



Information for Clinicians





OBJECTIVES

- Describe the epidemiology, clinical manifestations, management, and prevention of Zika virus disease.
- Discuss diagnostic testing for Zika virus infection.
- Articulate the importance of early recognition and reporting of cases.



OBJECTIVES

- Review the latest recommendations for pregnant women and others with possible Zika virus exposure.
- Discuss evaluation of infants with microcephaly, intracranial calcifications, and other abnormalities linked to maternal Zika virus infection.



ZIKA VIRUS

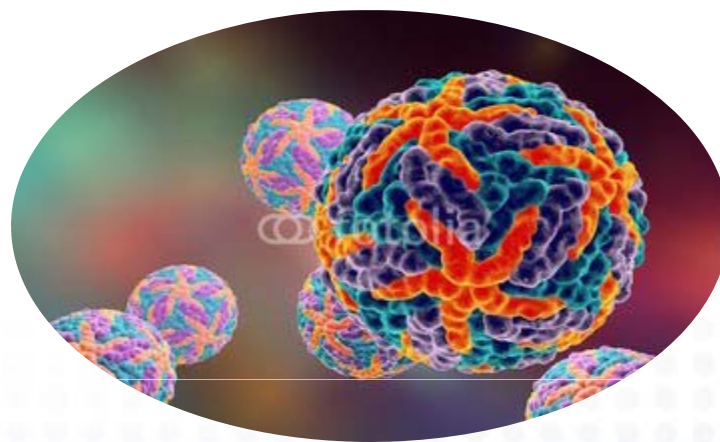
Information for Clinicians





Zika Virus

- Single stranded RNA Virus
- Genus *Flavivirus*, Family *Flaviviridae*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes (Stegomyia) species* mosquitoes



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Zika Virus Vectors: *Aedes* Mosquitoes



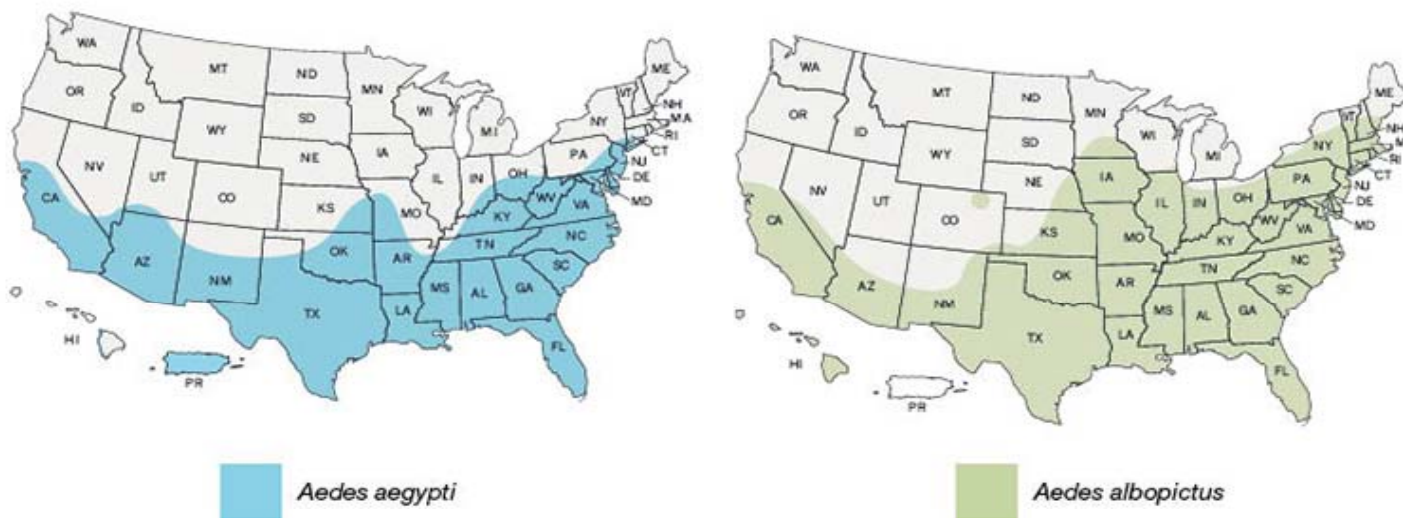
- *Aedes* species mosquitoes
 - *Ae aegypti* more efficient vectors for humans
 - *Ae albopictus*
- These mosquitoes can transmit dengue and chikungunya viruses.
- Species lays eggs in domestic water-holding containers.
- Typically live in and around households.
- Known to be aggressive daytime biters, but can also bite at night.



ZIKA

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Aedes aegypti and *Aedes albopictus* Mosquitoes: Geographic Distribution in the United States



Aedes aegypti

Aedes albopictus

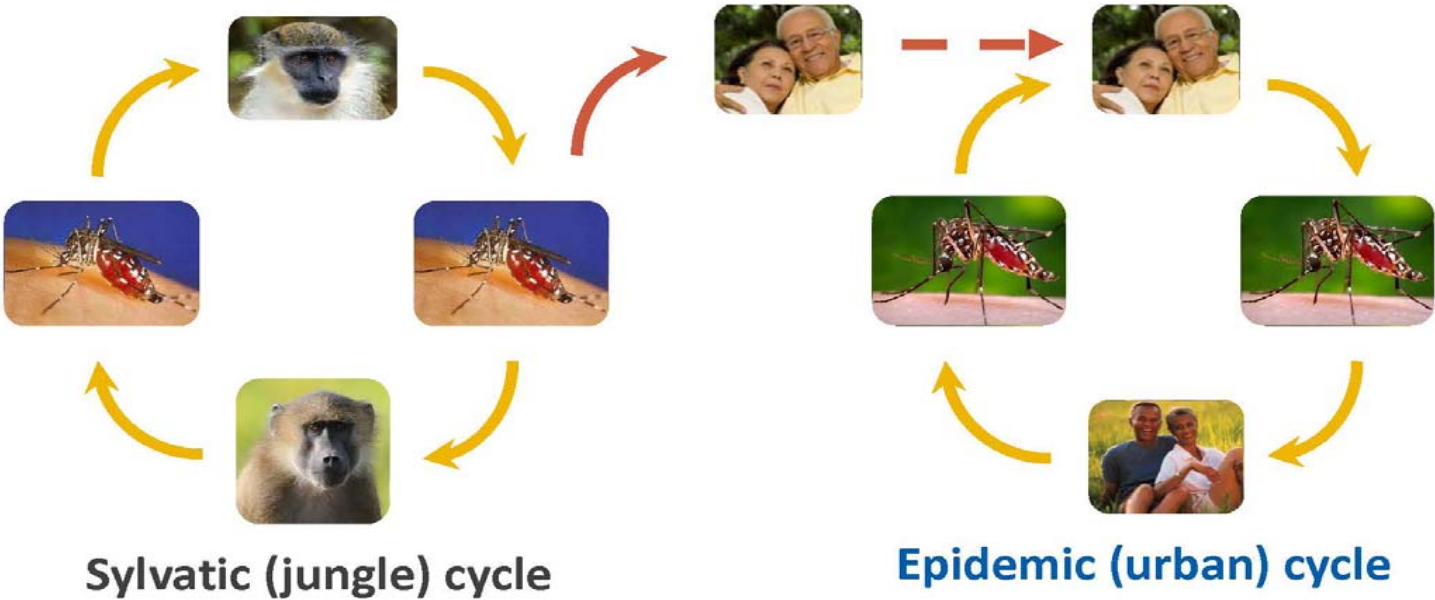
Currently in Alabama, *Ae albopictus* is found throughout the state, *Ae aegypti* has not been identified in over 25 years. Research suggests that *Ae albopictus* out-competed and displaced *Ae aegypti* in the late 1980s.



