



ZIKA VIRUS: INFORMATION FOR CLINICIANS

Updated September 10, 2019



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

These slides provide clinicians with information about:

- Zika epidemiology and clinical features
- Diagnosis and testing
- Reporting Zika cases
- Sexual transmission
- Preconception guidance
- Zika and pregnancy
- Evaluation and follow-up of infants with Zika infection
- Infection control
- What to tell patients



ZIKA EPIDEMIOLOGY AND CLINICAL FEATURES

Zika virus (Zika)

- Discovered in Uganda in 1947
- 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



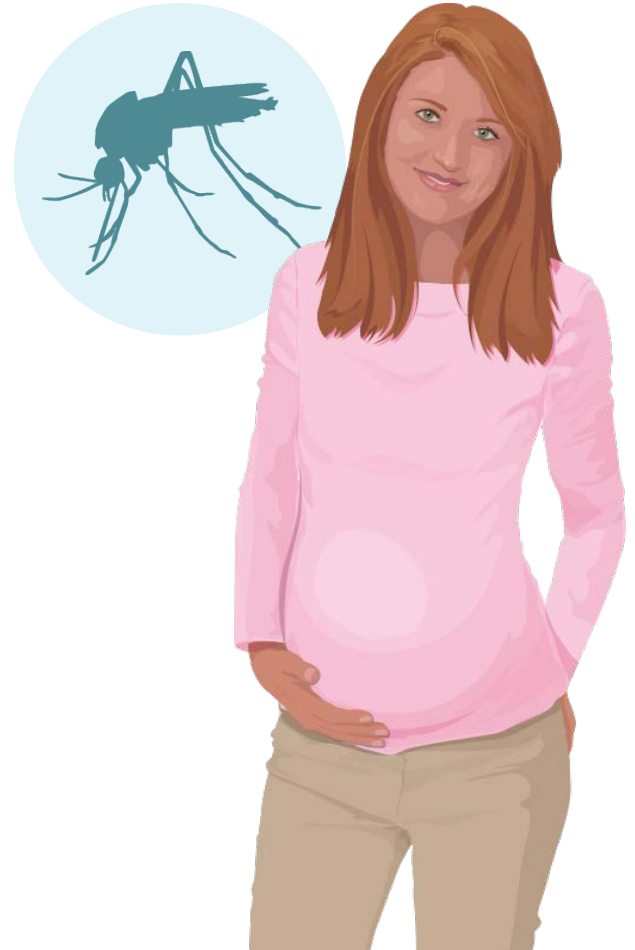
Aedes albopictus

Where has Zika virus been found?

- Before 2015, Zika outbreaks occurred in Africa, Southeast Asia, and the Pacific Islands
- A large outbreak occurred in the Americas in 2015 and 2016, which has since subsided
- No recent local transmission within the continental U.S.
- Zika is still potentially a risk internationally, particularly in areas of outbreaks
- For the latest on Zika transmission risk, visit <https://www.cdc.gov/zika/geo/index.html>

Transmission methods

- Bite from an infected mosquito
- Sexual transmission from an infected person to his or her partners
- Maternal-fetal
 - » Periconceptual
 - » Intrauterine
 - » Perinatal
- Potentially through breast milk
 - » Benefits of breastfeeding likely outweigh risks though



