

CDC Responds to **ZIKA**



Zika Virus: Information for Clinicians

Updated June 13, 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.
- As of June 20, 2016, outbreaks are occurring in 48 countries and territories.



Modes of transmission

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



Example Zika virus incidence and attack rates, Yap 2007

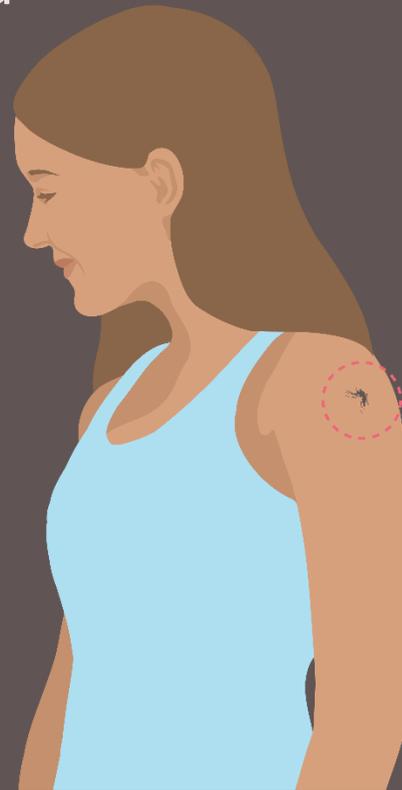
- Infection rate: 73% (95% CI 68–77)
- Symptomatic attack rate among infected: 18% (95% CI 10–27)
- All age groups affected
- Adults more likely to present for medical care
- No severe disease, hospitalizations, or deaths

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.
- Virus remains in semen longer than in blood.

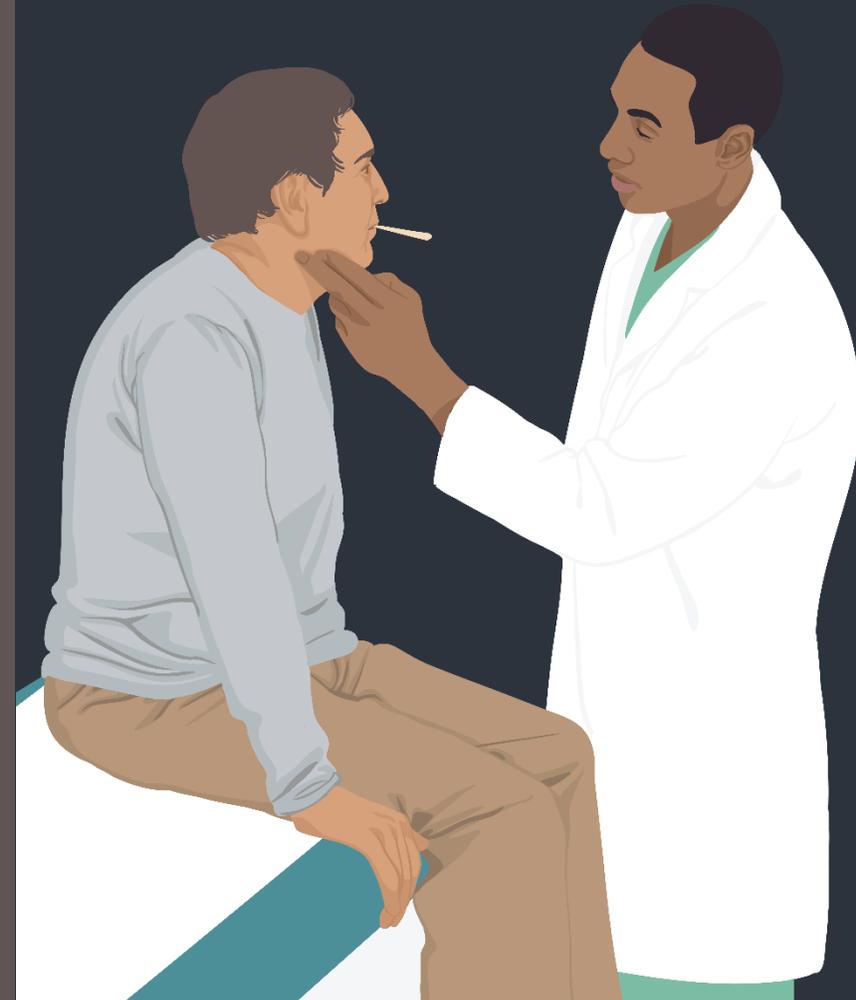


3 - 14 Days



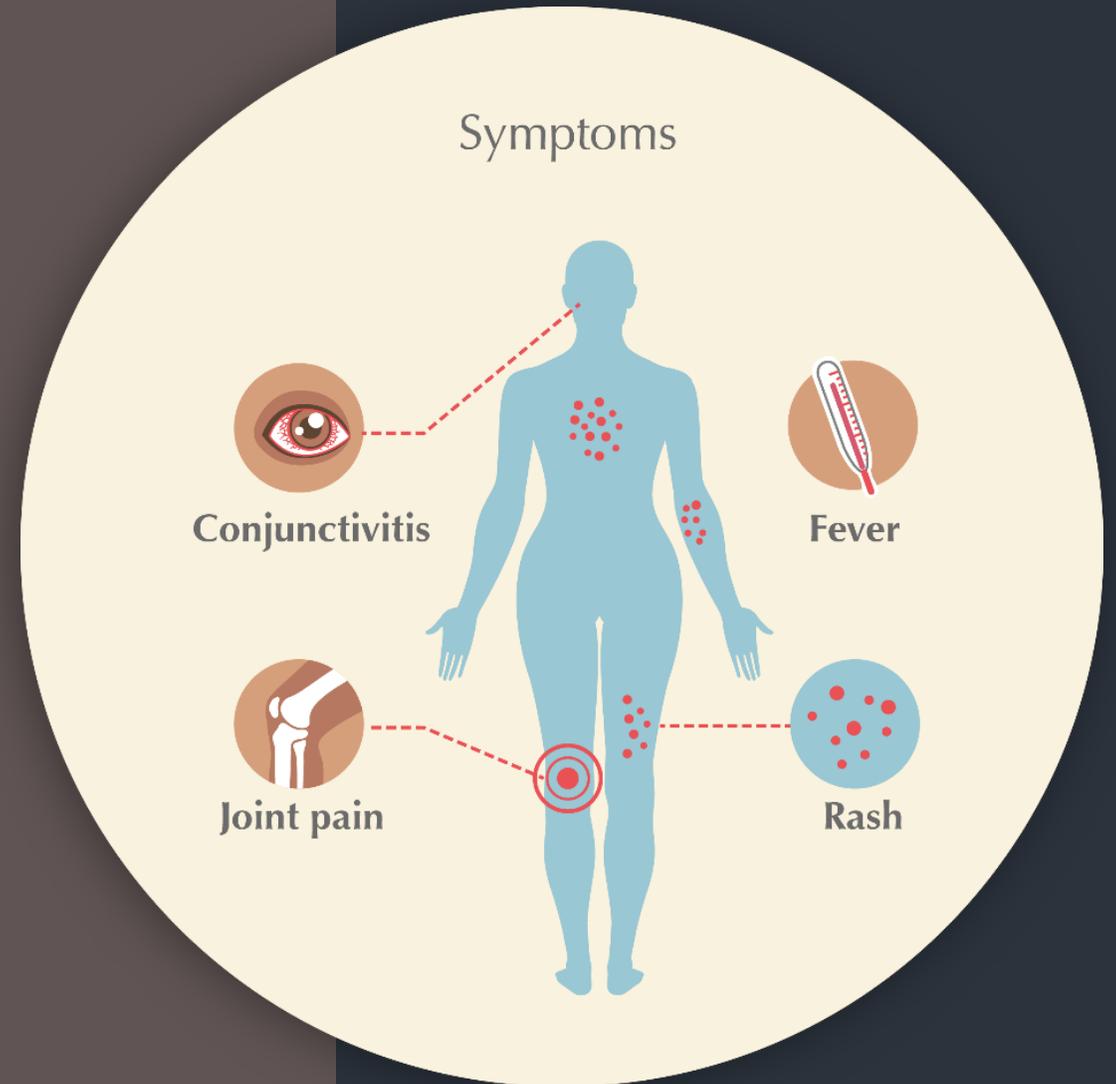
Zika virus clinical disease course and outcomes