ZIKA

VIRUS

Zika Virus Transmission Cycles





Other Modes of Transmission

- Maternal-fetal
 - Intrauterine
 - Perinatal

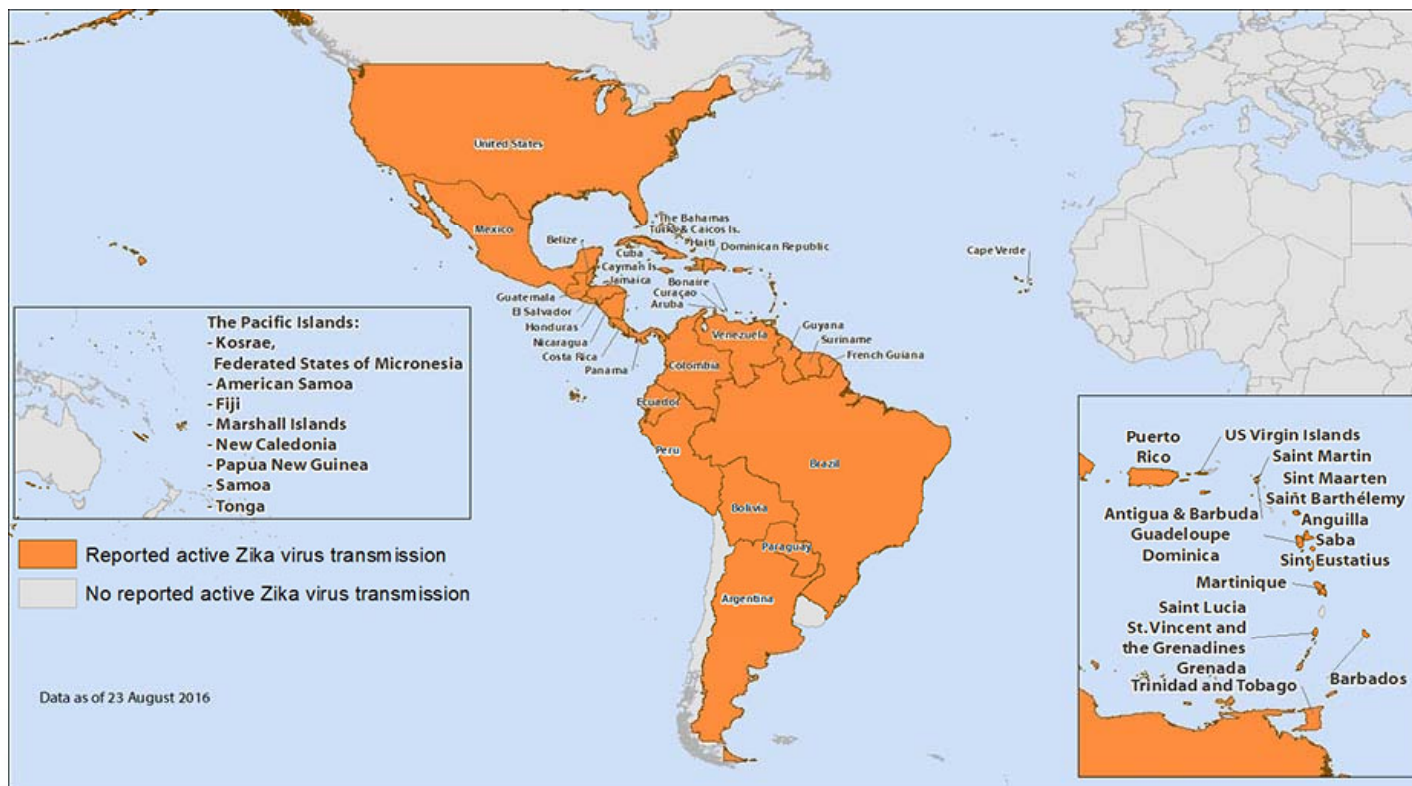
- Other
 - Sexual
 - Blood transfusion
 - Laboratory exposure

- Theoretical
 - Organ or tissue transplantation
 - Breast milk





Countries and Territories with Active Zika Virus Transmission





Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013–2014, more than 28,000 suspected cases reported from French Polynesia*

*<http://ecdc.europa.eu/en/publications/Publications/Zika-virus-French-Polynesia-rapid-risk-assessment.pdf>





Zika Virus in the Outbreaks in the Americas

- Before 2007, at least 14 confirmed cases of human Zika virus had been documented, although other cases were likely to have occurred but were not identified because the symptoms of the virus are similar to other diseases.
- In May 2015, the first locally-acquired cases in the Americas were reported in Brazil.
- The virus is likely to spread to other countries, because the mosquitoes that spread Zika are found throughout the world.