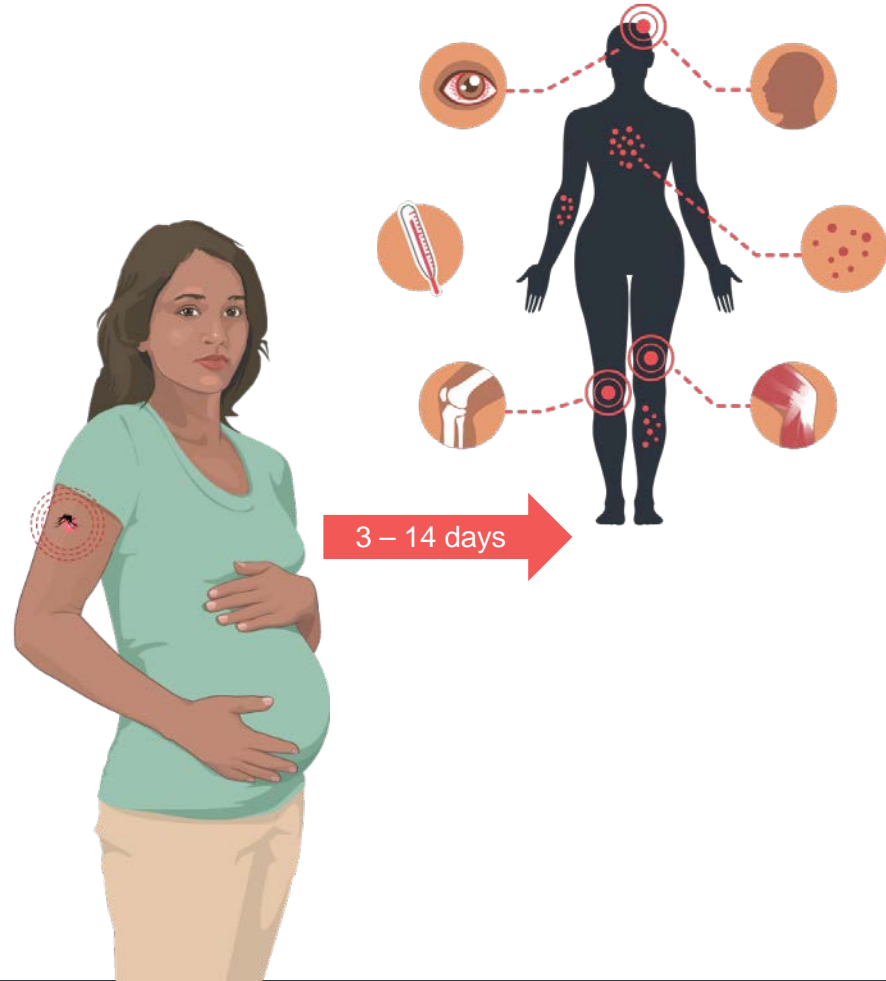
Transmission methods

- Potentially through blood transfusion
 - » Reported cases in Brazil
 - » No cases in U.S. to date
 - » FDA recommends screening blood
- Potentially by laboratory exposure
 - » Routes not clearly established



Zika incubation and viremia

- Incubation is 3–14 days
- 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 urine and semen longer than in blood



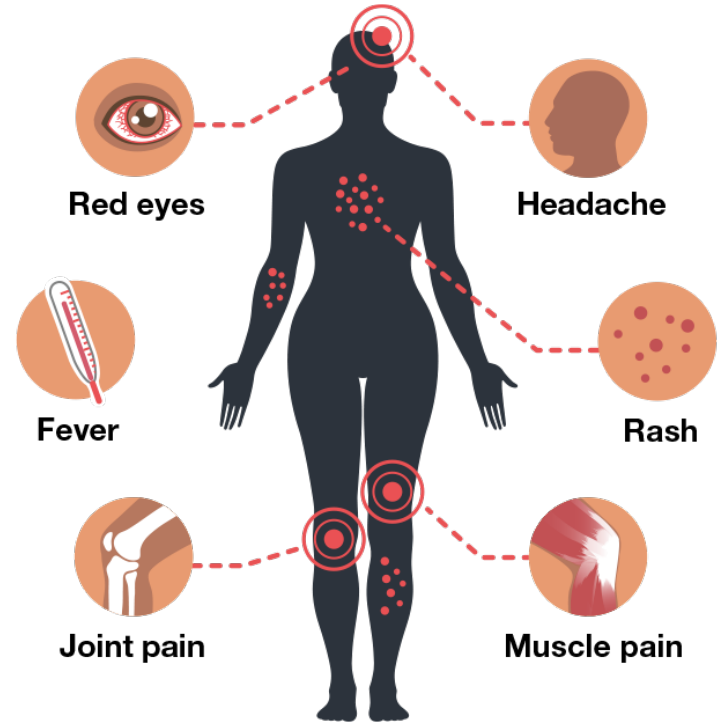
Clinical disease course and outcomes

- Many infections are asymptomatic
- Clinical illness is usually mild
- Symptoms last several days to a week
- Severe disease requiring hospitalization is uncommon
- Fatalities are rare
- Research suggests that Guillain-Barré syndrome (GBS) is strongly associated with Zika
 - » Only a small proportion of people with recent Zika infection get GBS



Common Zika symptoms

- Acute onset of fever
- Maculopapular rash
- Headache
- Conjunctivitis (red eyes)
- Muscle pain
- Joint pain



Reported clinical symptoms among confirmed Zika virus disease cases

Symptoms	N (n=31)	%
Macular or popular 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 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)

