symptoms develop, wait at least 8 weeks after last date of exposure before attempting conception.
 - During that time, use condoms every time during sex or do not have sex to protect partner.



Couples interested in conceiving who DO NOT reside in an area with active Zika virus transmission

- For Men with possible exposure to Zika virus
 - If Zika virus disease diagnosed or symptoms develop, wait at least 6 months after symptom onset to attempt conception.
 - If NO symptoms develop, wait at least 8 weeks after exposure to attempt conception.
 - During that time, use condoms every time during sex or do not have sex to protect partner.
 - Discuss contraception and use of condoms.



Couples interested in conceiving who reside in an area with active Zika virus transmission

- Women and men interested in conceiving should talk with their HCPs
- Factors that may aid in decision-making
 - Reproductive life plan
 - Environmental risk of exposure
 - Personal measures to prevent mosquito bites
 - Personal measures to prevent sexual transmission
 - Education about Zika virus infection in pregnancy
 - Risks and benefits of pregnancy at this time

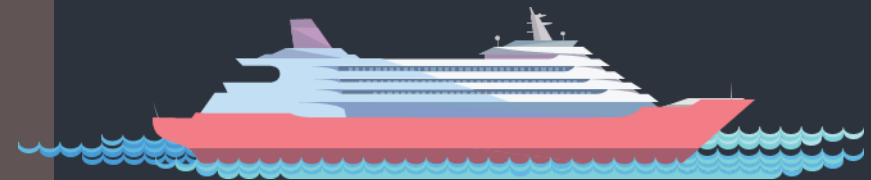


WHAT TO TELL PATIENTS ABOUT ZIKA

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Pregnant women

- Should not travel to areas with Zika.
- If they must travel to areas with Zika, tell pregnant patients to protect themselves from mosquito bites and take steps to prevent sexual transmission during and after travel.



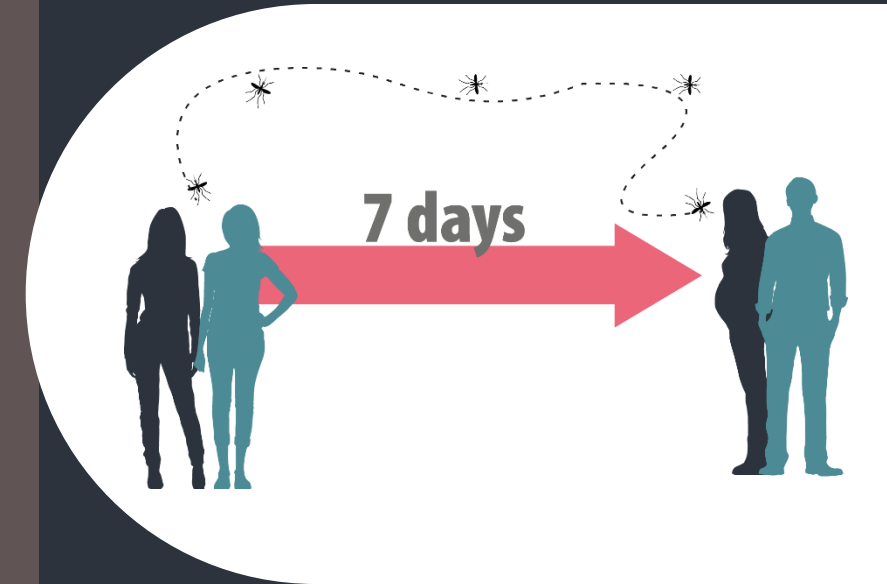
Treating patients who test positive

- There are no vaccine or medicine Zika.
- Treat the symptoms of Zika
 - Rest
 - Drink fluids to prevent dehydration
 - Take acetaminophen (Tylenol®) to reduce fever and pain
 - Do not take aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) until dengue can be ruled out to reduce the risk of bleeding.