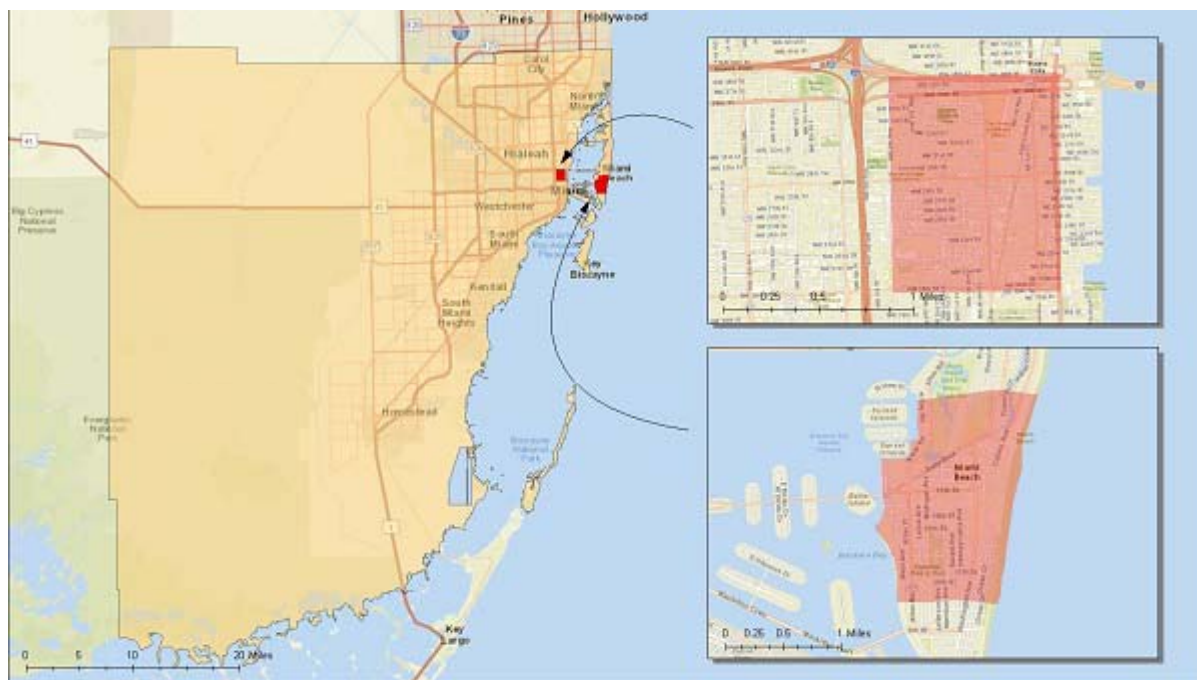
Zika Virus in the Outbreaks in the Americas

- Currently, outbreaks are occurring in many countries or territories in the Americas, including the Commonwealth of Puerto Rico and the U.S. Virgin Islands.
- Local transmission in the continental United States was reported on June 29 in Florida.





Local Map of Florida Zika-Affected Area





Zika Virus in the Continental United States

- On August 1, 2016, the Governor of Florida announced that the Florida Department of Public Health identified that 14 people in the state had been infected with locally transmitted Zika virus.
- As of August 15, 2016, Florida reported 30 locally transmitted cases
- As of August 17, 2016, U.S. states have reported a total of 2,245 (529 in pregnant women) travel-associated cases to CDC. Additionally, U.S. territories have reported 35 travel-associated and 8,000 locally-acquired cases (691 in pregnant women).





Zika Virus Incidence and Attack Rates: Serosurvey on Yap Island, 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)
Duffy M. N Engl J Med 2009





Reported Clinical Symptoms Among Confirmed Zika Virus Disease Cases on Yap Island, 2007

Symptoms	Number of cases (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%

Duffy M. N Engl J Med 2009
Yap Island, 2007





Zika Virus Clinical Disease Course and Outcomes

- Clinical illness is usually mild.
- Only 1 out of 5 people realize they have the disease.
- Symptoms last several days to a week.
- Severe disease requiring hospitalization is uncommon.
- Fatalities are rare.





Zika Virus Clinical Disease Course and Outcomes

- Guillain-Barré syndrome (GBS) has been reported in patients following suspected and confirmed Zika virus infection.
- As of August 17, a total of 32 confirmed GBS cases have been in the U.S. and U.S. Territories combined.





Zika Virus and Gullian-Barré Syndrome (GBS)

- The Brazil Ministry of Health reported an increased number of people who have been infected with Zika virus who also have Guillain-Barré syndrome (GBS). Zika has now been linked to GBS.
- GBS is an uncommon sickness of the nervous system in which a person's own immune system damages the nerve cells, causing muscle weakness, and sometimes, paralysis.





Zika Virus and Gullian-Barré Syndrome (GBS)

- GBS symptoms include weakness of the arms and legs that is usually the same on both sides of the body.
- These symptoms can last a few weeks or several months. Although most people fully recover from GBS, some people have permanent damage, and in 1 out of 20 cases people have died.





Distinguishing Zika from Dengue and Chikungunya

- Dengue and chikungunya viruses are transmitted by the same mosquitoes with similar ecology.
- Dengue and chikungunya can circulate in the same area and rarely cause coinfections.
- The diseases have similar clinical features.
- Important to rule out dengue and chikungunya, as proper clinical management can improve outcome.*

*WHO dengue clinical management guidelines:
http://whqlibdoc.who.int/publications/2009/9789241547871_eng.pdf





Clinical Features: Zika Virus Compared to Dengue and Chikungunya

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



Diagnostic Testing for Zika Virus

- Reverse transcriptase-polymerase chain reaction (rRT-PCR) for viral RNA in serum and urine collected ≤ 14 days after illness onset
- MAC-ELISA IgM testing on all **Negative** rRT-PCR
- MAC-ELISA testing when more than 2 weeks (> 14 days) post symptom onset or for asymptomatic pregnant women since last possible exposure





Diagnostic Testing for Zika Virus

- Plaque reduction neutralization test (PRNT) in virus-specific neutralizing antibodies in paired sera
- Immunohistochemical (IHC) staining for viral antigens or rRT-PCR on fixed tissues





Zika Patient Information Fact Sheet



Your health care provider has evaluated you and consulted with the Alabama Department of Public Health (ADPH). You are being tested for the mosquito-borne diseases Zika, Dengue, and Chikungunya because of your exposure history.

