Questions and Answers for Pediatric Healthcare Providers: Infants and Zika Virus Infection

Summary

CDC has developed interim guidelines for healthcare providers in the United States caring for infants born to mothers who while pregnant traveled to or resided in an area with Zika virus transmission. These guidelines include recommendations for the evaluation, testing, and management of infants with and without microcephaly or intracranial calcifications detected. These interim guidelines will be updated as more information becomes available.

MMWR Interim Clinical Guidance for Pediatric Healthcare Providers (http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3er.htm?s_cid=mm6503e3er_e)

General Questions about Zika Virus Infection and Congenital Microcephaly

What is the link between Zika virus in Brazil and the high numbers of infants born there with microcephaly?

Zika virus infections have been confirmed in several infants with microcephaly from Brazil. The time frame and geographic location of reports of infants with microcephaly coincides with the outbreak of Zika virus infections in Brazil. The baseline prevalence of congenital microcephaly is difficult to determine because of underreporting, and the inconsistency of clinical criteria used to define microcephaly. Although population-based estimates of congenital microcephaly in Brazil vary, the number of infants with microcephaly currently being reported in Brazil is greater than would be expected.

What birth defects have been reported in in infants with confirmed Zika virus infection?

Brain abnormalities reported in infants with microcephaly and laboratory-confirmed congenital Zika infection include microcephaly and disrupted brain growth. Some infants with possible Zika virus infection have been found to have intracranial calcifications and abnormal eye findings. It is not known if Zika virus infection caused any of these abnormalities.

What birth defects have been reported in infants with suspected Zika virus infection?

A report of 35 infants with microcephaly (http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e2er.htm) who were born during an outbreak of Zikus virus infection in Brazil in 2015 described the following brain abnormalities: intracranial calcifications, ventriculomegaly, and neuronal migration disorders (lissencephaly and pachygyria). Other anomalies included congenital contractures and clubfoot. An important distinction is that neither these infants nor their mothers had laboratory-confirmed Zika virus; however, most of the mothers (~75%) reported symptoms consistent with Zika virus.

How is microcephaly diagnosed after birth?

Microcephaly is diagnosed when an infant's head is smaller than expected as compared to infants of the same age (or gestational age) and sex. Although a universally accepted definition of microcephaly does not exist, microcephaly is most often defined as head circumference (occipitofrontal circumference) greater than 2 standard deviations below the mean, or less than the 3rd percentile based on standard growth charts (e.g., Fenton, Olsen, CDC, or WHO growth curves (http://www.who.int/childgrowth/publications/technical_report_pub/en/)).

What are the potential sequelae of microcephaly?

For infants diagnosed with microcephaly, head size correlates with underlying brain size. However, these measurements do not consistently predict long term sequelae. Neurologic sequelae may include seizures, vision or hearing problems, and developmental disabilities. Symptoms vary with the extent of brain disruption.

Additional information about microcephaly.

What causes congenital microcephaly?

Causes of congenital microcephaly may include genetic conditions such as chromosomal abnormalities or maternal exposures (e.g., alcohol, mercury, or radiation) during pregnancy. Maternal infections that have been associated with microcephaly include cytomegalovirus (CMV), herpes simplex virus, rubella virus, lymphocytic choriomeningitis virus (LCMV), *Treponema pallidum* (i.e., syphilis), and *Toxoplasma gondii.*

What treatment exists for infants with congenital Zika virus infection?

No treatment is currently available for Zika virus infection. Care for these infants is focused on diagnosing and managing conditions that are present, monitoring the child's development over time, and addressing problems as they arise.

What is the prognosis for a newborn with congenital Zika virus infection?

The prognosis for infants with congenital Zika virus infection is not known. In infants with severe microcephaly from other causes, a range of neurologic sequelae have been reported (e.g., intellectual disability, hearing loss, vision loss, and seizures). These problems can range from mild to severe, are often life-long, and in some cases can be life-threatening.

Clinical Guidance Questions

Which newborns should be tested for Zika virus infection?

Testing for Zika virus infection is recommended for infants born to women who traveled to or resided in an area with ongoing Zika virus transmission during pregnancy who were 1) diagnosed with microcephaly or intracranial calcifications detected prenatally or at birth, or 2) who have mothers with positive or inconclusive test results for Zika virus infection.

How are infants diagnosed with Zika virus infection?

Zika virus infection can be diagnosed by performing reverse transcriptase-polymerase chain reaction (RT-PCR) on infant serum. Serology assays can also be used to detect Zika virus-specific IgM and neutralizing antibodies. However, since it has not been established which test is most reliable for a diagnosis in infants, RT-PCR and IgM tests should both be performed. Plaque-reduction neutralization testing (PRNT) can also be performed to measure virus-specific neutralizing antibodies and differentiate from other flaviviruses.

If Zika virus testing of a newborn is indicated, how is the test ordered?

There are no commercially available tests for Zika virus. Zika virus testing is performed at the CDC Arbovirus Diagnostic Laboratory and at some state and territorial health departments. Healthcare providers should contact their state and local health department to facilitate testing. See the Diagnostic Testing webpage for information on how to obtain Zika testing (http://www.cdc.gov/zika/hc-providers/diagnostic.html).

