

Zika Virus: Information for Clinicians

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**Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division**

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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

- **State the recommendations for pregnant women and others to prevent possible Zika virus exposure**
- **Discuss evaluation of infants with microcephaly and the relationship of Zika and microcephaly**

Zika Virus

- **Single stranded RNA Virus**
- **Genus *Flavivirus*, Family *Flaviviridae***
- **Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses**

Zika Virus

- Transmitted to humans primarily by *Aedes (Stegomyia) species* mosquitoes

Zika Virus Vectors: Aedes Mosquitoes

- *Aedes species* mosquitoes
 - *Ae aegypti* more efficient vectors for humans
 - *Ae albopictus*

Zika Virus Vectors: Aedes Mosquitoes

- 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

Other Modes of Transmission

- Maternal-fetal
 - Intrauterine
 - Perinatal
- Other
 - Sexual
 - Blood transfusion
 - Laboratory exposure

Other Modes of Transmission

- Theoretical
 - Organ or tissue transplantation
 - Breast milk

Zika Virus Epidemiology

- First isolated from a monkey in Uganda in 1947
- Prior to 2007, only sporadic human disease cases reported from Africa and southeast Asia
 - At least 14 cases of human Zika virus disease had been documented, although other cases were likely to have occurred and were not reported

Zika Virus Epidemiology

- Most likely other cases were not identified because the symptoms of Zika are similar to many other diseases
- In 2007, first outbreak reported on Yap Island, Federated States of Micronesia
- In 2013-2014, > 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 Outbreaks in the Americas

- Before 2007, at least 14 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

Zika Virus 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
- The virus is likely to spread to other countries though, because the mosquitoes that spread Zika are found throughout the world

Zika Virus in the Continental United States

- Local transmission of Zika virus has not been reported in the continental United States
- Since 2011, there have been laboratory - confirmed Zika virus cases identified in travelers returning from areas with local transmission

Zika Virus in the Continental United States

- As of February 24, 2016, U.S. states have reported a total of 107 travel - associated cases to CDC
 - Additionally, U.S. territories have reported 1 travel associated and 39 locally acquired cases

Zika Virus in the Continental United States

- With current outbreaks in the Americas, cases among U.S. travelers will most likely increase
- Imported cases may result in virus introduction and local spread in some areas of the U.S.

Zika Virus Incidence and Attack Rates

- 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

| 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% |

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

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
 - 4 out of 5 people do not even realize they have the disease
- Fatalities are rare

Zika Virus Clinical Disease Course and Outcomes

- Guillain - Barré syndrome has been reported in patients following suspected Zika virus infection
 - The relationship to Zika virus infection is not known

Zika Virus and Gullian-Barré Syndrome (GBS)

- The Brazil Ministry of Health has reported an increased number of people who have been infected with Zika virus who also have Guillain - Barré syndrome (GBS)
 - CDC is working with Brazil to study the possibility of a link between Zika and GBS

Zika Virus and Gullian-Barré Syndrome (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
- GBS symptoms include weakness of the arms and legs that is usually the same on both sides of the body

Zika Virus and Gullian-Barré Syndrome (GBS)

- 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

Zika Virus and Gullian-Barré Syndrome (GBS)

- Researchers do not fully understand what causes GBS
 - Most people with GBS report an infection before they have GBS symptoms
 - Rarely, vaccination has also been associated with the onset of GBS (for example, 1976 Swine influenza vaccine)

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

Distinguishing Zika From Dengue and Chikungunya

- 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 | - | + | - |

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

Diagnostic Testing for Zika Virus

- Reverse transcriptase - polymerase chain reaction (RT-PCR) for viral RNA in serum collected ≤ 7 days after illness onset
- Serology for IgM and neutralizing antibodies in serum collected ≥ 4 days after illness onset

Diagnostic Testing for Zika Virus

- Plaque reduction neutralization test (PRNT) for ≥ 4 -fold rise in virus - specific neutralizing antibodies in paired sera
- 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

Serology Cross-Reactions with Other Flaviviruses

- It is difficult to distinguish infecting virus 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

- No commercially - available diagnostic tests
- Testing performed at CDC and a few state health departments
- CDC is working to expand laboratory diagnostic testing in states
- ADPH must be contacted for approval for Zika diagnostic testing

Guidance for Zika Virus Specimen Collection Shipping and Testing: *Specimen Collection and 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. Serum should be kept refrigerated (2 - 8 degrees C) until ready to be shipped.