An exposure history means you have traveled recently to/from another country or an area within the United States with Zika virus transmission and developed symptoms within two weeks of travel, or you are pregnant with a travel history to a Zika-affected country, or you are pregnant and became symptomatic after a partner traveled to a Zika-affected area. Your health care provider will contact you with the results of the test. Please contact your health care provider with any questions you may have.

While waiting for your test results, please protect others by protecting yourself from additional mosquito bites. Please consistently use an EPA-approved insect repellent. Insect repellents containing DEET, IR3535, picaridin, some oil of lemon eucalyptus and para-methane-diol containing products provide long-lasting protection. You are also asked to wear long sleeves and pants to reduce the likelihood of bites.

Aspirin and other nonsteroidal anti-inflammatory medications (NSAIDs) should be avoided until Dengue virus infection can be ruled out. Medications which are NSAIDs are marketed under many product names including Advil, Motrin, Aleve and other generic names. If you have questions about products containing NSAIDs, please consult your pharmacist

You are being tested because of the following reason:

- You have an exposure history and are symptomatic (sick); or
- You are pregnant and have recently traveled to a Zika-affected area; or
- You are pregnant and have had unprotected sex with a partner who lives in or traveled to an area with active Zika transmission. (Please begin using barrier methods immediately or abstain from sex for the duration of pregnancy for the protection of your unborn child. The CDC recommends the use of barrier protection such as condoms and dental dams.)

Note: Zika can be passed through sex, even if the infected person does not have symptoms. Sex includes vaginal, anal, and oral sex, and the sharing of sex toys. Couples with a partner who lives in or has traveled to an area with active Zika transmission should use condoms (or other barrier methods to protect against infection). For couples in which the partner has symptoms during or on return from an area with active Zika transmission;

- *If partner traveling was female, use barrier methods or abstain from sex for at least 8 weeks after returning.*
- *If the partner traveling was male, use barrier methods or abstain from sex for at least 6 months after returning.*
- *If the partner who traveled has a pregnant partner, barrier protection should be used or abstain from sex for the duration of the pregnancy.*

If a partner travelled (male or female) and never developed symptoms, barrier protection should be used or abstain from sex for at least 8 weeks after returning.

ADDITIONAL INFORMATION CAN BE FOUND ON THE FOLLOWING WEBSITES:
The Alabama Department of Public Health (ADPH): www.adph.org/mosquito

The Centers for Prevention and Control (CDC), Fact Sheets and Posters:
www.cdc.gov/zika/fs-posters/index.html

Zika Patient Information Fact Sheet | August 16, 2016 | Alabama Department of Public Health



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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.
- It is difficult to distinguish infection in people previously infected with or vaccinated against a related flavivirus.
- Health care providers should work with state and local health departments to ensure test results are interpreted correctly.





Laboratories for Diagnostic Testing

- The Bureau of Clinical laboratories can perform the RT-PCR Triplex testing for Zika, dengue and chikungunya and the MAC-ELISA for Zika and dengue.
- As of August 17, 2016, there were seven commercially available Zika tests. Only one of them had the ability to test both the rRT-PCR and the MAC-ELISA tests. The number of commercially available tests continues to increase.
- Zika Consultation Forms should be submitted for Zika diagnostic testing, regardless of the laboratory conducting the testing. Any Zika diagnostic testing ordered should be done in accordance with CDC guidance.

URL to Emergency Use Authorizations for Zika Testing

<http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>

Accessed on August 17, 2016





Zika Virus Testing: Who should be tested?

- All persons with symptoms who:
 - traveled to any Zika affected area within 14 days of symptom onset.
 - had unprotected sexual contact* with a person that was diagnosed with Zika virus or traveled to an affected area.

- All pregnant women (including asymptomatic) who:
 - traveled to a Zika affected area during their pregnancy.
 - had unprotected sexual contact* with a person that was diagnosed with Zika virus or traveled to an affected area.

*Sexual contact includes vaginal sex, anal sex, oral sex and the sharing of sex toys.





Zika Virus Testing: Who should be tested?

- Symptomatic persons with an epidemiologic link to a positive individual or potential exposure(s) as determined by the State Epidemiologist using current information.
- All must present to their physician for specimen collection within 12 weeks of symptom onset (or exposure for asymptomatic pregnant women) – testing may be approved on a case by case basis after 12 weeks with possible exposure only on pregnant women.





Zika Virus Testing: Approval process

- To request that specimens be tested for Zika, chikungunya, and dengue virus, Alabama providers should contact the ADPH Infectious Diseases & Outbreaks Division at 1-334-206-5971 or 1-800-338-8347.
- The provider must complete the consultation form and submit to ADPH for review – the form is available online at <https://www.adph.org/Extranet/Forms/Form.asp?ss=s&formID=5910>
- **Effective September 9, 2016**, calls for authorization prior to submitting the Zika Consultation Form are only required for testing at birth and for fetal losses. Zika consultation forms should continue to be submitted for all patients for which Zika testing is indicated per CDC's guidance.

A blue circular logo with the text "ALABAMA PUBLIC HEALTH" in white, stacked vertically.

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Zika Virus Testing: Approval Process

- The form will be reviewed by an ADPH clinician to determine:
 - ✓ If the patient meets current testing criteria
 - ✓ Correct diagnostic test(s) to be performed – rRT-PCR, MAC-ELISA

- Upon approval of testing, specimens may be sent to BCL or a commercial laboratory.





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Collection and Storage*

- Proper collection of specimens to be tested for Zika, chikungunya, and dengue virus:
 - ✓ Collect blood specimen in a tiger top tube, centrifuge, and extract serum and place in a sterile tube. Approximately 2-3 mL of serum is needed to test for Zika, dengue, and chikungunya. Serum should be kept refrigerated (2 - 8°C) until ready to be shipped.
 - ✓ Collect 2-3 ml of urine (within 14 days of illness onset) in a sterile container and seal with parafilm. Urine should be kept refrigerated (2 - 8°C) until ready to be shipped.





Guidance for Zika Virus Specimen Collection Shipping and Testing

<http://www.adph.org/bcl/assets/ZikaVirus.pdf>



Guidance for Zika Virus Specimen Collection, Shipping, and Testing



Recommended Diagnostic Testing for Zika Virus

- ✓ CDC is recommending that for any suspect cases of Zika virus infection, testing should be considered for chikungunya and dengue.
- ✓ Please caution your patient against NSAID use including aspirin until dengue is ruled out.
- ✓ Healthcare providers wishing to arrange testing for Zika virus must contact ADPH Infectious Diseases & Outbreaks Division for consultation and approval at 1.800.338.8374.