DIAGNOSIS AND TESTING FOR ZIKA

Zika and dengue virus infections can present similarly

- Zika and dengue virus infections can cause similar clinical presentations
 - » Fever, joint pain, rash, muscle pain, or headache may be caused by Zika or dengue
- Zika and dengue are found in similar areas throughout the world
- Zika and dengue are spread by the same mosquitoes
- Both viruses should be kept on the differential

Additional differential diagnosis

In addition to dengue, additional infections that may present similarly to Zika include:

- Adenovirus
- Chikungunya and other alphaviruses (e.g., Mayaro, Ross River, Barmah Forest, o'nyong-nyong, and sindbis viruses)
- Enterovirus
- Leptospirosis
- Malaria
- Measles
- Parvovirus
- Rickettsia
- Rubella
- (Group A) Streptococcus
- Many others!

Whom to test

- Dengue and Zika virus testing is recommended for:
 - » Patients with a clinically compatible illness who live in or recently traveled to an area where there is risk for infection with Zika and dengue viruses
 - This includes symptomatic pregnant women.
- Zika virus testing is recommended for:
 - » Symptomatic patients who had sex with someone who lives in or recently traveled to an area with Zika virus
 - » Asymptomatic pregnant women with ongoing possible Zika virus exposure (i.e., residence in or frequent travel to an area with risk of Zika)
 - » Pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus infection
- Zika testing is not routinely recommended, but may be considered, for:
 - » Asymptomatic pregnant women with recent possible but no ongoing exposure to Zika virus (i.e., travelers)

Whom not to test

- Zika virus testing is not recommended for:
 - » Non-pregnant asymptomatic persons
 - » Preconception screening
- Dengue virus testing is not recommended for:
 - » Individuals without a clinically compatible illness

Diagnostic tests available for Zika and dengue

- RNA nucleic acid amplification testing (NAAT)
 - » on serum and urine
 - » and possibly whole blood, cerebral spinal fluid, or amniotic fluid
- Serology assays (e.g., ELISA)
 - » to detect virus-specific IgM antibodies, which typically develop toward the end of the first week of illness
- Plaque reduction neutralization tests (PRNTs)
 - » to confirm presence of virus-specific neutralizing antibodies in serum samples

Symptomatic non-pregnant persons (with serum collected ≤ 7 days after symptom onset):

- Dengue and Zika virus NAAT should be performed on serum
 - » Other specimen types including plasma, whole blood, cerebrospinal fluid, or urine may be acceptable for some NAATs
- A positive NAAT result typically provides adequate evidence of infection
 - » Sometimes a repeat NAAT may be performed to confirm the initial result
- A negative NAAT does not rule out infection; dengue and Zika virus IgM antibody testing is then recommended
- If both dengue and Zika virus NAATs are negative, but either IgM antibody test is positive, confirmatory PRNTs can be performed if clinically or epidemiologically necessary

Symptomatic non-pregnant persons (with serum collected > 7 days after symptom onset):

- Dengue and Zika virus IgM antibody testing should be performed on serum specimens
- If either IgM antibody test is positive, confirmatory PRNTs can be performed if clinically or epidemiologically necessary

Symptomatic pregnant women (with recent possible exposure and available specimens within 12 weeks of symptom onset):

- The following diagnostic testing should be performed at the same time:
 - » Dengue and Zika virus NAAT and IgM antibody testing on a serum specimen, and
 - » Zika virus NAAT on a urine specimen
- A positive NAAT result on any specimen typically provides adequate evidence of recent infection
 - » If NAAT is only positive for Zika virus on a single specimen and IgM antibody testing is negative, the NAAT should be repeated on newly extracted RNA from the same specimen to rule out false-positive NAAT results
- If both dengue and Zika virus NAATs are negative, but either IgM antibody test is positive, confirmatory PRNTs should be performed

Asymptomatic pregnant women (with ongoing possible Zika virus exposure):

- Zika virus NAAT testing is recommended three times during pregnancy
 - » Once at the initial prenatal care visit
 - » Followed by two additional Zika virus NAAT tests performed at non-consecutive prenatal visits
- Zika virus IgM antibody testing is no longer routinely recommended
 - » IgM can persist for months after infection
 - » IgM results cannot reliably determine whether an infection occurred during the current pregnancy

Asymptomatic pregnant women (with recent possible exposure to Zika virus but no ongoing exposure):

- Zika virus testing may be considered
 - » Although not routinely recommended, testing may be considered on a case-by-case basis and in line with jurisdictional recommendations
 - » If Zika virus testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure

