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DHEC Health Advisory

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Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection – United States, 2016

On January 26, 2016 Centers for Disease Control and Prevention (CDC) published Interim Guidelines for the evaluation and testing of infants with possible congenital Zika virus infection in the Morbidity and Mortality Weekly Report (MMWR). This Health Advisory summarizes the CDC interim recommendations for the evaluation and testing of infants with possible congenital Zika virus infection, along with long-term follow-up recommendations. The full article can be accessed at http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3er.htm.

Summary

CDC has developed interim guidelines for health care providers in the United States caring for infants with possible congenital Zika virus infection. These guidelines include recommendations for testing and management of infants with microcephaly or intracranial calcifications born to women who traveled to or resided in an area with Zika virus transmission while pregnant or for infants born to mothers with positive or inconclusive test results for Zika virus infection. Guidance is subject to change as more information becomes available; the latest information, including answers to commonly asked questions, can be found online at http://www.cdc.gov/zika.

Background

Zika virus is a mosquito-borne flavivirus transmitted primarily by *Aedes aegypti* mosquitoes. These vectors also transmit dengue and chikungunya virus and are found throughout much of the Americas, including parts of the United States. Zika virus infections have also been documented through both intrauterine transmission resulting in congenital infection and intrapartum transmission from a viremic mother to her newborn.

Zika Virus Testing Considerations and Classification

The diagnosis of Zika virus infection is made through molecular and serologic testing. This includes reverse transcription-polymerase chain reaction (RT-PCR) for viral RNA, and immunoglobulin (Ig) M ELISA and plaque reduction neutralization test (PRNT) for Zika virus antibodies. Because it is currently not known which type of testing most reliably establishes the diagnosis of congenital infection, CDC recommends both molecular and serologic testing of infants who are being evaluated for evidence of a congenital Zika virus infection.

Indications for Testing Include:

- 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 Laboratory Testing for Infants when Indicated

- Test infant serum for Zika virus RNA, Zika virus immunoglobulin (Ig) M and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies. The initial sample should be collected either from the umbilical cord or directly from the infant within 2 days of birth, if possible.
- If cerebrospinal fluid is obtained for other studies, test for Zika virus RNA, Zika virus IgM and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies.
- Consider histopathologic evaluation of the placenta and umbilical cord with Zika virus immunohistochemical staining on fixed tissue and Zika virus RT-PCR on fixed and frozen tissue.
- If not already performed during pregnancy, test mother's serum for Zika virus IgM and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies.

Recommended Clinical Evaluation and Laboratory Testing for Infants with Possible Congenital Zika Virus Infection.

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

- Comprehensive physical examination, including careful measurement of the occipitofrontal circumference, length, weight, and assessment of gestational age.
- Evaluation for neurologic abnormalities, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions. Full body photographs and any rash, skin lesions, or dysmorphic features should be documented. If an abnormality is noted, consultation with an appropriate specialist is recommended.
- Cranial ultrasound, unless prenatal ultrasound results from third trimester demonstrated no abnormalities of the brain.
- Evaluation of hearing by evoked otoacoustic emissions testing or auditory brainstem response testing, either before discharge from the hospital or within 1 month after birth. Infants with abnormal initial hearing screens should be referred to an audiologist for further evaluation.
- Ophthalmologic evaluation, including examination of the retina, either before discharge from the hospital or within 1 month after birth. Infants with abnormal initial eye evaluation should be referred to a pediatric ophthalmologist for further evaluation.
- Other evaluations specific to the infant's clinical presentation.

For Infants with Microcephaly or Intracranial Calcifications, Additional Evaluation Includes the Following