Specimen Collection & Storage

- ✓ To request that specimens be tested for Zika, chikungunya, or dengue virus, follow the instructions below to properly collect.
 - Collect blood specimen in a tiger top tube, centrifuge, and **extract serum and place in a sterile tube**. Approximately 2-3 mL of serum is needed to test for Zika, dengue, and chikungunya. Serum should be kept refrigerated (2 – 8°C) until ready to be shipped.
 - Collect 2-3 mL of urine (within 7 days of illness onset) in a sterile container and seal with parafilm. Urine should be kept refrigerated (2 – 8°C) until ready to be shipped.

Specimen Shipping

- ✓ The urine specimen can be shipped together with the serum specimen.
- ✓ **Complete one (1) BCL Requisition Form and submit with the specimen to BCL.** Select Arboviral testing and indicate Zika, dengue, and chikungunya as the agents suspected. Include specimen collection date, date of symptom onset, as well as dates, locations of recent travel, and relevant vaccine history.
- ✓ **Complete one (1) CDC's Specimen Submission Form (CDC DAS) 50.34 and submit with the specimen to BCL.** Include specimen collection date, date of symptom onset, as well as dates, locations of recent travel, and relevant vaccine history.
 - Specimen origin (top left corner): HUMAN
 - Test order name: ARBOVIRUS SEROLOGY
 - **Note:** Zika virus testing is not an option in the *suspected* -down menu (located on 1st page, top left); therefore, select "ARBOVIRUS SEROLOGY" and then type "Zika virus testing" in the Brief Clinical Summary field located at the top of the second page of the form.
 - Click the following link to print the completed form: [Instructions to enable printing of CDC submission form.](#)
- ✓ The specimen should be kept cold not frozen.
- ✓ The specimen should be placed in an insulated container with frozen ice packs for shipping.
- ✓ The specimen may be taken to your local county health department to be couriered to BCL overnight (at no cost). Please contact your local county health department to coordinate courier pick up time.
OR
- ✓ Ship specimen directly to BCL-EID at 8140 AUM Drive, Montgomery, AL 36117 (at your expense).
- ✓ If you have a question about specimen collection and shipping, call BCL at 334-260-3400 or email clab@adph.state.al.us

Resources

- ✓ For more information about Zika virus, <http://adph.org/mosquito/>





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

- Proper shipping of specimens to be tested for Zika, chikungunya, and dengue virus:
 - ✓ The urine specimen can be shipped together with the serum specimen.
 - ✓ **For ALL pregnant patients** –Collect and submit both serum and urine specimens.
 - ✓ Must complete one (1) BCL Requisition Form AND one (1) CDC's Specimen Submission Form (CDC DASH 50.34) and submit with the specimen(s) to BCL.





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

http://www.adph.org/bcl/assets/BCL_Requisition_Form.pdf

- Complete ALL requested patient and provider information.
- Select **Arboviral testing** and indicate **Zika, dengue, and chikungunya** as the agents suspected. Include specimen collection date, date of symptom onset, as well as dates of travel, locations of recent travel, and relevant vaccine history.





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

- Must complete one (1) **CDC's Specimen Submission Form (CDC DASH 50.34)** and submit with the specimen to BCL. Include specimen collection date, date of symptom onset, as well as dates, locations of recent travel, and relevant vaccine history.





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

- Specimen origin (top left corner): HUMAN
- Test order name: ARBOVIRUS SEROLOGY
- Note: Zika virus testing is not an option in the *suspected -down menu* (located on 1st page, top left); therefore, select “ARBOVIRUS SEROLOGY” and then type “Zika, dengue, chikungunya virus testing” in the Brief Clinical Summary field located at the top of the second page of the form.
- Click the following link to print the completed form: [Instructions to enable printing of CDC submission form.](#)





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

- The specimen should be kept cold **not frozen**.
- The specimen should be placed in an insulated container with frozen ice packs for shipping.
- The specimen may be taken to your local county health department to be couriered to BCL overnight (at no cost). If it is Friday, please follow the steps above and hold until Monday (or Tuesday if a Monday holiday). Please contact your local county health department to coordinate courier pick up time.

OR

Guidance for Zika Virus Specimen Collection, Shipping, and Testing (07/28/2016)





Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Shipping*

- Ship specimen directly to BCL-EID at 8140 AUM Drive, Montgomery, AL 36117 (**at your expense**).
- If you have a question about specimen collection and shipping, call BCL at 334-260-3400 or email clab@adph.state.al.us .

Guidance for Zika Virus Specimen Collection, Shipping, and Testing (07/28/2016)

Information for Clinicians





Initial Assessment and Treatment

- There is no specific antiviral therapy for Zika.
- Current treatment is supportive (i.e., rest, fluids, analgesics, antipyretics).
- Suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infections.
- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage.





Zika Virus Disease Clinical Evaluation

- Zika virus disease should be considered in travelers with acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis within two weeks after return from a [Zika-affected area](#).
- Inform and evaluate women who traveled to areas with Zika virus transmission while they were pregnant or had unprotected sex with a partner who traveled to an area with active transmission or shared sex toys with a partner who traveled to an area with active Zika transmission.





Zika Virus Disease Clinical Evaluation

- Couples who traveled to Zika-affected areas should follow guidance to wait before trying to become pregnant.
- Evaluate fetuses/infants of women infected during pregnancy for possible congenital infection and microcephaly.
- Testing of asymptomatic males is NOT recommended by the CDC.





Reporting Zika Virus Disease Cases

- As an arboviral disease, Zika virus disease is a nationally notifiable disease.
- Healthcare providers must report suspected cases to the Alabama Department of Public Health, Infectious Diseases and Outbreaks Division at 334-206-5971 or 800-338-8374.
- Timely reporting allows health departments to assess and reduce the risk of local transmission or mitigate further spread of the virus.





Zika Virus Preventive Measures

- There is no vaccine or medication to prevent infection or disease.
- The primary prevention measure is to reduce mosquito exposure.
- Pregnant women should NOT travel to areas with ongoing Zika virus transmission.
- Infected people should protect themselves from mosquito exposure during first 3 weeks of illness to prevent further transmission.