- 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

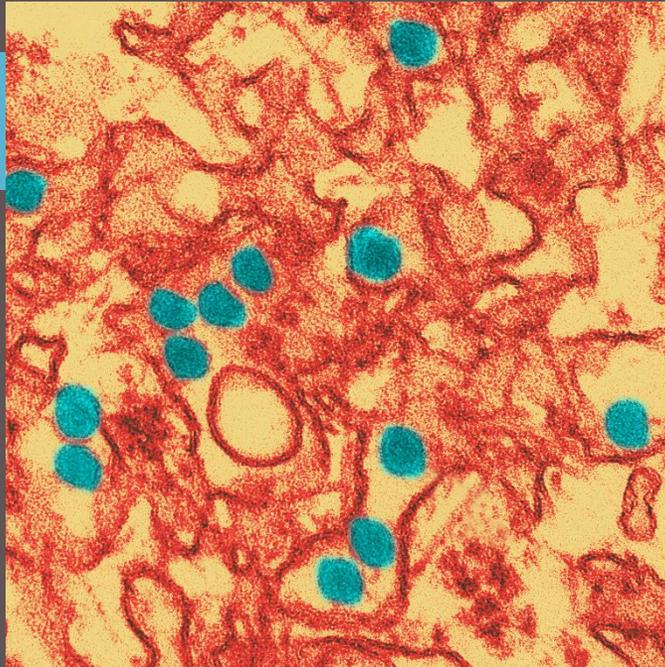
Duffy M. N Engl J Med 2009

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)

