

Zika Virus: An Update for Clinicians

**Satellite Conference and Live Webcast
Tuesday, May 24, 2016
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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 latest information on management and prevention of Zika virus disease**
- **Discuss current recommendations on diagnostic testing for Zika virus infection**
- **Articulate the importance of early recognition and reporting of cases**

Objectives

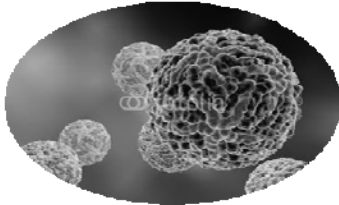
- **Review the latest recommendations for pregnant women and others with possible Zika virus exposure**
- **Discuss evaluation of infants with microcephaly, intracranial calcifications, and other abnormalities linked to maternal Zika virus infections**

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

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

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

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

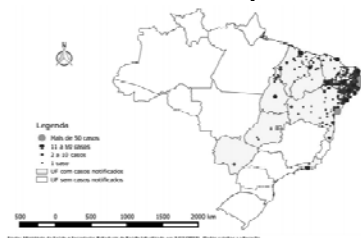
Zika Virus Epidemiology

- 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

- 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 May 11, 2016, U.S. states have reported a total of 503 travel-associated cases to CDC, including 48 in pregnant women and 10 cases of sexual transmission
 - Additionally, U.S. territories have reported 3 travel associated and 698 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 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

Zika Virus and Guillain-Barré Syndrome (GBS)

- The Brazilian 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
 - 6 cases (so far) in the U.S. and U.S. territories

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: Diagnostic Testing

Diagnostic Testing for Zika Virus

- Reverse transcriptase - polymerase chain reaction (rRT-PCR) for viral RNA in serum collected ≤ 7 days after illness onset
- Reverse transcriptase - polymerase chain reaction (rRT-PCR) for viral RNA in urine collected ≤ 14 days after illness onset

Diagnostic Testing for Zika Virus

- The Bureau of Clinical Laboratories (BCL) is performing Zika virus testing using the TrioPlex rRT-PCR which tests for Zika, dengue, and chikungunya
- Testing is performed on serum and urine

Diagnostic Testing for Zika Virus

- A commercial serum Zika test is currently available from Quest Diagnostics
- Real-time Reverse Transcriptase-polymerase chain reaction (rRT-PCR)
 - Indicated ≤ 7 days after illness onset

Diagnostic Testing for Zika Virus

- MAC-ELISA testing
 - Serology for IgM and neutralizing antibodies in serum collected ≥ 4 days after illness onset
 - Also performed in pregnant women between 2-12 weeks after return from travel

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 rRT-PCR on fixed tissues

Diagnostic Testing for Zika Virus

- HAN Alert sent out on May 18, 2016 asks all providers to continue to contact ADPH for consultation prior to ordering Zika testing
 - The Notifiable Disease Rules require reporting of all arboviral test results

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 appropriate tests are ordered and test results are interpreted correctly

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 14 days of illness onset) in a sterile container and seal with parafilm. Urine should be kept refrigerated (2 – 8 degrees C) until ready to be shipped.

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

- ✓ Urine and serum specimens should be shipped together.
- ✓ 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 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 drop-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 a local county health department to be couriered to BCL overnight (at no cost to submitter). Please contact the local county health department to coordinate with courier pick up times.

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 submitter's expense).
- ✓ If you have a question about specimen collection and shipping, call BCL at 334-260-3400 or email clab@adph.state.al.us

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 Division 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, microcephaly, intracranial calcifications and other congenital abnormalities
- 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 required to report suspected cases to the Alabama Department of Public Health, Infectious Diseases and Outbreaks Division, at 334-206-5971 or 1-800-338-8374

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 postpone travel to areas with ongoing Zika virus outbreaks

Zika Virus Preventive Measures

- People returning from a Zika-affected area should protect themselves from mosquito exposure for 3 weeks post return to prevent further transmission
 - To protect family, friends, and neighbors

Zika Virus and Pregnancy

Zika Virus and Pregnancy

- Now known that Zika virus infection can cause severe birth defects in some women exposed during pregnancy
- 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 and at the time of delivery
- No evidence to suggest pregnant women will have more serious illness if infected

Zika Virus and Pregnancy

- Illness onset occurs 2-12 days following the mosquito bite
- Illness is short lived, normally lasting less than one week
- Infected individuals usually do not require hospitalization or experience serious morbidity

Zika Virus and Pregnancy

- Zika virus is now known to cause adverse pregnancy outcomes, including birth defects and fetal loss

Perinatal Counseling: Limiting Exposure

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

Perinatal Counseling: Limiting Exposure

- No antiviral treatment, no prophylactic medication or vaccination is currently available for Zika virus infection

CDC Recommendations: Pregnant Women Considering Travel

- Pregnant women in any trimester should not 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 abstain from insertive sexual activity for the duration of the pregnancy

Recommendations for Evaluating Pregnant Travelers

- Ask pregnant women 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

- Testing (rRT-PCR) is recommended for pregnant women with clinical illness, i.e., the presence of one 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