Asymptomatic pregnant women (with possible exposure and prenatal ultrasound findings consistent with congenital Zika syndrome):

- Zika virus NAAT and IgM testing should be performed on maternal serum and NAAT on maternal urine
- If amniocentesis is being performed already as part of clinical care, Zika virus NAAT testing of amniotic fluid should also be performed
 - » Results should be interpreted cautiously given the limitations of amniotic fluid testing
 - » It is unknown how sensitive or specific RNA NAAT testing of amniotic fluid is for congenital Zika virus infection
 - » Or what proportion of infants born after infection will have abnormalities
- Testing of placental and fetal tissues may also be considered

Testing of infants

- CDC recommends laboratory testing for
 - » All infants born to mothers with laboratory evidence of possible Zika virus infection during pregnancy
 - » Infants who have abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a mother with a possible exposure to Zika virus
- Specimens should be collected ideally within the first 2 days of life
 - » However, testing specimens collected within the first few weeks to months after birth may still be useful in the evaluation for possible congenital Zika virus infection, especially among infants born in areas without risk of Zika

REPORTING ZIKA CASES

Reporting cases

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



SEXUAL TRANSMISSION

About sexual transmission

- Zika can be passed through sex
 - » From a person with Zika infection before, during, and after their symptoms
 - » May also be passed by a person who never has symptoms
- Sexual exposure includes:
 - » sex without a condom (including vaginal, anal, and oral sex)
 - » sharing of sex toys
- There is evidence of sexual transmission of Zika from male-to-female, male-to-male, and female-to-male sex partners
 - » Female-to-female sexual transmission has not yet been reported but is biologically plausible



Zika in semen (and other fluids)

- Zika can remain in semen longer than in other body fluids (including vaginal fluids, urine, and blood)
- Current reports show the longest period from symptom onset to potential sexual transmission was between 32–41 days
- The longest reported period potentially infectious virus has been detected in semen was 69 days after symptom onset
- In the largest study to date, Zika virus RNA shedding declined during the 3 months after symptom onset
 - » At >90 days after illness onset, semen of $\leq 7\%$ of participants had detectable Zika virus RNA
 - » The estimated mean time to clearance of Zika virus RNA from semen was 54 days



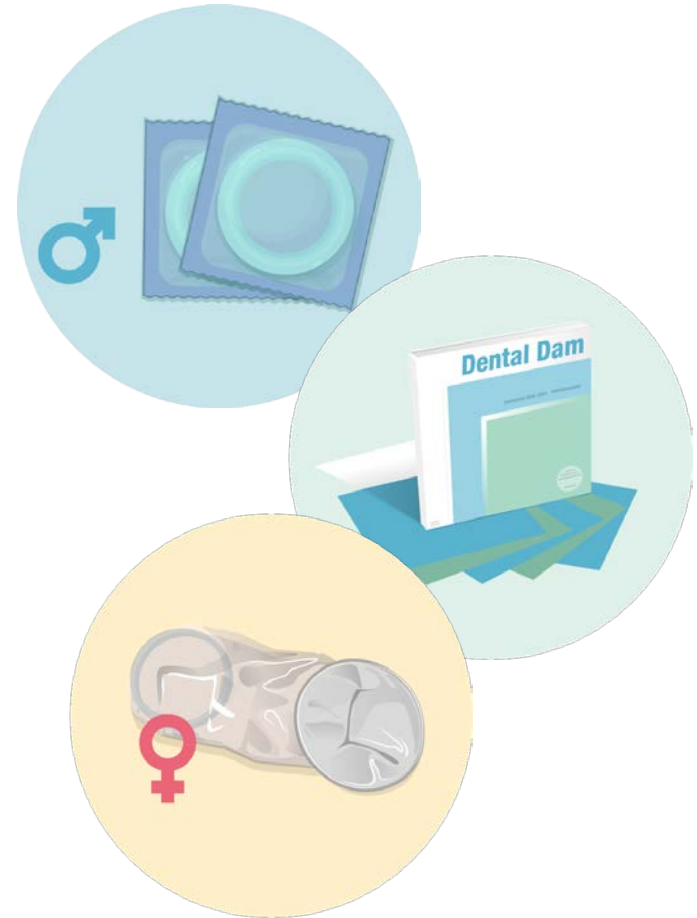
What we do not know about sexual transmission

- CDC and other public health partners continue research that may help us find out:
 - » How common it is for Zika to be passed during sex
 - » If Zika passed to a pregnant woman during sex has a different risk for birth defects than Zika transmitted by a mosquito bite