ZIKA VIRUS AND PREGNANCY

Information for Clinicians





Zika Virus and Pregnancy

- Existing data show:
 - No evidence of increased susceptibility
 - Infection can occur in any trimester
 - Incidence of Zika virus in this population is not known
 - No evidence of more severe effect of the disease in the woman herself, but this is being studied





CDC Recommendations: Pregnant Women Considering Travel

- Pregnant women in any trimester should NOT travel to areas where Zika is present
- Pregnant women who have to travel to one of these areas should talk to their health care provider and strictly follow steps to avoid mosquito bites during the trip.
- Pregnant women who have a partner who has traveled to a Zika-affected area should ask their partner to consistently and correctly use condoms or abstain from sexual activity (vaginal, anal, and oral sex and the sharing of sex toys) for the duration of the pregnancy.

A blue circular logo with the text "ALABAMA PUBLIC HEALTH" in white, bold, uppercase letters.

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Recommendations for Serology Testing

- Testing is recommended for all pregnant women with travel to a [Zika-affected area](#).
- ADPH also asks that Zika specimens on pregnant women meeting CDC's criteria for testing be submitted to the Bureau of Clinical Laboratories after consultation.
- Instructions on specimen collection, packaging, and shipping are provided following consultation and authorization.





Recommendations for Serology Testing

- **Future Pregnancies**

“Based on the available evidence, we think that Zika virus infection in a woman who is not pregnant would not pose a risk for birth defects in future pregnancies after the virus has cleared from her blood. From what we know about similar infections, once a person has been infected with Zika virus, he or she is likely to be protected from a future Zika infection.”

Source: CDC http://www.cdc.gov/zika/healtheffects/birth_defects.html

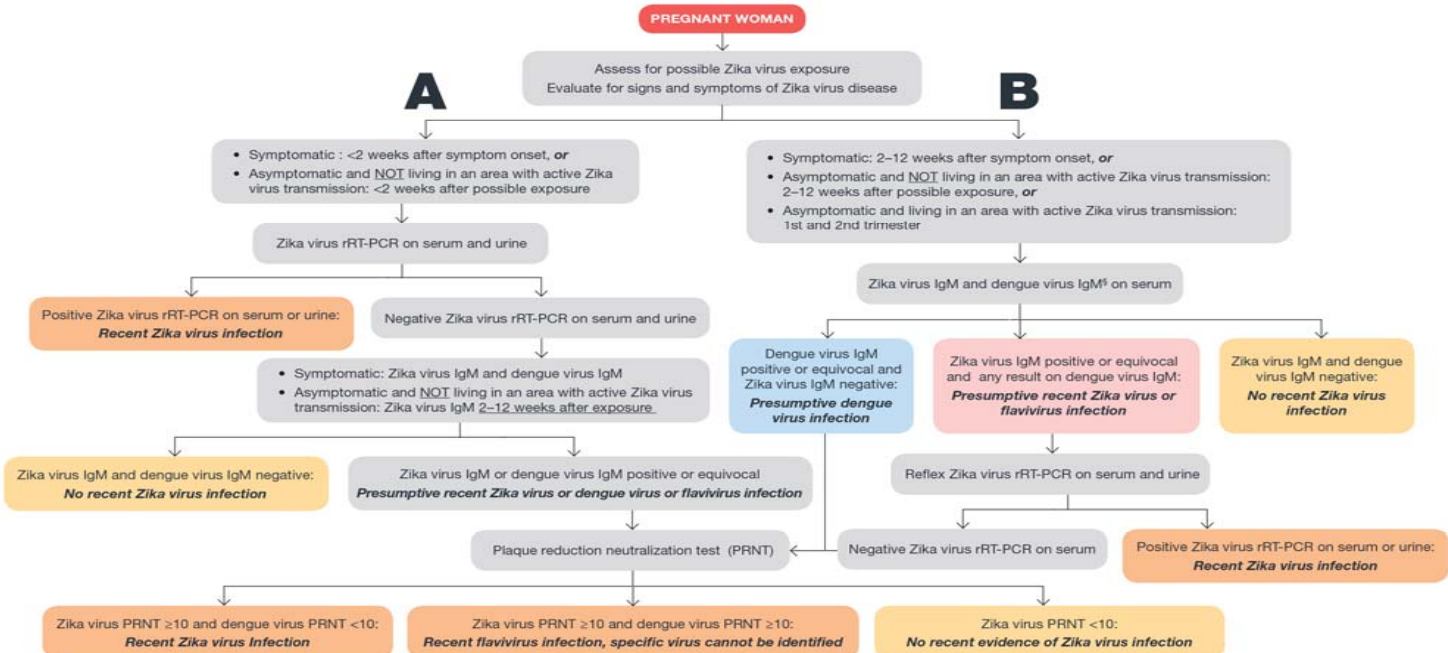


ZIKA VIRUS

CDC's Response to Zika

UPDATED INTERIM PREGNANCY GUIDANCE:

Testing and interpretation recommendations^{*,†,§,¶} for a pregnant woman with possible exposure to Zika virus^{**} — United States (including U.S. territories)



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.



Information for Clinicians



Zika and Pregnancy: Clinical Management

- Confirmed maternal or fetal infection:
 - Antepartum:
 - Consider serial ultrasounds every 3-4 weeks.
 - Consider referral to a maternal fetal medicine specialist with expertise in pregnancy management.





Zika and Pregnancy: Clinical Management

- Confirmed maternal or fetal infection:
 - Peripartum:
 - Histopathologic examination of the placenta and umbilical cord;
 - Testing of frozen placental tissue and cord tissue for Zika virus RNA
 - Testing of infant blood for Zika and dengue virus IgM and neutralizing antibodies





Zika Virus Disease Prevention for Pregnant Women

- Avoid mosquito bites:
 - Use EPA-registered insect repellent
- EPA-registered repellents including DEET are considered safe to use in pregnant and lactating women





Zika Virus Disease Prevention for Pregnant Women

- Wear long-sleeved shirts and pants to cover exposed skin
- Wear Permethrin-treated clothes
- Stay and sleep in screened-in or air-conditioned rooms
- Practice mosquito prevention strategies throughout the entire day



ZIKA VIRUS AND SEXUAL TRANSMISSION

Information for Clinicians





Zika Virus and Sexual Transmission – What We Know

- There is evidence that the Zika virus can be sexually transmitted by both men and women to their sex partners.
- As of August 17, 2016, 22 cases of sexually transmitted Zika virus infection confirmed in the U.S.

