



The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
305 South Street, Jamaica Plain, MA 02130

CHARLES D. BAKER
Governor

KARYN E. POLITO
Lieutenant Governor

MARYLOU SUDDERS
Secretary

MONICA BHAREL, MD, MPH
Commissioner

Recommended Perinatal Testing and Evaluation of Infants Born to Mothers with Possible Zika Virus Exposure and Infants with Congenital Zika Virus Syndrome
August 3, 2017

1. Clinical Guidance and Testing Recommendations

Zika virus can be transmitted transplacentally leading to complications of pregnancy and birth defects. The complete range of adverse birth outcomes associated with Zika virus infection is unknown, but includes: microcephaly; intracranial calcifications; ventriculomegaly; arthrogryposis; abnormalities of the corpus callosum, cerebrum or cerebellum; fetal loss; and abnormalities in both vision and hearing. In addition, congenital Zika infection may result in a normal-appearing neonate, with developmental delay or other clinical problems emerging as the infant develops.

Given the potential range of adverse birth outcomes and the possibility that not all outcomes will be detectable at birth, laboratory testing of infants is recommended in the following situations:

- Infants born to mothers who had laboratory evidence of Zika virus infection during pregnancy;
- Infants who have abnormal clinical or neuroimaging findings consistent with congenital Zika virus syndrome, and a risk factor suggestive of possible maternal infection (including either travel or unprotected sexual contact with a partner who has traveled), regardless of maternal Zika virus test results.

Laboratory testing of placenta and fetal membrane tissue, or the mother, may also be indicated, depending upon circumstances.

Clinical Evaluation Recommendations for Infants with Known or Possible Congenital Exposure to Zika Virus

Pediatric providers must inquire about possible maternal and congenital Zika virus exposure for every infant. Infants meeting the criteria above should be tested within 2 days after birth (see below). All infants born to mothers with risk factors for Zika exposure during pregnancy or the periconceptual period (travel to or residence in an area with Zika virus - [See CDC world map of areas with Zika](#)) or unprotected sexual contact with a partner with travel to or residence in such area) should receive a comprehensive physical examination including standardized measurement of head circumference and a standard newborn hearing assessment prior to being discharged from the hospital.

In addition, based on maternal risk of Zika virus infection and the gestational timing of that exposure, providers should exercise clinical judgment and have a low threshold for consideration of ophthalmologic exam and head ultrasound, as abnormalities may exist even in apparently healthy infants. Comprehensive assessment, including evaluation for developmental delays, should continue until the infant is at least one year.

Assessment of increased risk for maternal Zika virus exposure and potential for congenital infection should include:

- Likelihood of patient's exposure based on recent reports of Zika virus activity at the travel destination;
- Likelihood of exposure to mosquitoes (based on time of year, scheduled activities, type of accommodations) duration of travel (longer stays may increase exposure risk) and adherence to mosquito bite prevention strategies;
- Likelihood of sexual exposure (evidence of RNA persistence in semen up to 6 months has been reported); and
- Infection during first and early second trimester, which carries greater risk for severe congenital defects.

If an infant is born with abnormalities consistent with congenital Zika virus syndrome, additional evaluation and management by a neurologist, infectious disease specialist, ophthalmologist, geneticist, and endocrinologist may be helpful in the first month of life. Please see CDC's MMWR [Updated Guidance for the Evaluation and Management of Infants with Possible Zika Virus Infection - United States, August 19, 2016](#) for additional information on clinical management of these infants.

2. Available Laboratory Testing Methods

Depending on the specific circumstances and the results of any previous Zika virus testing, specimens for testing may include infant serum and urine, maternal serum, and placental tissue and fetal membranes.

1. **RT-PCR:** Detection of Zika virus RNA indicates the presence of the virus itself. PCR for Zika RNA can be done on serum and urine collected within 2 days after birth.

Availability: Infant testing should be conducted at the Massachusetts State Public Health Laboratory rather than through commercial laboratories.

Interpretation and Limitations: A Zika positive PCR result in an infant specimen collected within 2 days of birth confirms congenital Zika virus infection. Few infants, even with clinically compatible evidence of congenital Zika virus syndrome, have tested positive for Zika virus infection.

2. **Anti-Zika virus IgM antibodies:** These may provide evidence of recent exposure in certain patients. Serum samples with a positive or equivocal anti-Zika virus IgM result must be confirmed by testing serum for the presence of neutralizing antibodies using the plaque reduction neutralization test (PRNT).

Availability: Infant testing should be conducted at the Massachusetts State Public Health Laboratory rather than through commercial laboratories.