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

- ✓ 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.

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

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

- ✓ 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 virus testing" in the Brief Clinical Summary field located at the top of the second page of the form.*

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

- Click the following link to print the completed form: Instructions to enable printing of CDC submission form.
–<http://www.cdc.gov/ncezid/dvbd/specimensub/arboviral-shipping.html>

**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. If received warm, specimens will be unsatisfactory for testing
- ✓ The outer container must be labeled as UN3373 - Biological Substance Category B

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

**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 (2/23/2016)

Most Common Errors

- **NO Ice** - Affects integrity of specimen; warm specimens can result in hemolysis of RBCs and viral protein denaturation
- **NO Labels** - Category B packaging instructions must be followed
- **NO Consultation** - ADPH Infectious Diseases and Outbreaks must be contacted for consultation and approval to send specimens

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

Initial Assessment and Treatment

- Aspirin and other NSAIDs should be avoided until dengue can be ruled out to reduce the risk of hemorrhage

Zika Virus Disease Surveillance

- Surveillance 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

Zika Virus Disease Surveillance

- Evaluate fetuses / infants of women infected during pregnancy for possible congenital infection and microcephaly
- Be aware of possible local transmission in areas where *Aedes species* mosquitoes are active

Reporting Zika Virus Disease Cases

- As an arboviral disease, Zika virus disease is a nationally notifiable disease
- Health care providers are encouraged to report suspected cases to the Alabama Department of Public Health, Infectious Diseases and Outbreaks Division at 334-206-5971

Reporting Zika Virus Disease Cases

- 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 consider postponing travel to areas with ongoing Zika virus outbreaks

Zika Virus Preventive Measures

- Infected people should be protected from mosquito exposure during first week of illness to prevent further transmission

Zika Virus and Pregnancy

- Limited information is available
- Existing data shows
 - Pregnant women are not known to have increased susceptibility to Zika virus when compared with the general population

Zika Virus and Pregnancy

- Infection can occur in any trimester and maternal - fetal transmission of the virus can occur throughout pregnancy
- No evidence to suggest pregnant women will have more serious illness if infected

Zika Virus and Pregnancy

- The illness is short lived, occurring 2-12 days following the mosquito bite
- Infected individuals usually do not require hospitalization or experience serious morbidity

Perinatal Counseling: Limiting Exposure

- No antiviral treatment, no prophylactic medication or vaccination is currently available for Zika virus infection
- Because of the virus's significant association with adverse pregnancy outcomes, birth defects and fetal loss - avoid travel to Zika affected areas

Perinatal Counseling: Limiting Exposure

- Outbreaks occurring throughout South and Central America, the Pacific Islands and Africa and are expected to spread with international air travel

CDC Recommendations: Pregnant Women Considering Travel

- Pregnant women in any trimester should consider postponing travel to areas where Zika is present
- If travel to these areas is inevitable, pregnant women should talk to their health care provider and take rigorous precautions to avoid exposure to mosquito bites and infection

CDC Recommendations for Evaluating Pregnant Travelers

- Pregnant women who have a male partner who has traveled to a Zika affected area should ask their partner to consistently and correctly use condoms or consider abstaining from insertive sexual activity for the duration of the pregnancy

Recommendations for Evaluating Pregnant Travelers

- Ask pregnant woman about travel history
- If history of travel to an area with ongoing Zika virus transmission during pregnancy evaluate for symptoms of and test for Zika virus infection

Recommendations for Serology Testing

- Antibody Testing for Zika virus is now recommended for ALL pregnant women who have traveled to an affected area regardless of the presence of clinical illness

Recommendations for Serology Testing

- Testing is recommended for pregnant women with clinical illness, presence of two or more of the following symptoms (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) during or within two weeks of travel to a Zika affected area