* Sexually transmitted cases are not reported for areas with local mosquito-borne transmission of Zika virus because it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.





Zika Virus and Sexual Transmission – What We Know

- Zika virus RNA has been found in semen up to 188 days after symptoms began. It has also been found in vaginal fluid 3 days after symptom onset and in cervical mucus up to 11 post symptom onset.
- Some recent case studies have determined that the virus can persist longer in some pregnant women.

* Sexually transmitted cases are not reported for areas with local mosquito-borne transmission of Zika virus because it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.





Recommendations for Couples to Prevent Sexual Transmission

- Zika can be passed through sex from a person with or without symptoms to partners.
- Sex includes vaginal, anal, and oral sex and the sharing of sex toys.
- CDC recommends that pregnant women use protection or not have sex for the duration of pregnancy when there is a partner with travel to an area with active transmission regardless of whether the partner had symptoms or not.
- Not having sex is the best way to be sure that someone does not get sexually transmitted Zika virus.





Recommendations for Couples to Prevent Sexual Transmission

- For couples in which the partner has symptoms during or on return from an area with active Zika transmission:
 - ❑ If partner traveling was female, use barrier methods and wait for at least 8 weeks before having unprotected sex;
 - ❑ If the partner traveling was male, use barrier methods and wait for at least 6 months before having unprotected sex.
 - ❑ If the partner who traveled has a pregnant partner, barrier protection should be used for the duration of the pregnancy.
 - ❑ “Sex” includes vaginal, anal, and oral sex and the sharing of sex toys.

NOTE: CDC recommends that pregnant women with “possible exposure” now defined as the pregnant woman traveling or living in an area with active Zika virus transmission or unprotected sex or shared use of sex toys with a partner who traveled to an area with active Zika transmission.





Recommendations to Prevent Sexual Transmission

At this time, testing a person's blood, urine, or genital secretions to determine their potential risk of sexually transmitting Zika virus is not recommended for the following reasons:

A negative blood test or antibody test could be falsely reassuring. This can happen when:

- The blood test is performed after the virus is no longer in the blood (detected by RT-PCR) but could still be present in other bodily fluids (e.g., semen).
- The antibody test is performed early after infection when the antibody levels are not yet high enough to be detected, or later after infection when the antibody levels have fallen to undetectable levels.
- The test is falsely negative.





Recommendations to Prevent Sexual Transmission

Second, we currently have limited understanding of Zika virus shedding in genital secretions, or of how to interpret the results of tests of semen or vaginal fluids. For more information on diagnostic testing for Zika, see [Testing for Zika](#).



ZIKA VIRUS IN INFANTS AND CHILDREN

Information for Clinicians

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Case Definitions - Microcephaly

- **Definite congenital microcephaly live births:**

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





Case Definitions - Microcephaly

- Definite congenital microcephaly - **still births/early termination**
 - HC at delivery less than 3rd percentile for gestational age and sex



Definitions for Possible Congenital Microcephaly

- Possible congenital microcephaly live births
 - If earlier HC is not available, HC less than 3rd percentile for age and sex beyond 6 weeks of age
- Possible congenital microcephaly for all birth outcomes
 - Microcephaly diagnosed or suspected on prenatal ultrasound in the absence of available head circumference





What is Microcephaly?

- Clinical finding of a small head when compared to infants of same sex and age
- Measured by head circumference (HC) or occipitofrontal circumference (OFC)
- Reliable assessment of intracranial brain volume
- Often leads to cognitive and/or neurologic issues





What is Microcephaly?

- Mechanisms
 - primary due to abnormal development (often with a genetic etiology)
 - secondary due to arrest or destruction of normally-forming brain tissue (by infection, vascular disruption)
- Difficult birth defect to monitor because of inconsistent definition and use of terminology



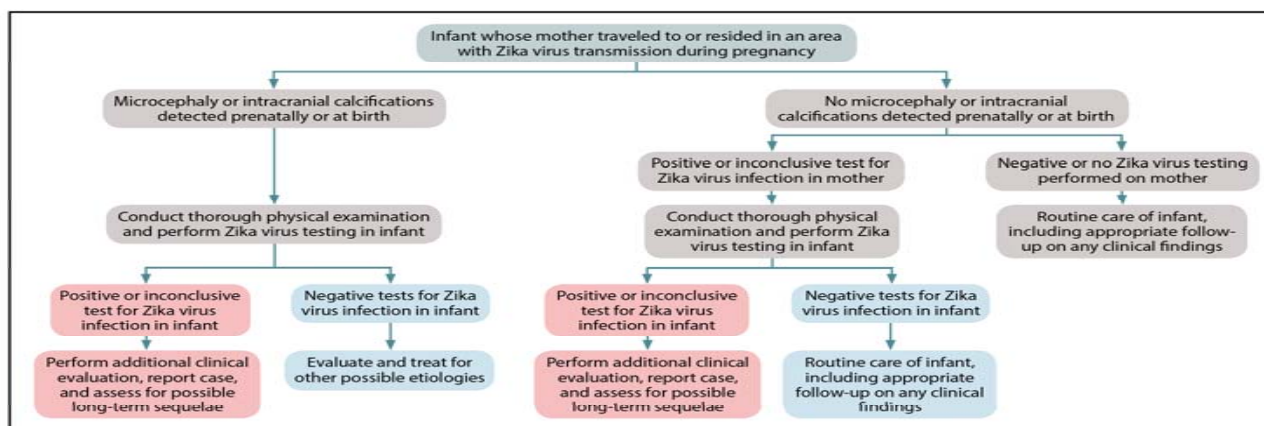
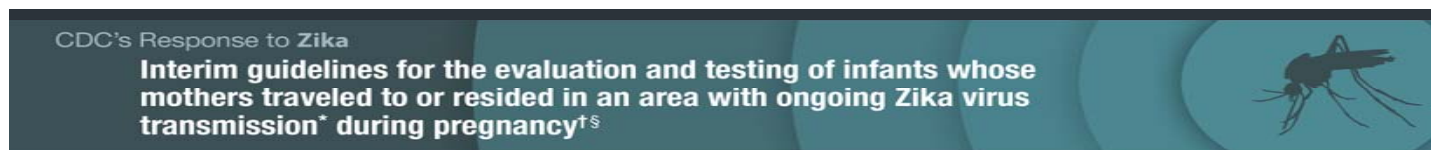
What is Microcephaly?