If Zika virus testing of a newborn is indicated, what specimens are recommended?

Zika virus RT-PCR and serology assays can be performed on infant serum or serum or plasma collected from the umbilical cord. If cerebrospinal fluid (CSF) specimens are available, Zika virus RT-PCR should be performed; however, CSF specimens should not be collected for the sole purpose of Zika virus testing. Other specimens that can be tested include the placenta and the umbilical cord. Histopathologic examination and immunohistochemical staining can be performed. Zika virus RT-PCR on fixed and frozen tissue should also be considered.

When is a newborn considered to have congenital Zika virus infection?

A newborn is considered to be congenitally infected if 1) Zika virus RNA is detected in any newborn specimen or during testing of amniotic fluid or the placenta, or 2) Zika virus IgM antibodies are detected along with confirmatory neutralizing antibody tiers that are ≥4-fold higher than dengue virus neutralizing antibody titers in the infant serum or cerebrospinal fluid (CSF). Testing for congenital infection is considered inconclusive if Zika virus IgM antibodies are detected but Zika virus neutralizing antibody titers are <4-fold higher than dengue virus neutralizing antibody titers.

What are the challenges in interpreting Zika virus testing in a newborn?

Zika virus testing in newborns has several challenges. RT-PCR tests may not detect Zika virus RNA in a newborn who had Zika virus infection *in utero* if the period of viremia has passed. Serologic tests for Zika virus can often be falsely positive because of cross-reacting antibodies against related flaviviruses (e.g., dengue and yellow fever viruses). Plaque-reduction neutralization testing (PRNT) can be performed to measure virus-specific neutralizing antibodies to Zika virus, but neutralizing antibodies may still yield cross-reactive results in newborns due to maternal antibodies that were transferred to the infant. It is important to work closely with state or territorial health departments to ensure the appropriate test is ordered and interpreted correctly.

Should health care providers report infants with positive or inconclusive Zika virus test results?

Health care providers should report positive or inconclusive results to their state or territorial health department. As an arboviral disease, Zika virus disease is a nationally notifiable condition.

What should health care providers do to evaluate infants with positive or inconclusive Zika virus test results?

A thorough physical examination should be performed, including careful measurement of the head circumference, length, weight, and assessment of gestational age. Cranial ultrasound is recommended unless it was performed as part of prenatal screening in the third trimester and clearly showed no abnormalities of the brain. Ophthalmologic evaluation is recommended as well as repeat hearing screen at six months of age. Continued evaluation of developmental characteristics and milestones, including head circumference, is recommended through the first year of life.

What additional evaluation is recommended for infants with positive or inconclusive Zika virus test results who have microcephaly or intracranial calcifications?

Consultations are recommended with a clinical geneticist or dysmorphologist, a pediatric neurologist, and a pediatric infectious disease specialist. A complete blood count, platelet count, and liver function tests should also be conducted. If any additional congenital anomalies are identified through clinical examination and imaging studies, genetic and other teratogenic causes should be considered.

What should health care providers do for an infant with negative test results for Zika virus infection?

For infant without suspected abnormalities, health care providers should continue with routine pediatric care. If the infant has microcephaly or intracranial calcifications, health care providers should continue to evaluate and treat for other possible etiologies.

If a mother had Zika virus infection during pregnancy but the newborn tests negative for Zika virus, what is recommended for additional follow-up?

If the newborn does not have abnormal findings on examination, the infant should receive routine pediatric care including measurement of growth and development, and appropriate evaluation and follow-up for any clinical findings that arise. If the newborn has abnormal findings on examination, diagnostic testing for other causes of the newborn's conditions should be performed including testing for other congenital viral infections if indicated.

If a mother had Zika virus infection during pregnancy, should she breastfeed her infant?

Although Zika virus RNA has been detected in breast milk, transmission of Zika infection through breastfeeding has not been documented. Based on available evidence, the benefits of breastfeeding infants outweigh any theoretical risk related to Zika virus infection.

For more information, please visit:

- CDC Travel Notices (http://wwwnc.cdc.gov/travel/notices/)
- CDC Zika Virus Home Page (http://www.cdc.gov/zika/index.html)
- CDC Zika Virus Obstetrical Healthcare Provider Q&A (http://www.cdc.gov/zika/pdfs/questions-answers-clinicians.pdf)
- **MMWR Clinical Guidance for Obstetrical Provider** (http://www.cdc.gov/mmwr/volumes/65/wr/mm6502e1er.htm?s_cid=mm6502e1er_e)

(http://www.cdc.gov/Other/plugins/#pdf)

Page last reviewed: January 26, 2016

Page last updated: January 26, 2016

Content source: Centers for Disease Control and Prevention (http://www.cdc.gov/)

National Center for Emerging and Zoonotic Infectious Diseases (NCEZID) (http://www.cdc.gov/ncezid)

Division of Vector-Borne Diseases (DVBD) (http://www.cdc.gov/ncezid/dvbd/index.html)