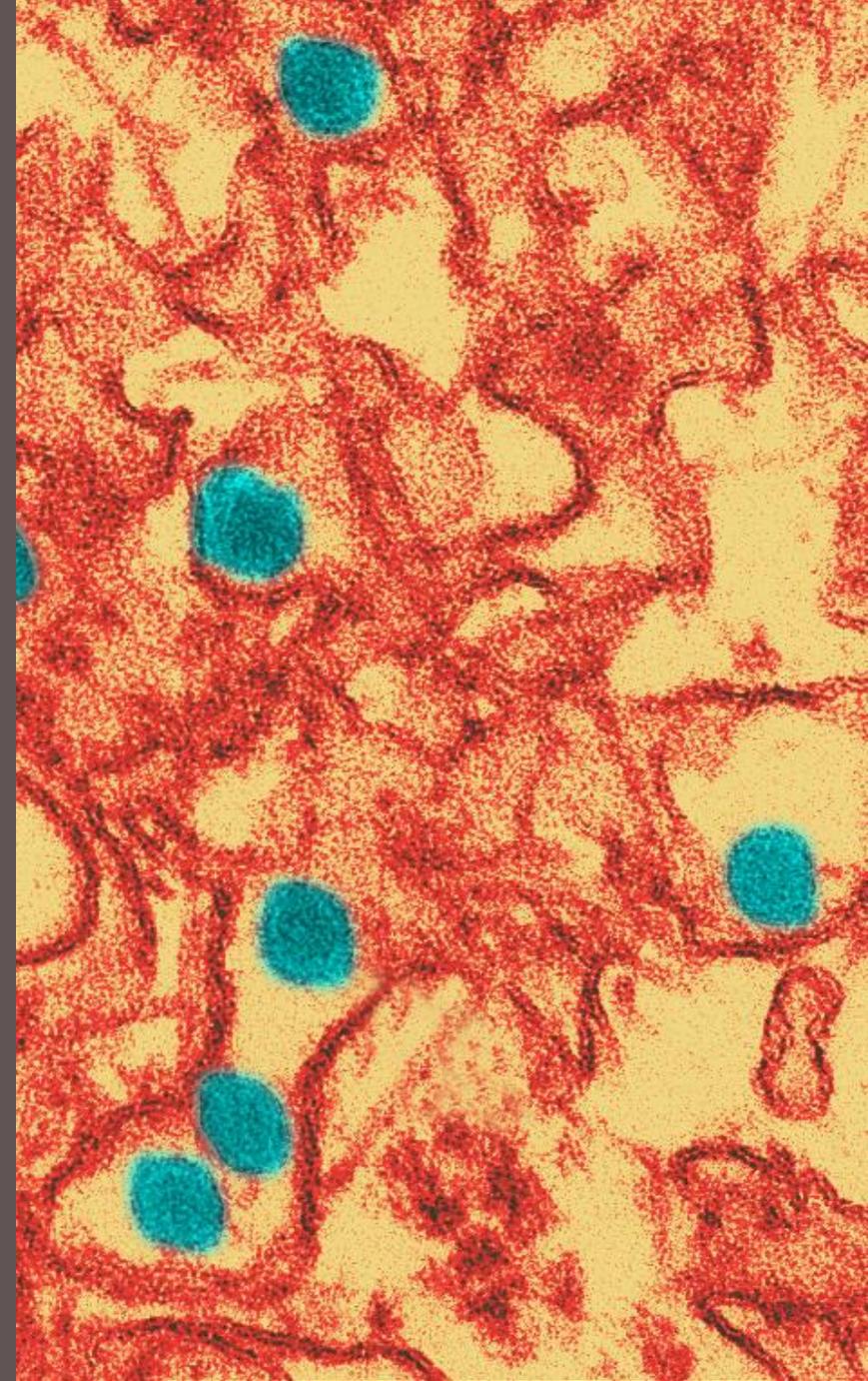
DIAGNOSES AND TESTING FOR ZIKA



Differential diagnosis

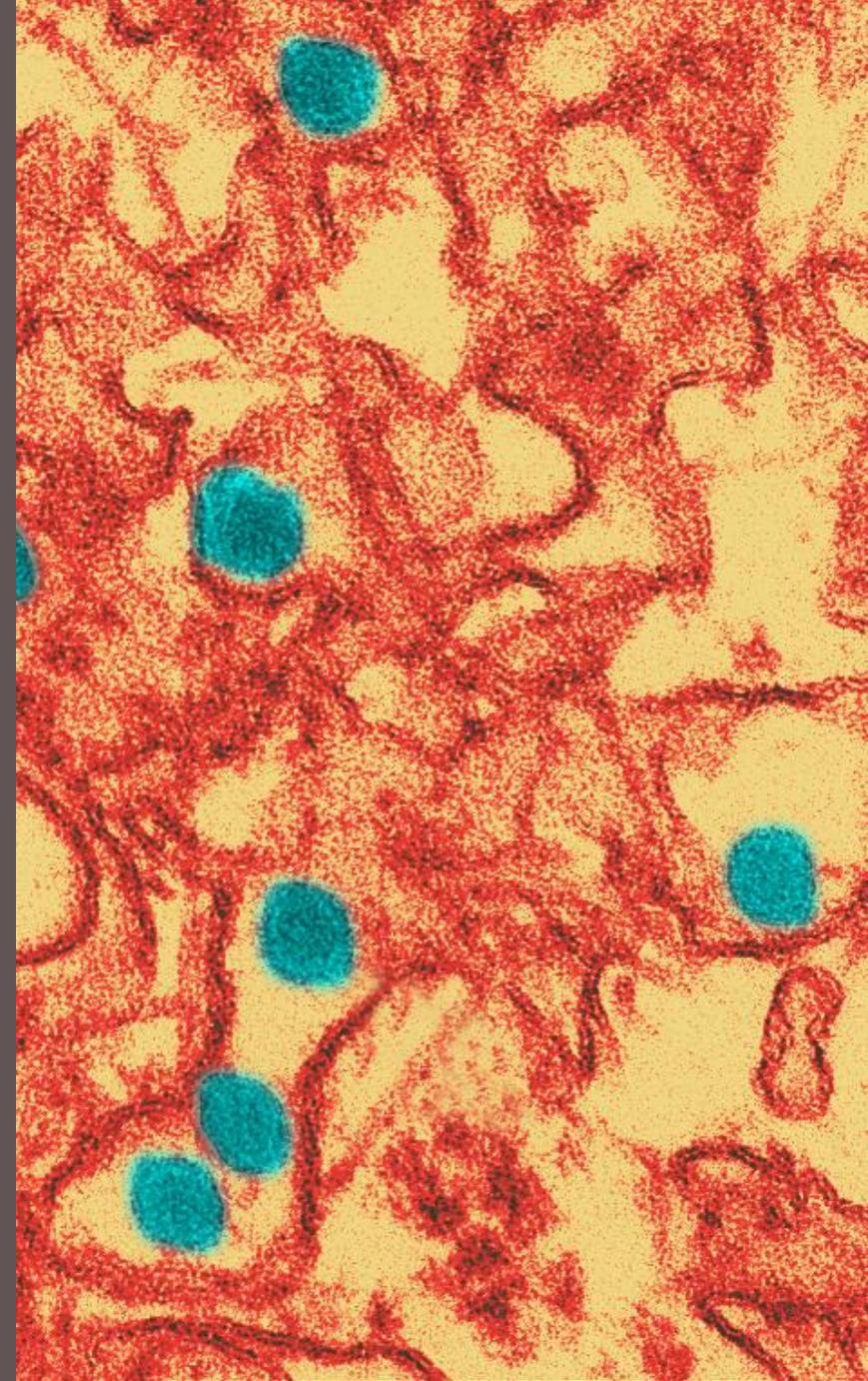
Based on typical clinical features, the differential diagnosis for Zika virus infection is broad. Considerations include

- 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)