Preventing or reducing the chance of sexual transmission

- Not having sex eliminates the risk of getting Zika from sex
- Condoms can reduce the chance of getting Zika from sex
 - » Dental dams (latex or polyurethane sheets) may also be used for certain types of oral sex (mouth to vagina or mouth to anus)
 - » Not sharing sex toys can also reduce the risk of spreading Zika to sex partners
- Pregnant couples with a partner who lives in or recently traveled to an area with risk of Zika should use condoms correctly every time they have sex (or not have sex) during the duration of pregnancy



Preventing or reducing the chance of sexual transmission

- Non-pregnant couples with a partner who traveled to an area with risk of Zika can use condoms/protection or not have sex
 - » If traveler is female: For at least 2 months after travel or symptom onset
 - » If traveler is male: For at least 3 months after travel or symptom onset
 - This longer period for males is because Zika virus can persist longer in semen than in other body fluids (including vaginal fluids and blood)
- People living in an area with risk of Zika can use condoms or not have sex if they are concerned about sexually transmitting Zika



PRECONCEPTION GUIDANCE

Asymptomatic couples interested in conceiving

- Testing is NOT recommended for asymptomatic couples in which one or both partners has had possible exposure to Zika virus:
 - » No test is 100% accurate
 - » A negative blood test or antibody test could be falsely reassuring
 - » We have limited understanding of Zika virus shedding in genital secretions or how to interpret test results of genital secretions
 - Zika shedding may be intermittent, in which case a person could test negative at one point but still carry the virus and shed it again in the future



Couples interested in conceiving who live in or frequently travel to an area with a Zika outbreak or other areas at risk of Zika ([Map](#))

- Women and men interested in conceiving should talk with their healthcare providers
- Factors that may aid in decision-making:
 - » Plans for having children
 - » 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



Couples interested in conceiving who DO NOT live in an area with risk of Zika

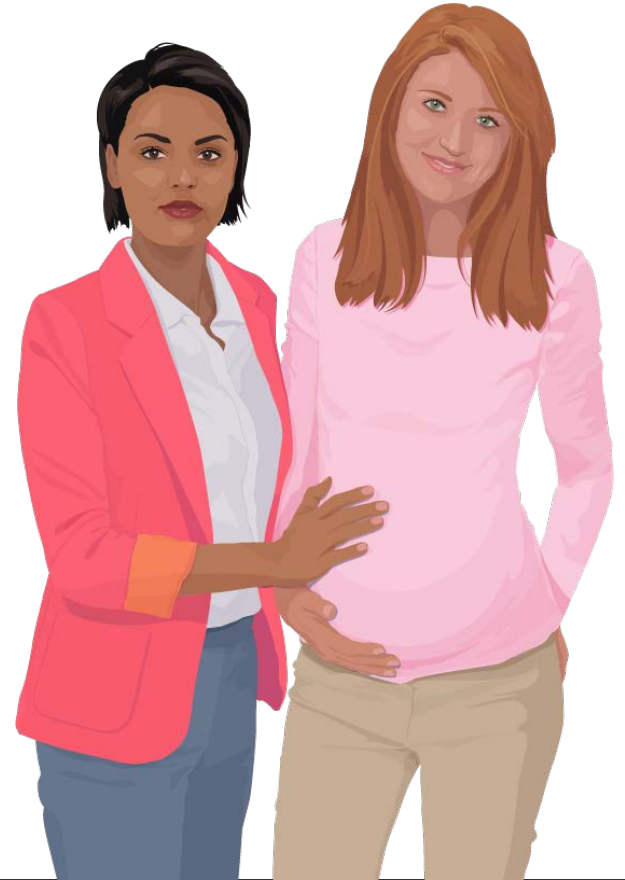
- For couples with exposure to an area with a Zika outbreak or other areas with risk of Zika ([Map](#))
 - » Discuss signs and symptoms of infection and potential adverse outcomes associated with Zika
 - » If only female partner was exposed, wait at least 2 months after last possible exposure to Zika or symptom onset before trying to conceive
 - » If male partner was also exposed, wait at least 3 months after his last possible exposure or symptom onset before trying to conceive
 - » During that time, use condoms every time during sex or do not have sex



ZIKA AND PREGNANCY

Zika and pregnancy

- Knowledge about Zika virus is increasing rapidly and researchers continue to work to better understand the extent of Zika virus' impact on mothers, infants, and children
- No evidence that previous infection will affect future pregnancies