Recommendations for Serology Testing

- Testing can be offered to pregnant asymptomatic women with a travel history to a Zika affected area
- IgM antibody testing should be performed 2 to 12 weeks after return from travel
- 80% of patients infected with Zika remain asymptomatic

Diagnosis of Maternal Zika Virus Infection

- Laboratory evidence of maternal Zika virus infection can include Zika virus RNA detected by RT-PCR in any clinical specimen
- Positive Zika virus IgM with confirmatory neutralizing antibody titers that are ≥ 4 fold higher than dengue virus neutralizing antibody titers in serum by PRNT
- Testing would be considered inconclusive if Zika virus neutralizing antibody titers are ≤ 4 fold higher than dengue virus neutralizing antibody titers

Testing for Zika virus Following Symptom Onset

- The best diagnostic test for infection is RT-PCR which should be completed ideally within 4 days of symptom onset
- Beyond 4 days of symptom onset, testing for Zika virus IgM specific Ab and neutralizing Ab should be performed in addition to the RT-PCR test

Recommendations for Serology Testing for Asymptomatic Patients

- A negative IgM test result obtained 2-12 weeks after travel suggests that a recent infection did not occur and could negate the need for serial ultrasound

Testing for Zika Virus Challenges:

- Interpretation of Ab testing can be problematic because of cross reacting with related arboviruses
- Zika viremia decreases rapidly overtime; therefore, if serum is collected even 5 - 7 days after onset, a negative test does not definitively exclude infection

Recommendations for Serology Testing

- CDC recommends offering re-testing in mid second trimester for women who were exposed very early in gestation
- Testing is not indicated for women without a history of travel to areas where Zika virus infection is endemic or without a history of unprotected sexual contact with someone who has been exposed to the infection

Case # 1

- How would you manage this patient?
 - A pregnant woman presents to your office at 26 weeks with a history of travel to Colombia on March 1 - March 8
 - She has noted bites, fever and a rash

Case # 1

- If your patient has a history of travel to a Zika virus affected area and presents with signs of an acute infection within 2 weeks of travel, serologic testing is needed

Case # 1

- Clinical illness consistent with Zika virus disease is defined by the CDC as 2 or more of the following signs or symptoms:
 - Acute onset of fever
 - Maculopapular rash
 - Arthralgia
 - Conjunctivitis

Case # 1

- If the serologic testing is positive or inconclusive, or ultrasound findings are consistent with Zika virus infection, amniocentesis with RT-PCR test for Zika virus should be considered

Case # 2

How would you manage this patient?

- A pregnant woman presents to your office at 20 weeks with a history of travel to Mexico between 16 weeks + 0 days and 16 weeks + 5 days
- She has noted mosquito bites but no illness

Case # 2

- In an asymptomatic patient with a history of travel to an endemic area, Serum IgM assay is now recommended between 2 and 12 weeks after exposure
- If the IgM result is positive or inconclusive, serial fetal ultrasound to screen for microcephaly and intracranial calcifications should be performed

Treatment is Supportive

- Includes rest, fluids with analgesics and antipyretics
- Aspirin should be avoided until dengue virus infection can be ruled out because of the related risk of bleeding with hemorrhagic fever

Treatment is Supportive

- Pregnant women with fever should be treated with acetaminophen
- NSAIDs should be avoided in the second half of pregnancy because of their effect on fetal renal blood flow and structure of the ductus arteriosus

Clinical Management

- Important for physicians to be aware that fetal ultrasound may not detect microcephaly or calcifications until late second trimester or early third trimester
- If markers are concerning for fetal infection, amniocentesis with RT-PCR testing should be considered

Clinical Management

- **Sensitivity and specificity of RT-PCR on amniotic fluid is unknown**
- **Maternal - fetal transmission risks from an invasive procedure are unknown**

Clinical Management

- **Even if the IgM is negative, a baseline screening ultrasound should be performed**
- **If the patient is negative for both serologic testing and ultrasound findings, the patient can resume routine prenatal care**

Clinical Management

- **Postpartum**
 - **Zika virus RNA has been detected in blood, amniotic fluid, semen, saliva, CSF, urine and breast milk**

Confirmed Maternal - Fetal Infection

- **Postpartum:**
 - **Detailed 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