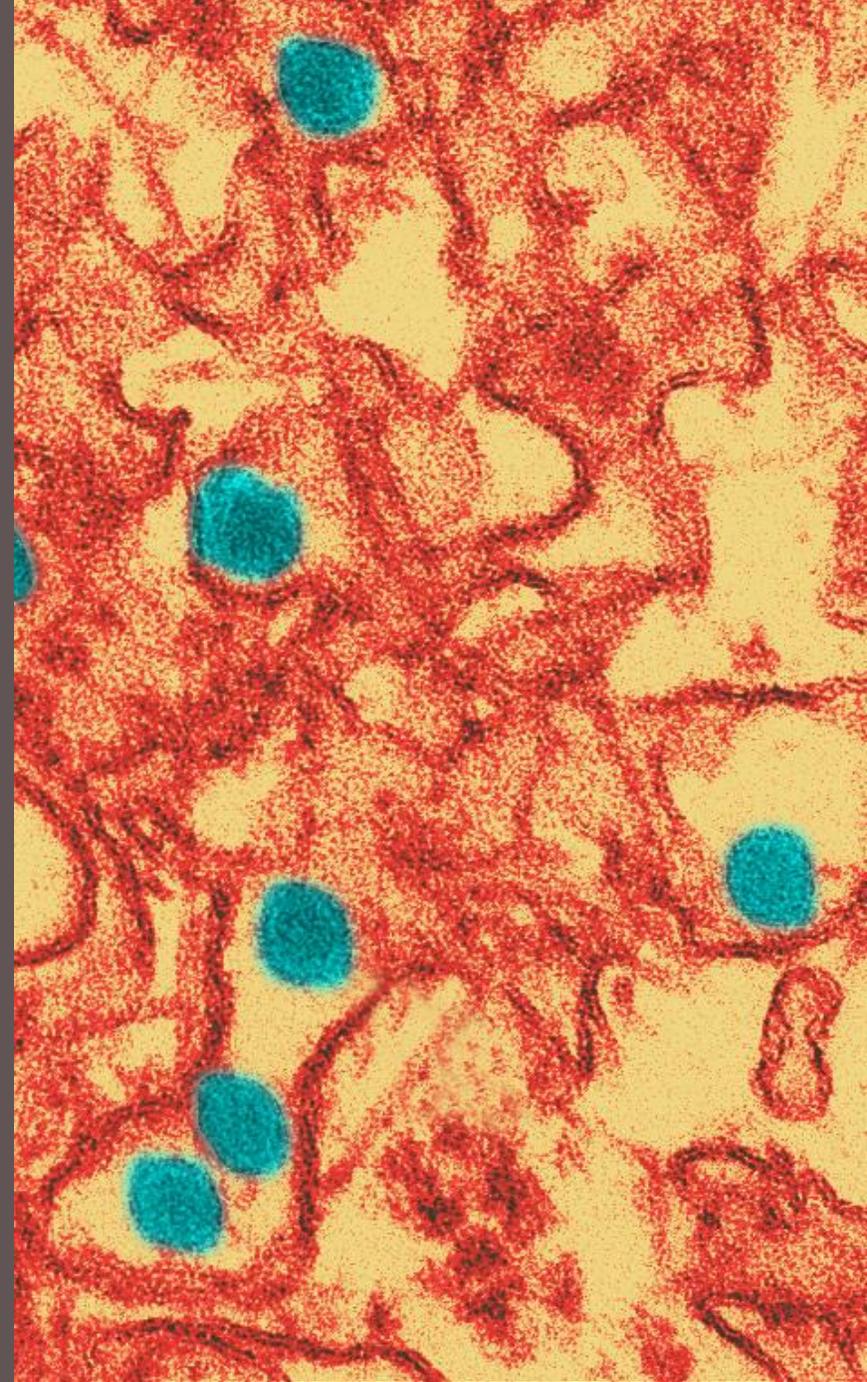
Diagnostic testing for Zika virus

- Real time reverse transcriptase-polymerase chain reaction (rRT-PCR) for viral RNA in clinical specimens collected < 7 days (serum) or \leq 14 days (urine) after illness onset.
- 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.



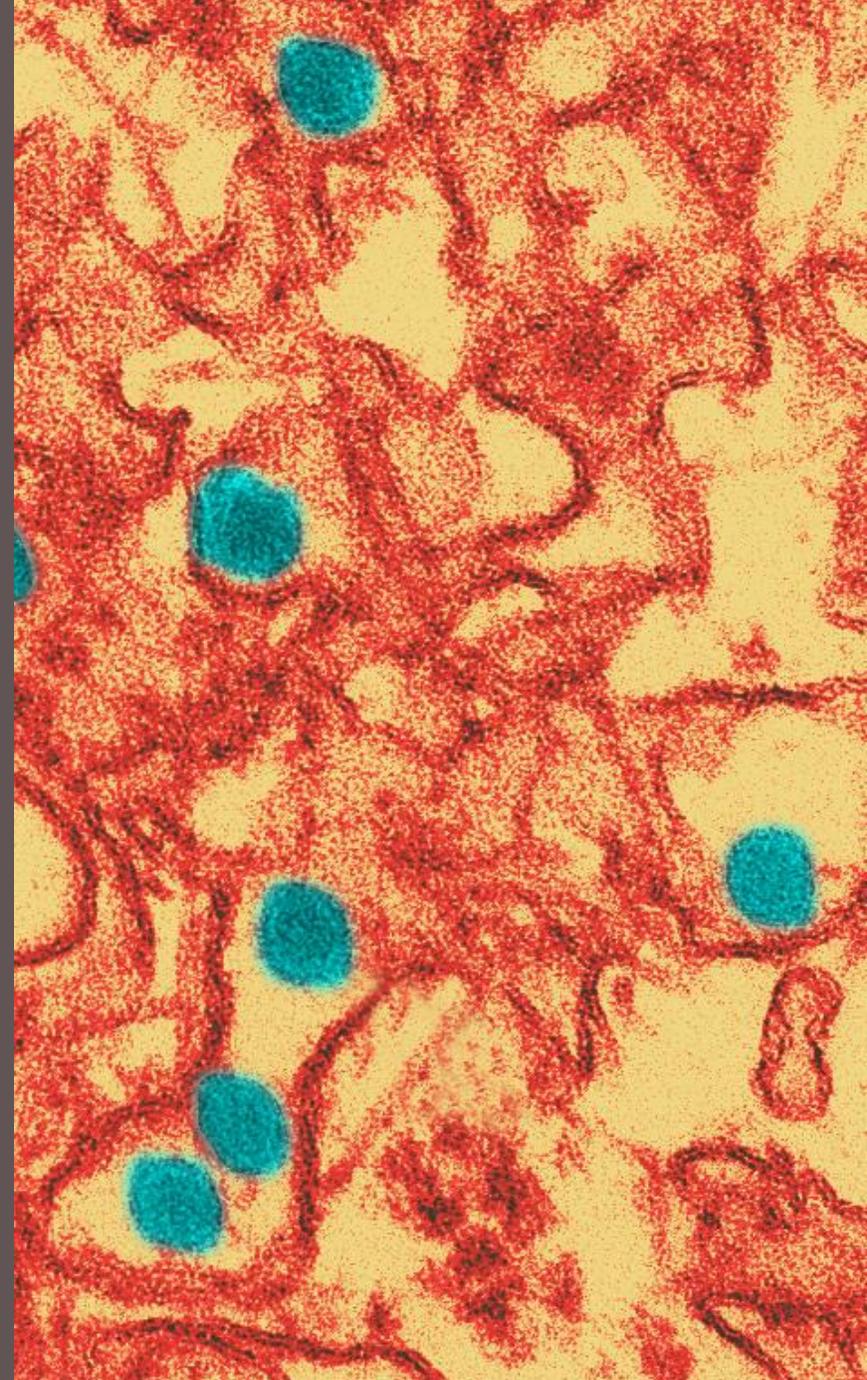
Serology cross-reactions with other flaviviruses

- Zika virus serology (IgM) can be positive due to antibodies against related *flaviviruses* (e.g., dengue and yellow fever viruses)
- 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*
- Healthcare providers should work with state and local health departments to ensure test results are interpreted correctly



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 contact their state health department to facilitate diagnostic testing.