Patients who test positive

- Protect from mosquito bites during the first week of illness, when Zika virus can be found in blood.
- The virus can be passed from an infected person to a mosquito through bites.
- An infected mosquito can spread the virus to other people.

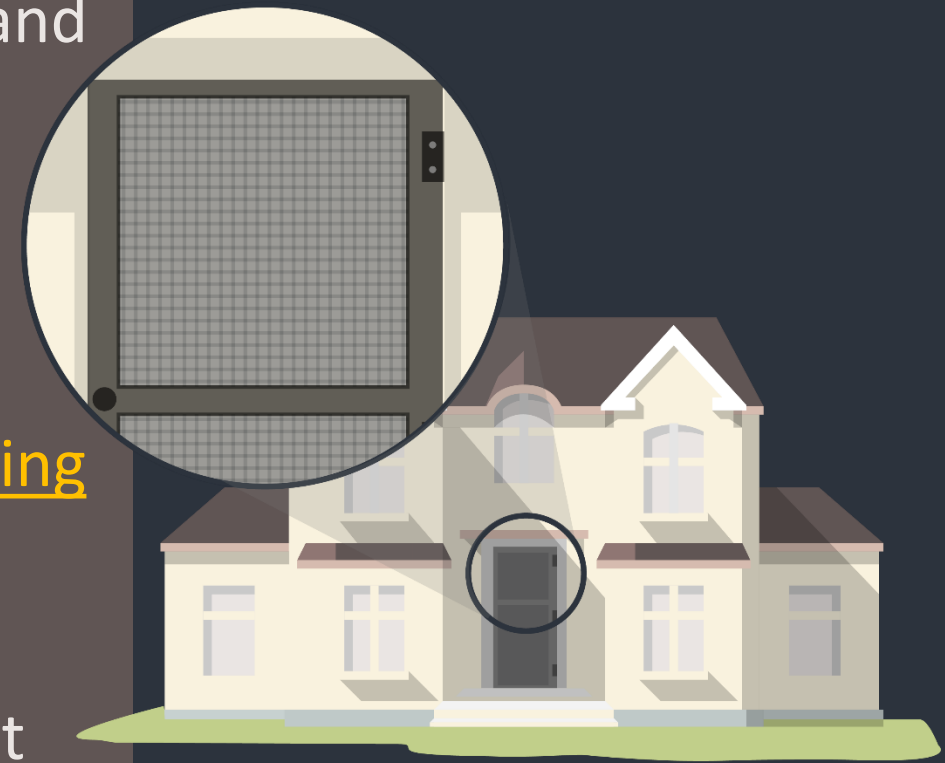


WHAT TO TELL PATIENTS ABOUT MOSQUITO BITE PROTECTION

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Mosquito bite protection

- Wear long-sleeved shirts and long pants.
- Stay and sleep in places with air conditioning and window and door screens to keep mosquitoes outside.
- Take steps to control mosquitoes inside and outside your home (<http://www.cdc.gov/zika/prevention/controlling-mosquitoes-at-home.html>).
- Sleep under a mosquito bed net if you are overseas or outside and are not able to protect yourself from mosquito bites.



Mosquito bite protection

- Use Environmental Protection Agency (EPA)-registered insect repellents with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-menthane-diol.
- Always follow the product label instructions.
- Do not spray repellent on the skin under clothing.
- If you are also using sunscreen, apply sunscreen before applying insect repellent.



Mosquito bite protection

- Do not use insect repellent on babies younger than 2 months old.
- Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.
- Dress children in clothing that covers arms and legs.
- Cover crib, stroller, and baby carrier with mosquito netting.
- Do not apply insect repellent onto a child's hands, eyes, mouth, and cut or irritated skin.
 - Adults: Spray insect repellent onto your hands and then apply to a child's face.



Additional resources

- <http://www.cdc.gov/zika/index.html>
- <http://www.cdc.gov/zika/hc-providers/index.html>
- <http://www.cdc.gov/zika/hc-providers/index.html>