- **Postpartum**
 - **Although the virus has been shown to be present in breast milk, there has been no evidence of viral replication in milk or reported transmission in breastfed infants**

Evidence of Maternal-Fetal Transmission of Zika Virus

Evidence of maternal-fetal transmission:

- **Zika virus infection has been confirmed in infants with microcephaly in Brazil and in infants whose mothers have traveled to Brazil but delivered in the U.S.**
- **Zika virus RNA identified in specimens of fetal losses**

Zika Virus and Microcephaly in Brazil

- Reports of a substantial uptick in number of babies born with microcephaly in 2015 in Brazil; true baseline unknown
 - Zika virus infection identified in several infants born with microcephaly (including deaths) and in early fetal losses
 - Some of the infants with microcephaly have tested negative for Zika virus

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
 - Wear long-sleeved shirts and long pants to cover exposed skin
 - Wear Permethrin-treated clothes

Zika Virus Disease Prevention for Pregnant Women

- Stay and sleep in screened-in or air-conditioned rooms
- Practice mosquito prevention strategies throughout the entire day

Special Consideration for Women of Reproductive Age

- Women of reproductive age with current or previous laboratory confirmed Zika virus infection should be counseled that there is no evidence that prior Zika virus infection poses a risk of birth defects in future pregnancies
- Viremia is expected to last approximately one week in patients with clinical illness

U.S. Zika Pregnancy Registry

- CDC recently established a national registry to learn about the risks of Zika during pregnancy
- Collaboration with local, state and health care providers to collect clinical information about pregnancy, infant at birth and the child throughout the first year of life
- Knowledge gained to assist in responding to the ongoing outbreak

Zika Virus and Sexual Transmission

Zika Virus and Sexual Transmission

- Sexual transmission of Zika virus is possible, and is of particular concern during pregnancy
- Current information about possible sexual transmission of Zika is based on reports of three cases

Zika Virus and Sexual Transmission

- The first was probable sexual transmission of Zika virus from a man to a woman, in which sexual contact occurred a few days before the man's symptom onset
- The second is a case of sexual transmission currently under investigation (Unpublished data, 2016, Dallas County Health and Human Services)

Zika Virus and Sexual Transmission

- The third is a single report of replication-competent Zika virus isolated from semen at least 2 weeks and possibly up to 10 weeks after illness onset; reverse transcriptase - polymerase chain reaction testing of blood plasma specimens collected at the same time as the semen specimens did not detect Zika virus
 - The man had no sexual contacts

Zika Virus and Sexual Transmission

- Because no further testing was conducted, the duration of persistence of Zika virus in semen remains unknown
- In all three cases, the men developed symptomatic illness

* Source: Interim Guidelines for Prevention of Sexual Transmission of Zika Virus - United States, 2016 *Weekly* / February 12, 2016 / 65(5); 120–121

Zika Virus and Sexual Transmission - What We Know

- There is evidence that the Zika virus can be sexually transmitted by a man to his sex partners
 - As of February 24, 14 cases of sexually transmitted Zika virus has been reported

Zika Virus and Sexual Transmission - What We Know

- In the two cases of likely sexual transmission, both men had Zika symptoms
- The virus is present in semen longer than in blood

Zika Virus and Sexual Transmission - What We Don't Know

- How long the virus is present in semen in men who have had Zika
- If infected men who never develop symptoms can have Zika virus in their semen

Zika Virus and Sexual Transmission - What We Don't Know

- If infected men who never develop symptoms can transmit Zika virus through sex
- If a woman can transmit Zika virus to her sex partners

Additional Zika Virus and Sexual Transmission Information

- At this time, there is no evidence that women can transmit Zika virus to their sex partners
- There are tests to detect Zika virus in semen, but they are not widely available

Additional Zika Virus and Sexual Transmission Information

- In addition, most clinicians have limited understanding of how to interpret the results of such tests, so CDC does not recommend testing semen at this time

Recommendation for Men Who Live in or Traveled to a Zika - Affected Area

- If the man's partner is pregnant, the couple should either not have sex or use condoms the right way every time they have vaginal, anal, and oral (mouth - to - penis) sex during the partner's pregnancy
- Condoms can also help prevent getting HIV and other sexually transmitted diseases