Clinical management of a pregnant woman with laboratory evidence of possible Zika virus infection

- Consider serial fetal ultrasounds (every 3–4 weeks) to assess fetal anatomy, particularly fetal neuroanatomy, and to monitor growth
- Given the length of time for the detection of prenatal microcephaly, prenatal ultrasounds should include detailed fetal anatomy, particularly neuroanatomy, to detect brain or structural abnormalities that might occur before microcephaly

EVALUATION AND FOLLOW UP

OF INFANTS WITH CONFIRMED OR POSSIBLE ZIKA VIRUS
INFECTION

Congenital Zika Syndrome (CZS)

- Zika virus infection during pregnancy can lead to **Congenital Zika Syndrome (CZS)**, a distinct pattern of birth defects and disabilities
- These five features are rarely seen with other infections or are unique to CZS:
 - » **Severe microcephaly** (small head size) resulting in a partially collapsed skull
 - » **Decreased brain tissue** with brain damage (as indicated by a specific pattern of calcium deposits)
 - » **Damage to the back of the eye** with a specific pattern of scarring and increased pigment
 - » **Limited range of joint motion**, such as clubfoot
 - » **Too much muscle tone** restricting body movement soon after birth



Case definition of microcephaly

Definite congenital microcephaly for live births

- Head circumference (HC) at birth 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 2 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



Case definition of *possible* 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



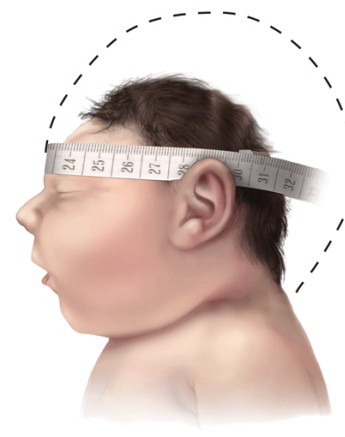
Measuring head circumference for microcephaly



Baby with typical head size



Baby with microcephaly



Baby with severe microcephaly

- Use a measuring tape that cannot be stretched
- Securely wrap 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 within 24 hours after birth.
 - » Commonly-used birth head circumference reference charts by age and sex based on measurements taken before 24 hours of age

Not every infection will lead to birth defects

- It is important to remember that even in places with Zika, women are delivering infants that appear to be healthy
- Many questions remain about the timing, absolute risk, and the spectrum of outcomes associated with Zika virus infection during pregnancy
- More lab testing and other studies are planned to learn more about the risks of Zika virus infection during pregnancy



Categories of infants born to mothers with possible exposure to Zika

1. Infants with birth defects consistent with congenital Zika syndrome born to mothers with possible Zika virus exposure during pregnancy
2. Infants without birth defects consistent with congenital Zika syndrome, but who were born to mothers with laboratory evidence of possible Zika virus infection during pregnancy
3. Infants without birth defects consistent with congenital Zika syndrome born to mothers with possible congenital Zika virus exposure during pregnancy but without laboratory evidence of Zika virus infection



Infants born to mothers with possible exposure to Zika

- All infants born to mothers with possible exposure to Zika virus during pregnancy should receive a standard evaluation at birth and at each well-child visit
 - » Comprehensive physical exam (including growth parameters)
 - » Age-appropriate vision screening
 - » Developmental screening and monitoring
 - » Standard newborn hearing screening (auditory brainstem response (ABR) preferred)



Infants born to mothers with laboratory evidence of Zika during pregnancy

- In addition to a standard evaluation, infants with clinical findings consistent with congenital Zika should receive:
 - » Zika virus NAAT and IgM testing
 - » Head ultrasound by 1 month
 - » Comprehensive ophthalmologic exam by 1 month
 - » ABR by 1 month if newborn hearing screen was performed by otoacoustic emissions method



Infants with birth defects consistent with Congenital Zika Syndrome (CZS)

- In addition to a standard evaluation, infants with clinical findings consistent with congenital Zika should receive:
 - » Zika virus NAAT and IgM testing
 - » Head ultrasound by 1 month
 - » Comprehensive ophthalmologic exam by 1 month
 - » ABR by 1 month if newborn hearing screen was performed by otoacoustic emissions method
 - » Evaluation for other causes of congenital anomalies