- 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



Algorithm: Infant Whose Mother Traveled to or Resided in an Area with 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>.

Updated Interim Guidelines and other resources for healthcare providers available at <http://www.cdc.gov/zika/hc-providers/index.html>
www.cdc.gov/zika



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





Update: Interim Guidance for Evaluation of Infants and Children
With Possible Congenital Zika Virus Infection - United States -
August 19, 2016

www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm

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Information for Clinicians



Zika Virus Laboratory Testing of Infants

- Recommended for
 - Infants with microcephaly/microencephaly, intracranial calcifications, other types of congenital abnormalities consistent with Zika infection born to women who traveled to or resided in an area with Zika virus transmission while pregnant or to women with other exposure as defined in CDC's guidance.
 - Infants born to mothers with positive or inconclusive test results for Zika virus infection





Recommended Zika Virus Testing for Infants*

- Recommended tests
 - Zika virus RNA (RT-PCR), IgM, and neutralizing antibodies
 - Dengue virus IgM and neutralizing antibodies
- Clinical specimens
 - Infant serum within 2 days of birth if possible
 - Cerebrospinal fluid, if obtained for other studies

*When indicated, including: 1) infants with microcephaly or intracranial calcifications born to women potentially exposed to Zika virus during pregnancy, or 2) infants born to mothers with positive or inconclusive test results for Zika virus infection.





Recommended Zika Virus Testing for Infants*

- Consider histopathologic evaluation (placenta and umbilical cord)
 - Zika virus immunohistochemical staining (fixed tissue)
 - Zika virus RT-PCR (fixed and frozen tissue)
- Additionally, if not already performed, test mother's serum
 - Zika virus IgM and neutralizing antibodies
 - Dengue virus IgM and neutralizing antibodies

*When indicated, including: 1) infants with microcephaly or intracranial calcifications born to women potentially exposed to Zika virus during pregnancy, or 2) infants born to mothers with positive or inconclusive test results for Zika virus infection.





Zika-Related Birth Defects

Brain abnormalities with and without microcephaly

- Confirmed or possible congenital microcephaly
- Intracranial calcifications
- Cerebral atrophy
- Abnormal cortical formation (e.g., polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia)
- Corpus callosum abnormalities
- Cerebellar abnormalities





Zika-Related Birth Defects

Brain abnormalities with and without microcephaly

- Porencephaly
- Hydranencephaly
- Ventriculomegaly / hydrocephaly (excluding “mild” ventriculomegaly without other brain abnormalities)
- Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)
- Other major brain abnormalities, including intraventricular hemorrhage *in utero* (excluding post-natal IVH)

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Zika-Related Birth Defects Continued

Early brain malformations, eye abnormalities, or consequences of central nervous system (CNS) dysfunction

- Neural tube defects (NTD)
 - Anencephaly / Acrania
 - Encephalocele
 - Spina bifida
- Holoprosencephaly / Arhinencephaly





Zika-Related Birth Defects Continued

- Structural eye abnormalities
 - Microphthalmia / Anophthalmia
 - Coloboma
 - Cataract
 - Intraocular calcifications
 - Chorioretinal anomalies involving the macula (e.g., chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage); excluding retinopathy of prematurity
 - Optic nerve atrophy, pallor, and other optic nerve abnormalities





Zika-Related Birth Defects Continued

- Congenital contractures (e.g., arthrogryposis, club foot, congenital hip dysplasia) with associated brain abnormalities
- Congenital deafness documented by postnatal testing



Evaluation and Testing for All Infants with Possible Congenital Zika Virus Infection

For all infants with possible congenital Zika virus infection, perform the following:

- Thorough physical examination, including careful measurement of the head circumference, length, weight, and assessment of gestational age*
- Cranial ultrasound, unless prenatal ultrasound results from third trimester demonstrated no abnormalities of the brain

*If any abnormalities are noted, consultation with the appropriate specialist is recommended





Evaluation and Testing for All Infants with Possible Congenital Zika Virus Infection

For all infants with possible congenital Zika virus infection, perform the following:

- Further evaluation
 - neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions*
 - hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth*
 - eye exam to include visualization of the retina, optic nerve, and macula either before discharge from the hospital or within 1 month after birth*
- Other evaluations specific to the infant's clinical presentation

*If any abnormalities are noted, consultation with the appropriate specialist is recommended





Zika Virus Laboratory Testing of Infants

- Recommended for:
 - Infants with microcephaly/microcephaly, intracranial calcifications, other types of congenital abnormalities consistent with Zika infection born to women who traveled to or resided in an area with Zika virus transmission while pregnant or to women with other exposure as defined in CDC's guidance.
 - Infants born to mothers with positive or inconclusive test results for Zika virus infection





Recommended Long-Term Follow-Up of Infants with Possible Congenital Zika Virus Infection

- Report cases to the Alabama Department of Public Health, 1-334-206-5971 or 1-800-338-8374 and monitor for additional guidance as it released.
- Cases will be entered into *U.S. Zika Pregnancy Registry*
- Carefully evaluate head circumference and developmental characteristics and milestones throughout the first year of life
- Use of appropriate consultations with medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy)
- Conduct additional hearing screen at age 6 months, plus any appropriate follow-up of hearing abnormalities detected through newborn hearing screening

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





U.S. Zika Pregnancy Registry

- CDC is requiring all states to submit information on pregnant women with Zika infection
- These women have the following time points for data collection: Initial Identification of case, 2nd and 3rd trimester, and at delivery
- Infants have the following time points for data collection: birth, 2 months, 6 months and 12 months





Summary

- Zika virus continues to circulate and cause locally-transmitted disease in the Americas.
- We still expect limited local transmission in the U.S. despite Florida cases
- Consider the possibility of Zika virus infection in travelers to any area with active Zika transmission with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return.
- Pregnant women in any trimester should NOT travel to areas with active Zika virus transmission.
- Contact ADPH for authorization for Zika testing.





Questions?





Contact Information

For consultation, Alabama physicians should contact the ADPH Infectious Diseases & Outbreaks Division at 1-800-338-8347.

Visit www.adph.org/mosquito for the most updated information.