Recommendation for Men Who Live in or Traveled to a Zika - Affected Area

- Men who live or are traveling in an area with active Zika transmission should also take steps to prevent mosquito bites
- If a man develops symptoms of Zika virus illness at any time during his travel or within two weeks after he returns, he should see his healthcare provider to see if he has Zika virus or another illness

Recommendation for Men Who Live in or Traveled to a Zika - Affected Area

- Not having sex is the best way to be sure that someone does not get sexually transmitted Zika virus

Zika Virus in Infants and Children

Microcephaly

- Clinical finding of a small head - more than 2 SD less than mean for age / gender / conceptual age
- Measured by occipitofrontal circumference (OFC)
- Reliable assessment of intracranial brain volume
- Can lead to cognitive / neurologic issues

Microcephaly

- Primary due to abnormal development (Often with a genetic etiology)
- Secondary due to arrest or destruction of normally - forming brain tissue (Infection and/or vascular disruption)
- Difficult birth defect to monitor- inconsistent definition/use of terminology

Microcephaly and Zika

What We Know

- Small number of positive test results for Zika virus infection in infants with microcephaly
- Microcephaly pattern consistent with Fetal Brain Disruption Sequence
- Based on photos / scans of a small number of affected infants from Brazil
- Retrospective investigation in French Polynesia outbreak in 2013-2014
- Infants with other intrauterine infections such as cytomegalovirus (CMV)

Microcephaly and Zika

What We Do Not Know

- Causal relation between Zika virus and microcephaly or other adverse pregnancy outcomes
- Full spectrum of phenotypes in affected Infants
- Impact of timing of infection during Pregnancy
- Impact of severity of maternal infection
- Magnitude of the possible risk of microcephaly and other adverse pregnancy outcomes

Zika Virus Laboratory Testing of Infants

- **Recommended for:**
 - Infants with microcephaly or intracranial calcifications born to women who traveled to or resided in an area with Zika virus transmission while pregnant
 - 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

*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*

- **Clinical specimens:**
 - Serum (umbilical cord or direct, 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)

*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*

- **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.

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

- **For all infants with possible congenital Zika virus infection, perform:**
 - Thorough physical examination
 - Careful measurement of the head circumference
 - Length, weight, assessment of gestational age*

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

- Cranial ultrasound, unless prenatal ultrasound results from third trimester demonstrated no abnormalities of the brain

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

- Hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth*

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

- Eye exam-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

Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- For infants with microcephaly, consultation with:
 - Clinical geneticist or dysmorphologist
 - Pediatric neurologist to determine appropriate brain imaging and additional evaluation (e.g., US, CT scan, MRI, and / or EEG)

Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- Pediatric infectious disease specialist to consider other congenital infections-syphilis, toxoplasmosis, rubella, cytomegalovirus, lymphocytic choriomeningitis virus, and herpes simplex viruses

Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- CBC, platelet count, and LFT and enzyme tests including ALT, AST, and bilirubin
- Consideration of genetic and other teratogenic causes based on additional congenital anomalies identified by clinical examination and imaging studies

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

- Report case to state, territorial, or local health department and monitor for additional guidance as released
- Conduct additional hearing screen at age 6 months, plus any appropriate follow-up of hearing abnormalities detected through newborn hearing screening

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

- Carefully evaluate head circumference and developmental characteristics and milestones throughout the first year of life
 - Appropriate consultations with medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy)

Summary

- Zika virus continues to circulate and cause locally - transmitted disease in the Americas
- Consider the possibility of Zika virus infection in travelers with acute fever, rash, arthralgia, or conjunctivitis within 2 weeks after return

Summary

- A substantial increase in rates of congenital microcephaly have been reported in Brazil
- Pregnant women in any trimester should consider postponing travel to areas of Zika virus transmission
- Contact ADPH for ZIKA testing approval

Contact Information

- For consultation, Alabama physicians can contact the Alabama Department of Public Health Infectious Diseases and Outbreaks Division at 1-800-338-8347
- Visit www.adph.org/mosquito for the most updated information