Recommendations

- CDC recommends Zika virus testing for symptomatic people living in an active Zika transmission area, or who have recently traveled to an area with Zika, or who have had unprotected sex with a man confirmed to have Zika virus infection.
- Testing blood, semen, or urine is not recommended to determine how likely a man is to pass Zika virus through sex. This is because there is still a lot we don't know about the virus and how to interpret test results.
- Available tests may not accurately identify the presence of Zika or a man's risk of passing it on through sex. As we learn more and as tests improve, these tests may become more helpful for determining a man's risk of passing Zika through sex.



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 outcomes

- 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.



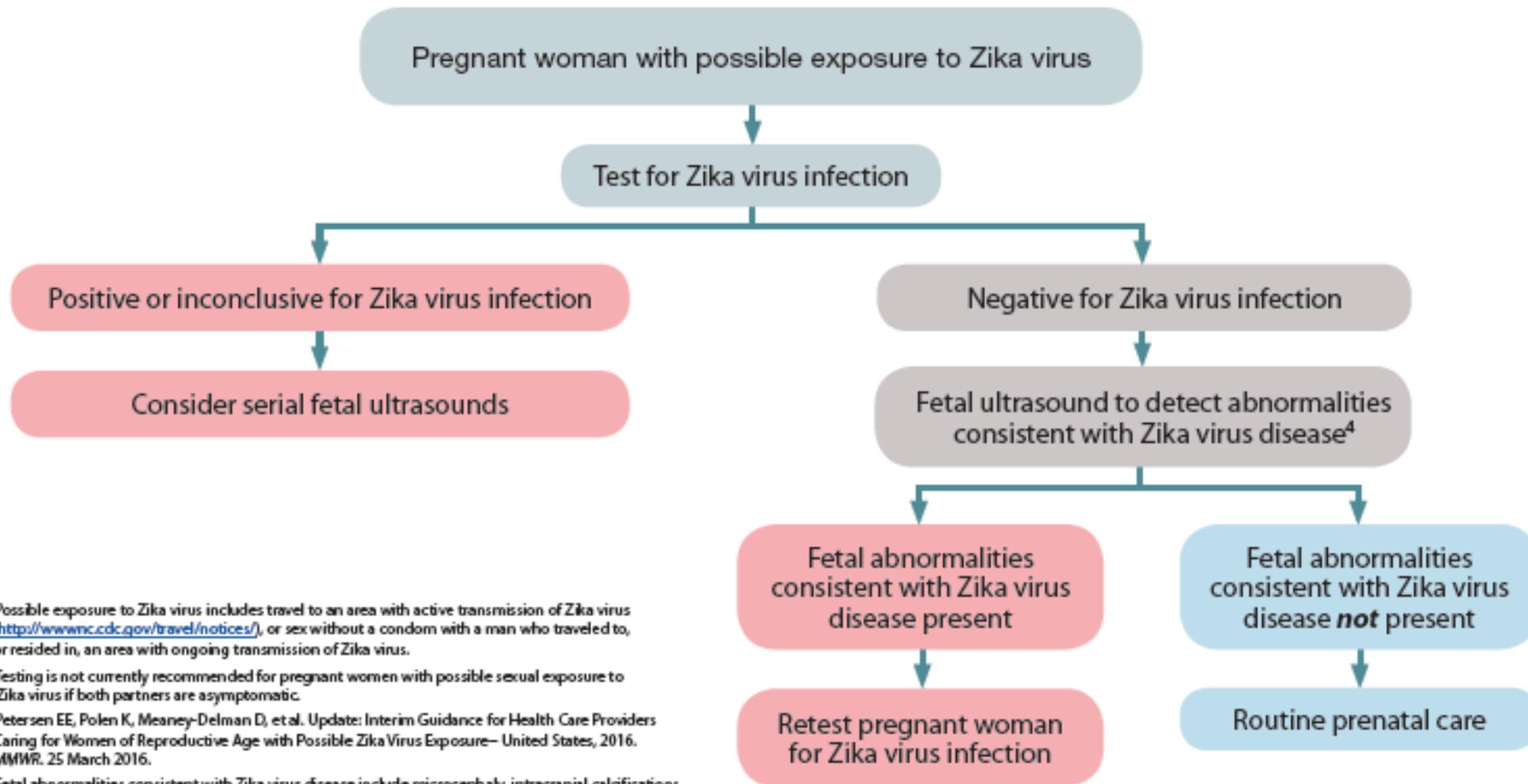
Who to test for Zika during pregnancy

- CDC does not recommend Zika virus testing for everyone.
- Pregnant women without symptoms should be tested if they have traveled to an area with Zika or live in an area with Zika.
- Pregnant women without symptoms should be tested if they have had sex without a condom with a man confirmed to have Zika virus infection.



CDC's Response to Zika
Updated Interim Guidance:

Testing Algorithm for a Pregnant Woman with Possible Exposure to Zika Virus^{1,2}, Not Residing in an Area with Active Zika Virus Transmission³