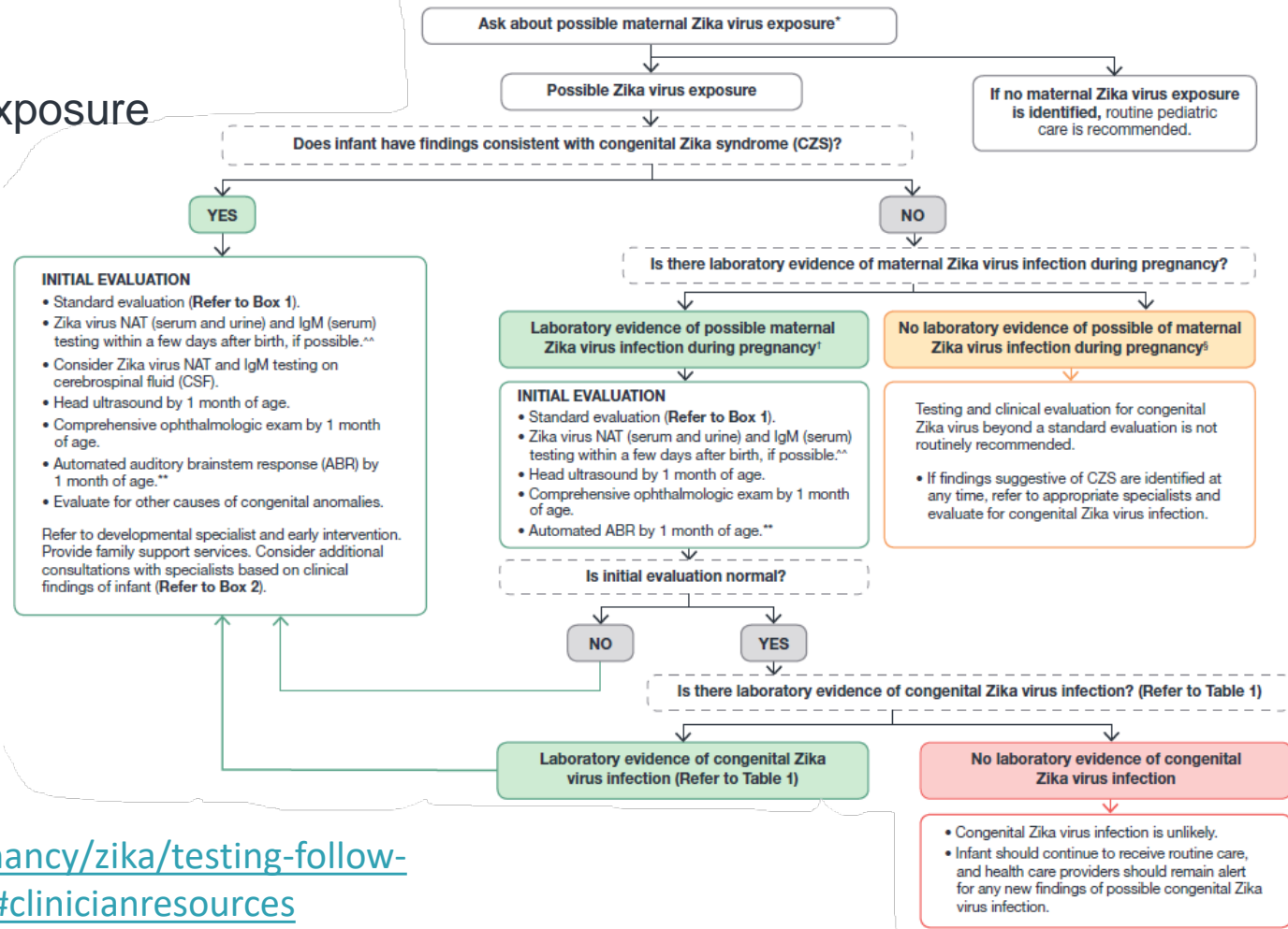


Infant testing

- Testing is recommended for
 - » Infants with birth defects consistent with Congenital Zika Syndrome born to mothers with possible Zika virus exposure during pregnancy (regardless of the mother's Zika virus testing results)
 - » Infants without birth defects consistent with congenital Zika syndrome who were born to mothers with laboratory evidence of possible Zika virus infection during pregnancy
- For infant testing, concurrent Zika virus RNA NAAT of serum and urine and Zika virus IgM testing of serum should be performed within a few days after birth, if possible



Algorithm: Possible maternal Zika virus exposure



<https://www.cdc.gov/pregnancy/zika/testing-follow-up/evaluation-testing.html#clinicianresources>

Recommended consultation for infants with features of CZS or lab evidence of congenital Zika virus infection