- Lab testing for Zika virus is recommended for **MOST** pregnant women who have traveled to an affected area regardless of the presence of clinical illness
 - If the patient presents to a provider within 2-12 weeks of return from a Zika-affected area, IgM antibody testing can be performed

Diagnosis of Maternal Zika Virus Infection

- Laboratory evidence of maternal Zika virus infection can include Zika virus RNA detected by rRT-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

Diagnosis of Maternal Zika Virus Infection

- 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 Challenges:

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

Recommendations for Serology Testing

- 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 May 8-May 14, 2016
 - She says she developed a fever and rash on May 16
 - She presents to your office on May 19

Case # 1

- She has a history of travel to Colombia, a Zika virus affected area
- She has onset of symptoms within 2 weeks of travel return
- You have your nurse to call ADPH ID&O at 1-800-338-8374 because testing is needed

Case # 1

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

Case # 2

How would you manage this patient?

- A pregnant woman presents to your office at 20 weeks
- History of travel to Mexico, April 3-9, 2016 (16+0 to 16+6 weeks)
- She noted mosquito bites but no other complaints

Case # 2

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

Treatment is Supportive

- Includes rest, fluids, 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 regardless of test results 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

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

Confirmation of 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

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**
 - Apply insect repellent after sunscreen is applied to get best results

Zika Virus Disease Prevention for Pregnant Women

- Wear long-sleeved shirts and long 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 and night

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**

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 and the infant from birth through the first year of life**
- **Knowledge gained will assist in responding to the ongoing outbreak**

U.S. Zika Pregnancy Registry

- **Data collection time points for pregnancy include**
 - Initiation into care
 - 2nd Trimester
 - 3rd Trimester
 - Delivery
- **For additional information on the U.S. Zika Pregnancy Registry please access the following link <http://www.cdc.gov/zika/hc-providers/registry.html>**

Zika Virus and Sexual Transmission

Zika Virus and Sexual Transmission - What We Know

- **Zika virus can be sexually transmitted by a man to his male or female sex partners**
 - **As of May 11, 2016, 10 cases of sexually transmitted Zika virus have been reported in the U.S.**

Zika Virus and Sexual Transmission - What We Know

- **In known cases of sexual transmission, the men had Zika symptoms**
- **The virus can be spread before, during or after symptoms are present**

Zika Virus and Sexual Transmission - What We Know

- **The virus is present in semen longer than in blood**
- **Live virus has been found in semen up to 2 weeks after symptoms began**
- **Viral particles have been found in semen up to 62 days after symptoms began**

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

- **How long the virus is present in semen in men who have had Zika**
- **How long the virus can be spread through sex**
- **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
- Testing of asymptomatic males is not recommended for the purposes of determining if they are infected
 - A negative result does not mean that there is no Zika virus infection

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

- Couples in which a man had confirmed Zika virus infection or clinical illness consistent with Zika virus disease should consider using condoms or abstaining from sex for at least 6 months after onset of illness

MMWR, April 1, 2016

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

- Couples in which a man traveled to an area with active Zika virus transmission but did NOT develop symptoms of Zika virus disease should consider using condoms or abstaining from sex for at least 8 weeks after departure from the area

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 in 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

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

Microcephaly and Zika

What We Know

- Causal relationship between Zika and microcephaly
- Positive test result in some infants with microcephaly
- Pattern consistent with Fetal Brain Disruption Sequence
- Retrospective investigation in French Polynesia outbreak in 2013-2014
- Other intrauterine infections (ex. CMV) can cause microcephaly

Microcephaly and Zika

What We Do Not Know

- 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, intracranial calcifications, other abnormalities consistent with Zika born to women who traveled/resided in 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 the following:**
 - Thorough physical examination, including careful measurement of the head circumference, length, weight, and 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

Further Evaluation for All Infants with Possible Congenital Zika Virus Infection

- 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*

Further Evaluation for All Infants with Possible Congenital Zika Virus Infection

- 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

Additional Evaluation for Infants with Microcephaly or Intracranial Calcifications

- For infants with microcephaly, consultations are recommended 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 should be considered after testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus, lymphocytic choriomeningitis virus, and herpes simplex viruses

Further Testing for Infants with Microcephaly or Intracranial Calcifications

- Complete blood count, platelet count, and liver function and enzyme tests including alanine aminotransferase, aspartate aminotransferase, and bilirubin
- Consideration of genetic and other teratogenic causes based on additional congenital anomalies that are identified through clinical examination and imaging studies

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

- Report case to Alabama Department of Public Health
 - 1-334-206-5971 or 1-800-338-8374 and monitor for additional guidance as released
- Cases will be entered into U.S. Zika Pregnancy Registry

U.S. Zika Pregnancy Registry

- Data collection time points for infants
 - Neonatal assessment
 - 2 months
 - 6 months
 - 12 months
- For additional information on the U.S. Zika Pregnancy Registry please access the following link <http://www.cdc.gov/zika/hc-providers/registry.html>

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

- Conduct additional hearing screen at 6 months of age including any appropriate follow up of hearing abnormalities detected through routine 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
 - Use of 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 postpone travel to areas of Zika virus transmission
- Contact ADPH for ZIKA testing approval and consultation

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