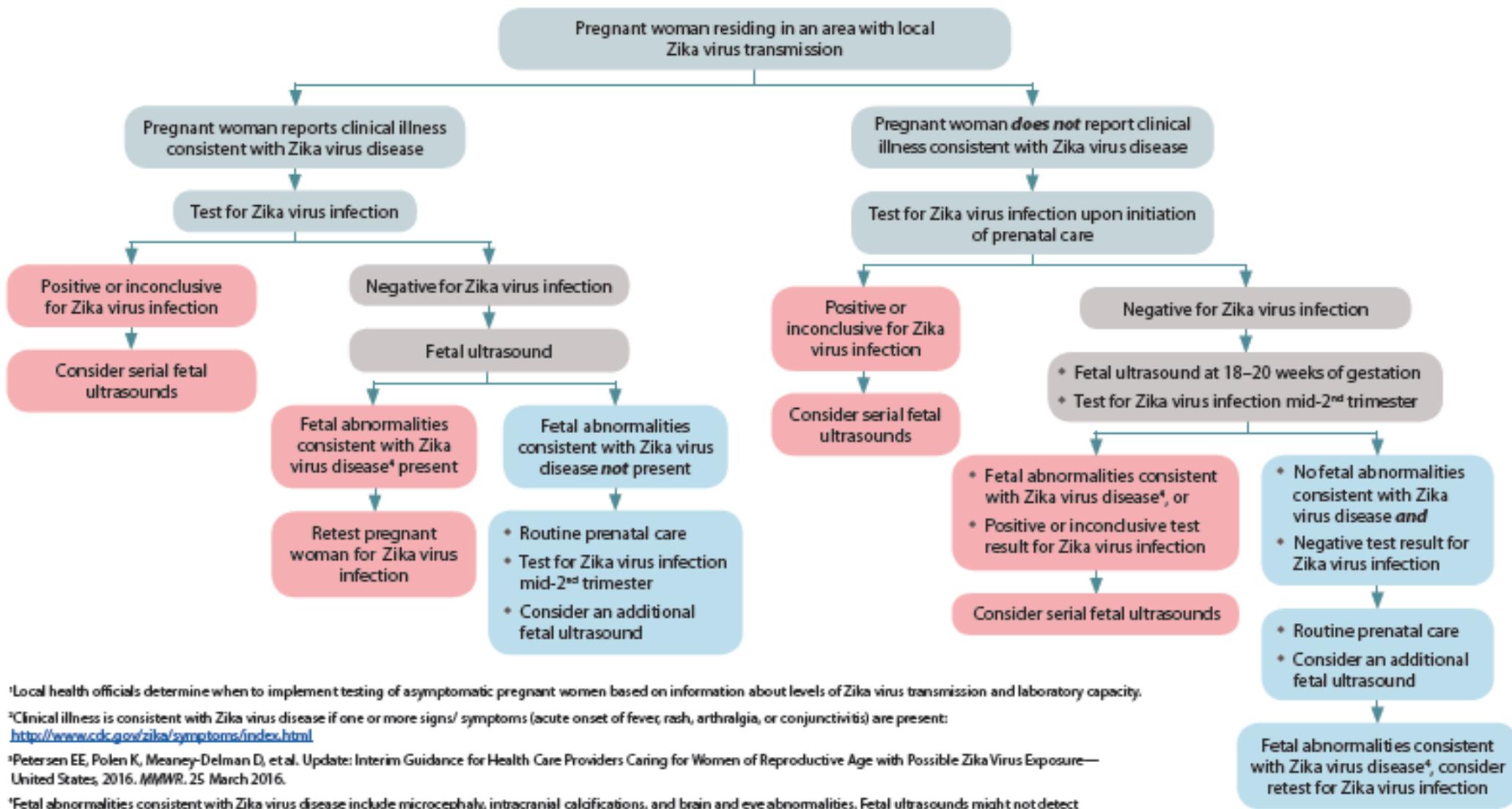
¹Possible exposure to Zika virus includes travel to an area with active transmission of Zika virus (<http://wwwnc.cdc.gov/travel/notices/>), or sex without a condom with a man who traveled to, or resided in, an area with ongoing transmission of Zika virus.

²Testing is not currently recommended for pregnant women with possible sexual exposure to Zika virus if both partners are asymptomatic.

³Petersen EE, Polen K, Meaney-Delman D, et al. Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure— United States, 2016. *MMWR*. 25 March 2016.

⁴Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.

Testing Algorithm for a Pregnant Woman Residing in an Area with Active Zika Virus Transmission¹, with or without Clinical Illness² Consistent with Zika Virus Disease³



¹Local health officials determine when to implement testing of asymptomatic pregnant women based on information about levels of Zika virus transmission and laboratory capacity.

²Clinical illness is consistent with Zika virus disease if one or more signs/ symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) are present: <https://www.cdc.gov/zika/symptoms/index.html>

³Petersen EE, Polen K, Meaney-Delman D, et al. Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure—United States, 2016. *MMWR*. 25 March 2016.

⁴Fetal abnormalities consistent with Zika virus disease include microcephaly, intracranial calcifications, and brain and eye abnormalities. Fetal ultrasounds might not detect abnormalities until late second or early third trimester of pregnancy.

Clinical management Positive or inconclusive Zika virus testing results during pregnancy

- Antepartum
 - Consider serial ultrasounds every 3-4 weeks.
 - Referral to maternal-fetal medicine specialist is recommended.
- Postpartum
 - Histopathologic examination of the placenta and umbilical cord.
 - Testing of frozen placental tissue and cord tissue for Zika virus RNA.
 - Testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies.



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

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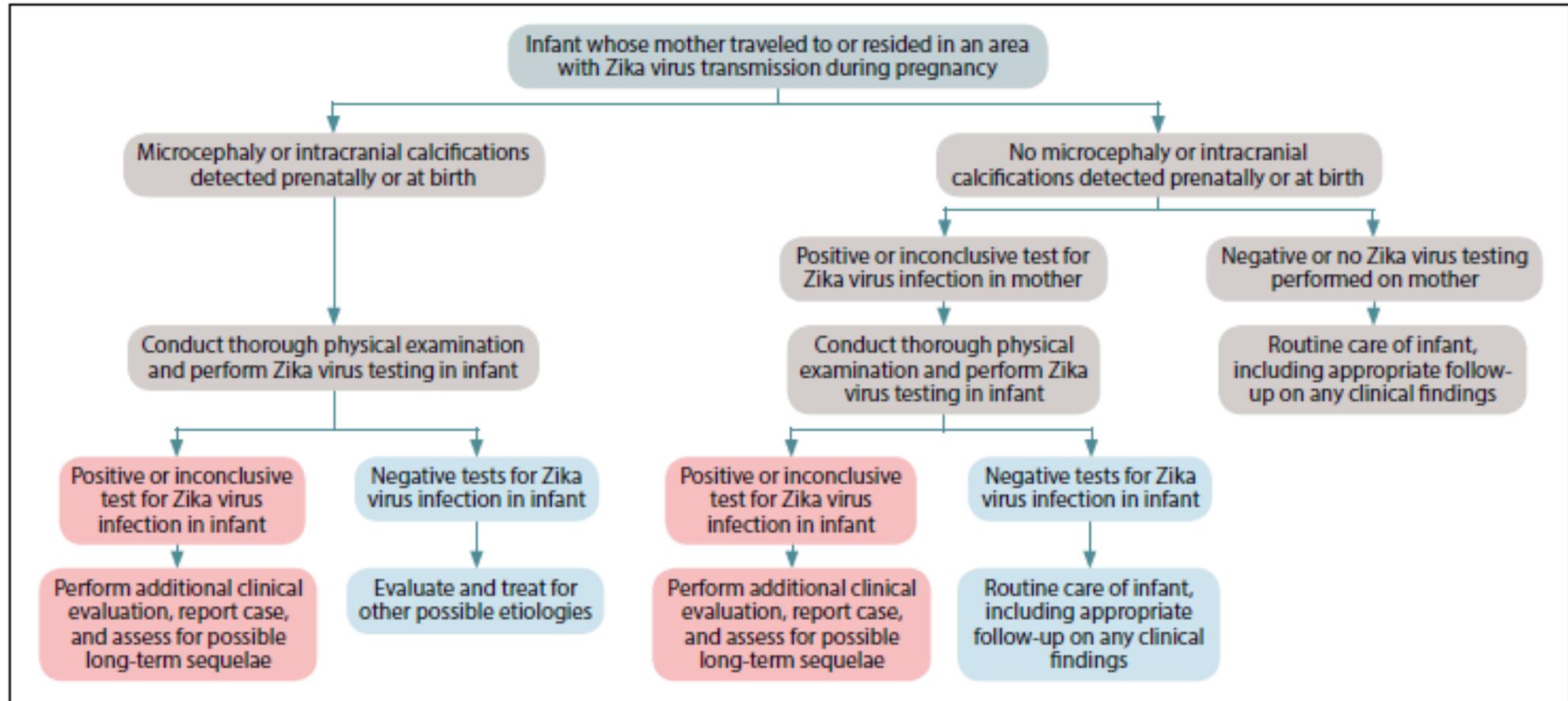
Infants with confirmed or possible Zika infection