Interpretation and Limitations: A positive IgM result on infant serum collected within 2 days of birth is interpreted as probable congenital Zika virus infection. PRNT (plaque reduction neutralizing testing) is not always indicated given this IgG test cannot distinguish between infant and maternal antibodies. It is estimated that maternal antibodies wane by 18 months and a test may be performed at that time to confirm or rule out congenital Zika virus infection.

3. **Tissue Testing:** Placental and fetal membrane tissue is tested using immunohistochemical methods.

Availability: Only with prior approval by CDC.

Interpretation and Limitations: Tissues positive for Zika virus by IHC do not necessarily indicate congenital infection, but can sometimes confirm the identity of the recently infecting flavivirus as Zika.

3. Collection of Specimens at Delivery

Please see the **Infant Diagnostic Testing Guidance Table** on page 4 to determine what tests are indicated for specific infants. Consultation with MDPH is required prior to submission and is available 24/7 by calling 617-983-6800.

The following information will be requested at the time of approval:

- Infant date of birth and gender;
- Gestational age at time of delivery;
- Infant measurements and percentiles, including head circumference, weight, and length;
- Presence of any abnormalities;
- Results of any testing (ex. hearing screening, head ultrasound, TORCH testing etc.); and
- Pediatrician contact information (if available).

Approved specimens should be submitted using the MA SPHL [clinical specimen submission form](#) and should include the information provided above for consistency.

Recommendations for Zika virus testing should be adapted to specific patient circumstances.

This table provides the current, best available guidance for the most common scenarios.

Specific information on [Specimen Collection, Storage and Shipment for Molecular, Serological and Tissue Testing for Zika Virus](#)

INFANT DIAGNOSTIC TESTING GUIDANCE TABLE - consultation with MDPH is required and available 24/7 by calling 617-983-6800

| Category | Sample Type | Timing | Additional Notes About Testing |
|--|--|---|--|
| Infants born to mothers with confirmed laboratory evidence of Zika virus infection ¹ | <ul style="list-style-type: none"> • Infant serum (≥1 mL) • Infant urine | Specimens from infant ≤ 2 days after delivery | Infant testing is recommended even if infant appears clinically well |
| Infants born to mothers with evidence of infection with a non-specified flavivirus ² | <ul style="list-style-type: none"> • Infant serum (≥1 mL) • Infant urine | Specimens from infant ≤ 2 days after delivery | Infant testing is recommended even if infant appears clinically well |
| Infants born with identified abnormalities OR Fetus with identified abnormalities detected on ultrasound AND Maternal risk factor for Zika virus infection ³ AND mother did NOT have laboratory-confirmed Zika virus infection | <ul style="list-style-type: none"> • Infant serum (≥1 mL) • Infant urine • Formalin-fixed placenta tissues • Maternal serum and urine if not previously tested • Amniotic fluid can be considered | Specimens from infant ≤ 2 days after delivery | Amniocentesis has inherent risks and a decision to perform it should be made in context and with informed discussion. The ability of a negative amniotic fluid RT-PCR to exclude infection is not known. |
| Fetal losses, miscarriages, or still births AND Maternal risk factor for Zika virus infection ³ AND mother did NOT have laboratory-confirmed Zika virus infection | Products of conception – contact MDPH to discuss whether testing is indicated and specific specimens to submit | Contact MDPH to discuss | Specific specimens will depend on gestational age of fetus and will require consultation with an epidemiologist |

¹Confirmatory laboratory evidence of Zika virus infection includes detection of viral RNA in maternal serum or urine (PCR positive), or an anti-Zika IgM antibody positive result **with** positive Zika neutralizing antibody titers and negative titers against dengue (<10)

²Evidence of infection with an unspecified flavivirus includes a positive or equivocal IgM antibody for Zika virus with positive neutralizing antibody titers for both Zika and Dengue

³Risk factors for maternal Zika virus infection include travel to or residence in an area with Zika virus ([See CDC world map of areas with Zika](#)) or unprotected sexual contact with a partner with travel to or residence in such area.

4. ADDITIONAL RESOURCES

Caring for Infants and Children

- [Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection - United States, August 2016](#) (Aug. 19, 2016)
- [Interim Guidelines for Healthcare Providers Caring for Infants and Children with Possible Zika Virus Infection – United States, February 2016](#) (Feb. 26, 2016)
- [Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection — United States 2016](#) (January 29, 2016)
- CDC: [Clinical Guidance for Healthcare Providers caring for Infants with possible congenital Zika virus](#)
- CDC: [Initial Evaluation and Outpatient Management During the First 12 Months of Life for Infants with Possible Congenital Zika Virus Infection](#)
- CDC: [Clinical Guidance: Evaluation and Potential Outcomes](#)
- CDC: [Resources and Guidance for Healthcare Providers Caring for Infants Affected by Zika Virus](#)