- Consultation with
 - » **Infectious disease specialist** - diagnostic evaluation of other congenital infections
 - » **Neurologist** - by age 1 month for comprehensive neurologic examination and consideration for other evaluations
 - » **Ophthalmologist** – by age 1 month for comprehensive eye exam and evaluation for possible cortical visual impairment
 - » **Clinical geneticist**- evaluate for other causes of microcephaly or other anomalies if present
 - » **Early intervention and developmental specialists**
 - » **Family and supportive services**



Additional possible consultations based on clinical findings

- Consider consultation with
 - » Endocrinologist for evaluation of hypothalamic or pituitary dysfunction and consideration for thyroid testing
 - » Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist for evaluation for dysphagia and management of feeding issues
 - » Orthopedist, physiatrist, and physical therapist for the management of hypertonia, club foot, or arthrogrypotic-like conditions
 - » Pulmonologist or otolaryngologist for concerns about aspiration



INFECTION CONTROL IN HEALTHCARE SETTINGS

Infection control

- Standard Precautions should be used
 - » Body fluids (including blood, vaginal secretions, and semen) have been implicated in transmission of Zika virus
 - » Percutaneous exposure or exposure of non-intact skin or mucous membranes to blood, body fluids, secretions, or excretions should be evaluated
- Pregnant healthcare personnel can care for patients with Zika using Standard Precautions
 - » However, facility managers and supervisors should exercise judgement in accommodating personnel concerned about potential exposure



Labor and delivery settings

- Assess the likelihood of the presence of body fluids or other infectious material
 - » Based on the condition of the patient, the type of anticipated contact, and the nature of the procedure or activity that is being performed
- Apply practices and personal protective equipment to prevent exposure as indicated



WHAT TO TELL PATIENTS ABOUT ZIKA

Travel for pregnant women

- Pregnant women should not travel to areas with current Zika outbreaks ([Map](#))
 - » Zika infection during pregnancy can cause serious birth defects
- Before travel to other areas with risk of Zika ([Map](#)), pregnant women should talk to a healthcare provider and carefully consider risks and possible consequences
- If pregnant women must travel to areas with risk of Zika, they should protect themselves from mosquito bites and sexual transmission during and after travel



Treating patients who test positive

- There is no specific vaccine or medicine for Zika
- Treat the symptoms of Zika
 - » Rest
 - » Drink fluids to prevent dehydration
 - » Take acetaminophen to reduce fever and pain
 - » Avoid aspirin and NSAIDs until dengue can be ruled out to reduce risk of bleeding



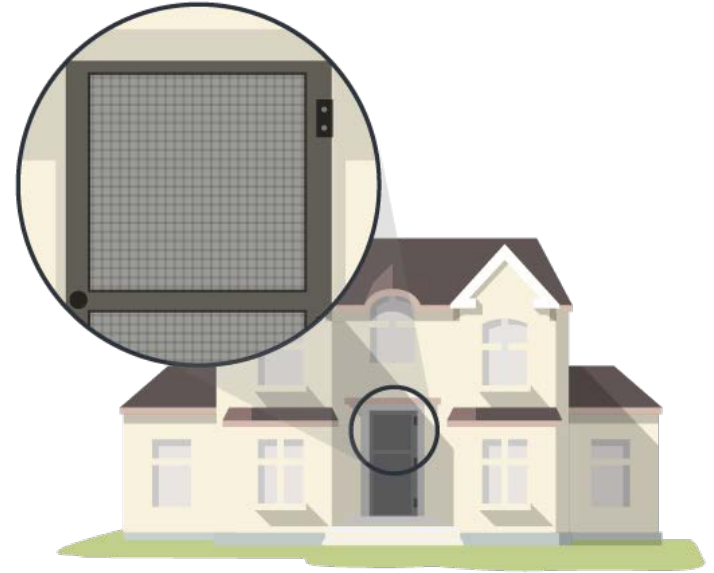
Patients who have Zika

- 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



Preventing Zika: Mosquito bite prevention

- 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
- Sleep under a mosquito bed net if air conditioned or screened rooms are not available, or if sleeping outdoors



Preventing Zika: Mosquito bite prevention

- Use Environmental Protection Agency (EPA)-registered insect repellents with one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone
- 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



Preventing Zika: [Mosquito bite prevention](#)

- 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
- Do not apply insect repellent onto a child's hands, eyes, mouth, cuts, or irritated skin



Additional resources

- [Zika virus homepage](#)
- [For Healthcare Providers](#)
- [Caring for Infants Tools](#)