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



Interim guidelines for the evaluation and testing of infants whose mothers traveled to or resided in an area with ongoing Zika virus transmission* 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

About sexual transmission

- A man with Zika virus can pass it to his female or male sex partners.
- Zika can be passed before, during, or after symptom onset.
- In known cases, the men had vaginal, anal, or oral (mouth-to-penis) sex without a condom.
- The virus can stay in semen longer than in blood, but we don't know exactly how long.



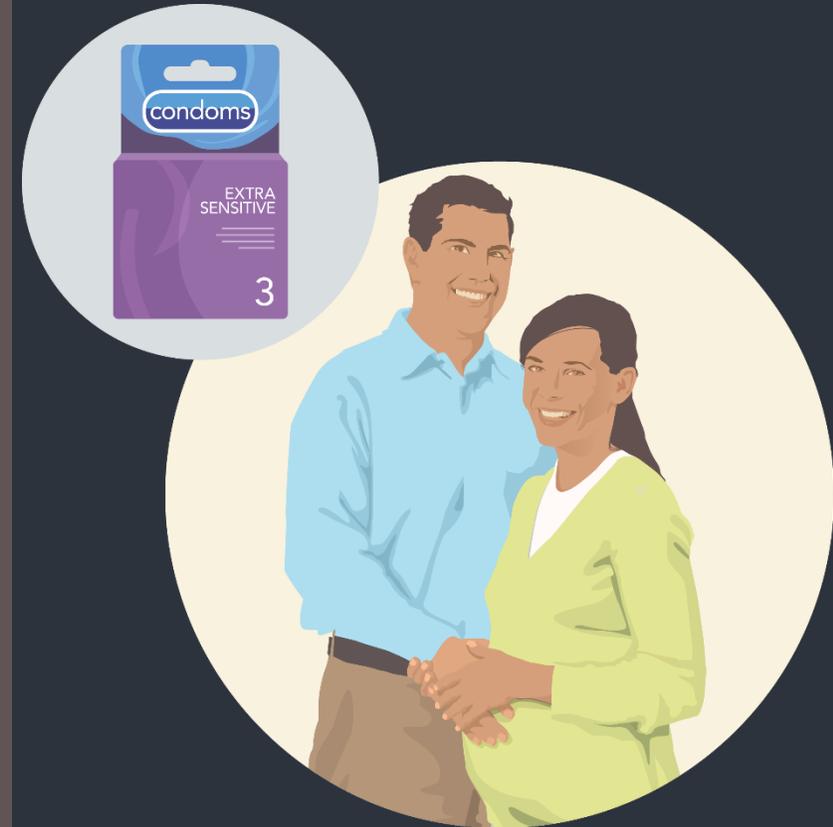
What we do not know about sexual transmission

- We do not know how often men with Zika who never develop symptoms can have the virus in their semen or if they can 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.
- If a woman with Zika can pass the virus to her sex partners.



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 male partner who lives in or recently traveled to an area with Zika should use a condom correctly from start to finish every time they have vaginal, anal, or oral (mouth-to-penis) sex throughout the pregnancy.



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

- For non-pregnant couples with a male partner who has recently traveled to an area with Zika
 - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for **at least 6 months** after symptoms begin.
 - If the male partner does not develop symptoms, the couple should consider using condoms or not having sex for **at least 8 weeks** after the man returns.



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

- For non-pregnant couples with a male partner who lives in an area with Zika
 - If the male partner has been diagnosed with Zika or has (or had) symptoms, the couple should consider using condoms or not having sex for **at least 6 months** after symptoms begin.
 - If the male partner does not develop symptoms, the couple should consider using condoms or not having sex as long as there is Zika in the area.



PRECONCEPTION GUIDANCE

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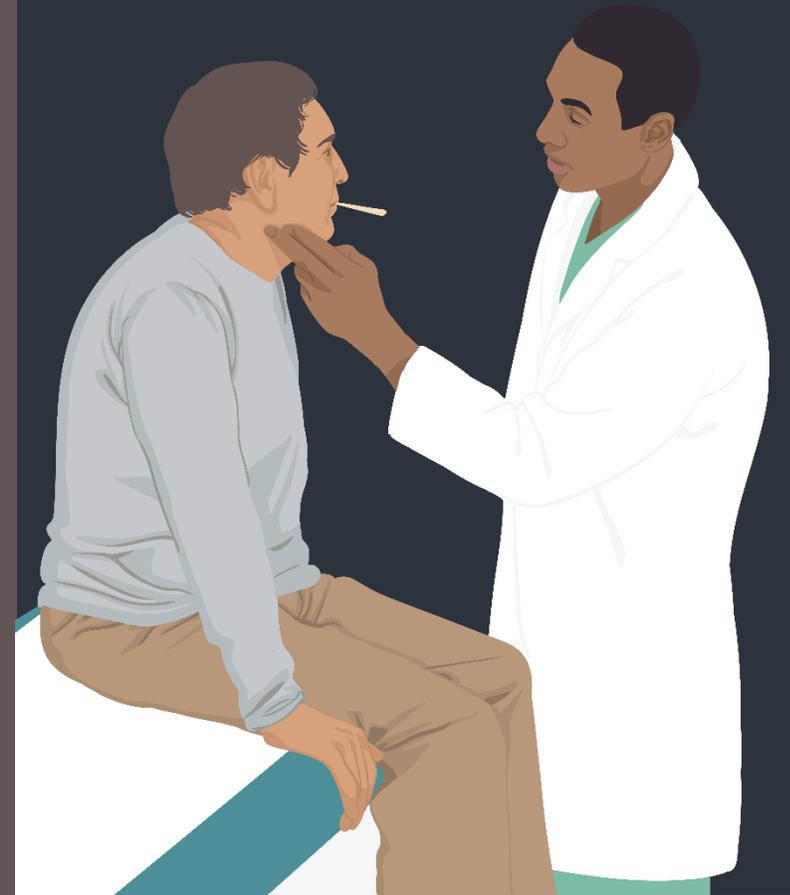
Couples interested in conceiving who DO NOT reside in an area with active Zika virus transmission