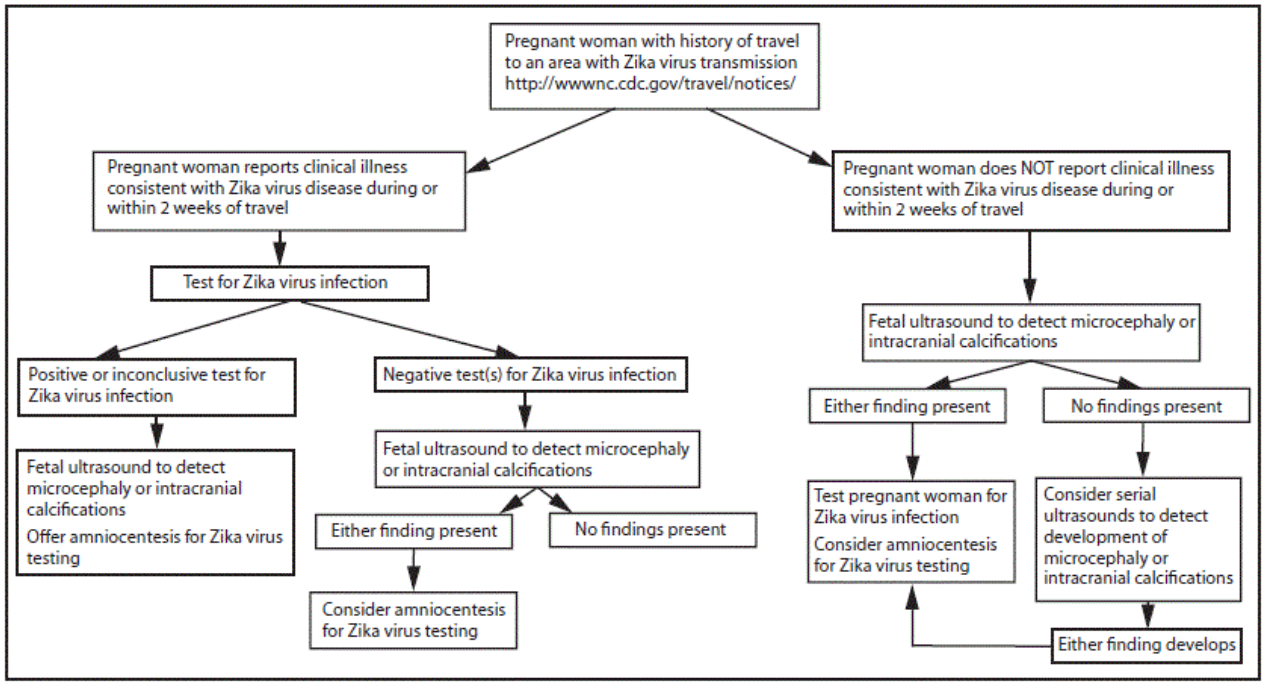
- Consultation with a clinical geneticist or dysmorphologist.
- Consultation with a pediatric neurologist to determine appropriate brain imaging and additional evaluation (e.g., ultrasound, computerized tomography scan, magnetic resonance imaging, and electroencephalogram).

- Testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infections. Consider consulting a pediatric infectious disease specialist.
- 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 for infants with possible congenital Zika virus infection

- Report case to state, territorial, or local health department and monitor for additional guidance as it is released.
- Conduct additional hearing screen at age 6 months, plus any appropriate follow-up of hearing abnormalities detected through newborn hearing screening.
- Carefully evaluate occipitofrontal circumference and developmental characteristics and milestones throughout the first year of life, with use of appropriate consultations with medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy).

Interim guidelines for the evaluation and testing of infants without microcephaly* or intracranial calcifications whose mothers traveled to or resided in an area with Zika virus transmission† during pregnancy§,¶,**



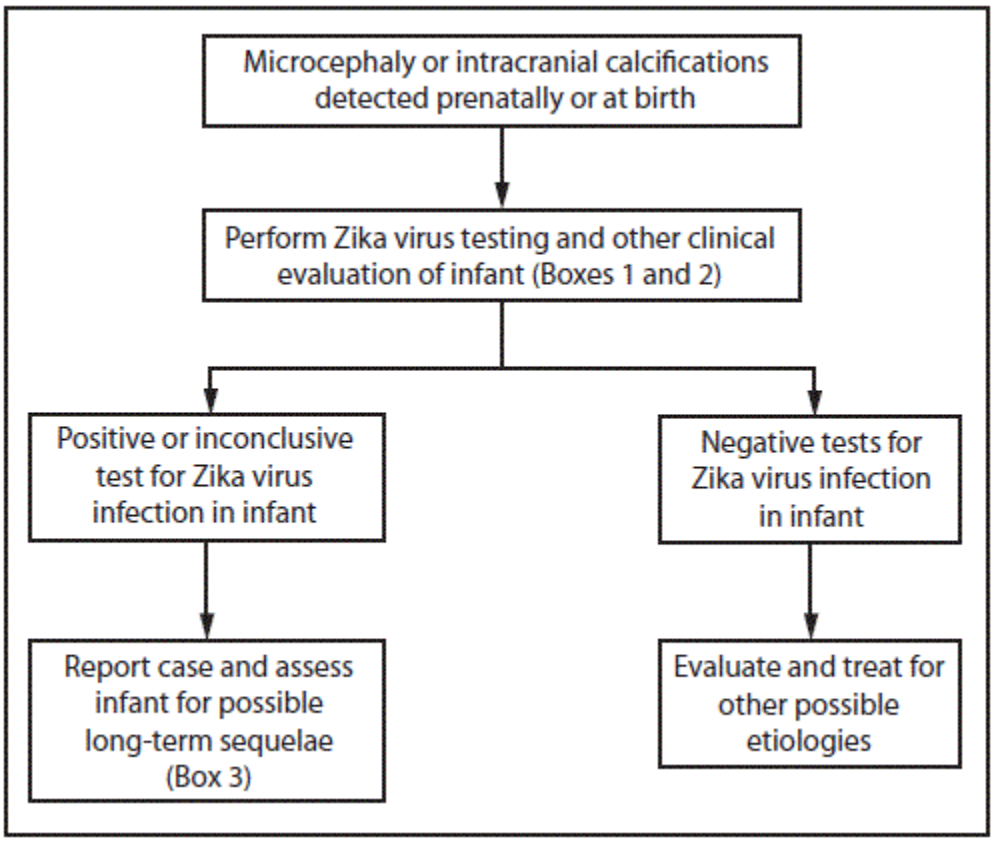
*Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex not explained by other etiologies.

† Areas with Zika virus transmission are listed on CDC's webpage. http://wwwnc.cdc.gov/travel/notices.

§ Laboratory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical sample, 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 would be considered inconclusive if Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers

¶ If mother reported clinical illness consistent with Zika virus disease during pregnancy and testing is indicated, perform Zika virus reverse transcription-polymerase chain reaction testing on serum specimen collected ≤7 days after illness onset when possible. Perform Zika and dengue virus IgM and neutralizing antibodies on serum specimens collected ≥4 days after illness onset. ** Clinical illness is consistent with Zika virus disease if two or more symptoms (including acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) are present during or within 2 weeks of any time spent in an area with ongoing Zika virus transmission.

Interim guidelines for the evaluation and testing of infants with microcephaly* or intracranial calcifications whose mothers traveled to or resided in an area with Zika virus transmission† during pregnancy§



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§ Laboratory evidence of Zika virus infection includes 1) detectable Zika virus, Zika virus RNA, or Zika virus antigen in any clinical sample, or 2) positive Zika virus immunoglobulin M with confirmatory neutralizing antibody titers that are ≥4-fold higher than dengue virus neutralizing antibody titers in serum or cerebrospinal fluid. Testing would be considered inconclusive if Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers.

Public Health Practitioners

- DHEC will investigate and facilitate testing for Zika virus disease reports in returning travelers from areas with documented transmission.
- Laboratory-confirmed Zika virus infections will be reported to CDC by DHEC.

DHEC contact information for reportable diseases and reporting requirements

Reporting of Zika virus is consistent with South Carolina Law requiring the reporting of diseases and conditions to your state or local public health department. (State Law # 44-29-10 and Regulation # 61-20) as per the DHEC 2016 List of Reportable Conditions available at: http://www.scdhec.gov/Library/CR-009025.pdf

Federal HIPAA legislation allows disclosure of protected health information, without consent of the individual, to public health authorities to collect and receive such information for the purpose of preventing or controlling disease. (HIPAA 45 CFR §164.512).

Regional Public Health Offices – 2016

Mail or call reports to the Epidemiology Office in each Public Health Region

MAIL TO:

Lowcountry	Midlands	Pee Dee	Upstate
4050 Bridge View Drive, Suite 600 N. Charleston, SC 29405 Fax: (843) 953-0051	2000 Hampton Street Columbia, SC 29204 Fax: (803) 576-2993	145 E. Cheves Street Florence, SC 29506 Fax: (843) 661-4859	200 University Ridge Greenville, SC 29602 Fax: (864) 282-4373

CALL TO:

Lowcountry	Midlands	Pee Dee	Upstate
Berkeley, Charleston, Dorchester Phone: (843) 953-0043 Nights/Weekends: (843) 441-1091	**Kershaw, Lexington, Newberry, Richland** Phone: (803) 576-2749 Nights/Weekends: (888) 801-1046	**Chesterfield, Darlington, Dillon, Florence, Marlboro, Marion** Phone: (843) 661-4830 Nights/Weekends: (843) 915-8845	**Anderson, Oconee** Phone: (864) 260-5801 Nights/Weekends: (866) 298-4442
Beaufort, Colleton, Hampton, Jasper Phone: (843) 322-2453 Nights/Weekends: (843) 441-1091	**Chester, Fairfield, Lancaster, York** Phone: (803) 286-9948 Nights/Weekends: (888) 801-1046	**Clarendon, Lee, Sumter** Phone: (803) 773-5511 Nights/Weekends: (843) 915-8845	**Abbeville, Greenwood, Laurens, McCormick** Phone: (864) 227-5947 Nights/Weekends: (866) 298-4442
Allendale, Bamberg, Calhoun, Orangeburg Phone: (803) 268-5833 Nights/Weekends: (843) 441-1091	**Aiken, Barnwell, Edgefield, Saluda** Phone: (803) 642-1618 Nights/Weekends: (888) 801-1046	**Georgetown, Horry, Williamsburg** Phone: (843) 915-8804 Nights/Weekends: (843) 915-8845	**Cherokee, Greenville, Pickens, Spartanburg, Union** Phone: (864) 372-3133 Nights/Weekends: (866) 298-4442

For information on reportable conditions, see http://www.scdhec.gov/Health/FHPF/ReportDiseasesAdverseEvents/ReportableConditionsInSC/

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Categories of Health Alert messages:

Health Alert	Conveys the highest level of importance; warrants immediate action or attention.
Health Advisory	Provides important information for a specific incident or situation; may not require immediate action.
Health Update	Provides updated information regarding an incident or situation; unlikely to require immediate action.
Info Service	Provides general information that is not necessarily considered to be of an emergent nature.