- For Women with possible exposure to Zika virus
 - Discuss signs and symptoms and potential adverse outcomes associated with Zika
 - If Zika virus disease diagnosed, wait at least 8 weeks after symptom onset to have sex and attempt conception.
 - If NO symptoms develop, wait at least 8 weeks after last date of exposure before having sex and attempting conception.



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, wait at least 6 months after symptom onset to have sex and attempt conception.
 - If NO symptoms develop, wait at least 8 weeks after exposure to have sex and attempt contraception.
 - 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

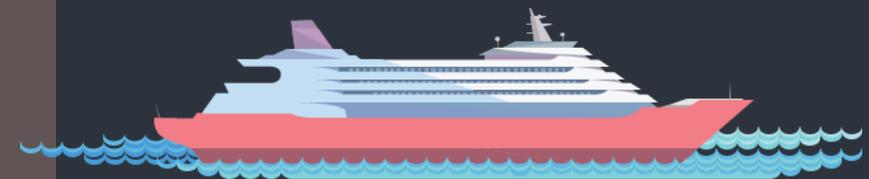


WHAT TO TELL PATIENTS ABOUT ZIKA

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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.



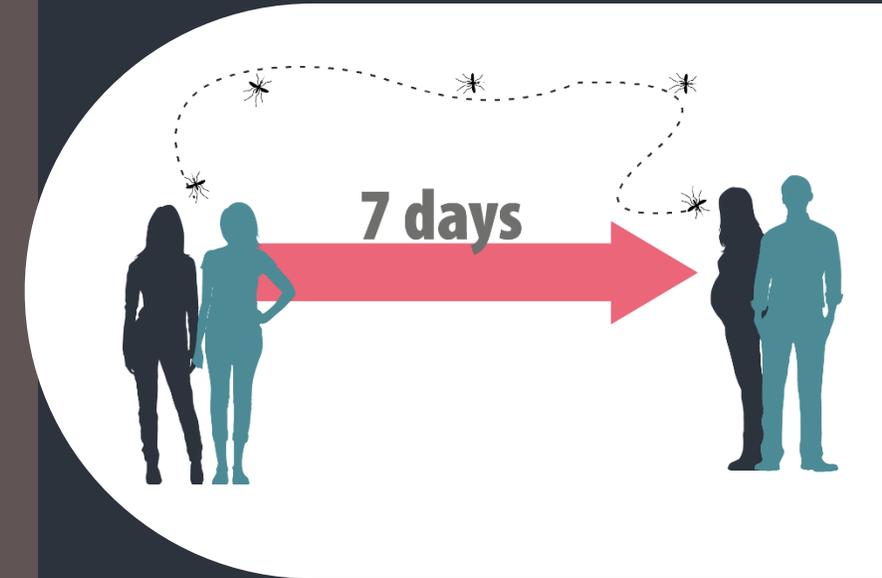
Treating patients who test positive

- 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.

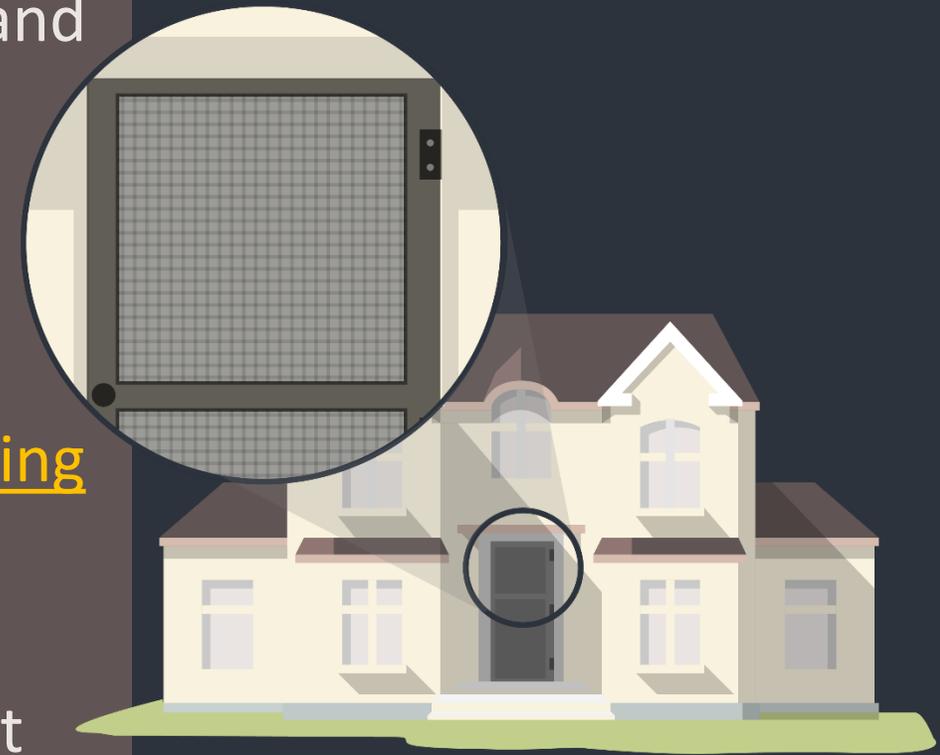


WHAT TO TELL PATIENTS ABOUT MOSQUITO BITE PROTECTION

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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>