Updated Interim Guidance for the Diagnosis, Evaluation and Management of Infants with Possible Congenital Zika Virus Infection

Margaret Fisher, MD, FAAP

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Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017

Tolulope Adebamjo, MD1,2; Shana Godfred-Cato, DO3; Laura Vien, MD4; Marc Fischer, MD5; J. Erin Staples, MD, PhD5; Wendi Kuhner-Tallman, PhD6; Henry Walke, MD7; Titilope Oduyebo, MD8; Kara Polen, MPH9; Georgina Peacock, MD10; Dana Meaney-Delman, MD4; Margaret A. Honein, PhD9; Sonja A. Rasmussen, MD11; Cynthia A. Moore, MD, PhD9; Contributors

OVERVIEW OF CHANGES

• Guidance defines three groups of infants:
  1. Infants with birth defects consistent with CZS born to mothers with possible Zika virus exposure during pregnancy (regardless of mother’s Zika virus test results)
  2. Infants without birth defects consistent with CZS born to mothers with lab evidence of possible Zika virus infection during pregnancy
  3. Infants without birth defects consistent with CZS born to mothers with possible Zika virus exposure during pregnancy but with no lab evidence of infection

• Updated information on interpreting lab testing results
• Updated recommendations for vision and hearing screening
• Some previously suggested screenings no longer recommended
FIGURE: Recommendations for the evaluation of infants with possible congenital Zika virus infection based on infant clinical findings, maternal testing results, and infant testing results

1. Ask about possible maternal Zika virus exposure
   - Possible Zika virus exposure
     - Does infant have findings consistent with CZS?
       - Yes
         - Initial evaluation:
           - Standard evaluation
           - Zika virus NAT and IgM testing
           - Consider Zika virus NAT and IgM testing on CSF
           - Head ultrasound by age 1 month
           - Comprehensive ophthalmologic exam by age 1 month
           - Automated ABR by age 1 month
           - Evaluate for other causes of congenital anomalies
           - Refer to developmental specialist and early intervention services
           - Provide family support services
           - Consider additional consultations with:
             - Infectious disease specialist
             - Clinical geneticist
             - Neurologist
             - Other clinical specialists based on clinical findings of infant
       - No
         - Initial evaluation normal?
           - Yes
             - Is there laboratory evidence of congenital Zika virus infection?
               - Laboratory evidence of congenital Zika virus infection
                 - Infant should continue to receive routine care, and health care providers should remain alert for any new findings of congenital Zika virus infection
               - No laboratory evidence of congenital Zika virus infection
                 - Testing and clinical evaluation for congenital Zika virus infection beyond a standard evaluation is not routinely recommended. If findings suggestive of CZS are identified at any time, refer to appropriate specialists and evaluate for congenital Zika virus infection.
           - No
             - Is there laboratory evidence of possible maternal Zika virus infection during pregnancy?
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                 - Initial evaluation:
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                   - Zika virus NAT and IgM testing
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STANDARD EVALUATION FOR ALL INFANTS WITH POSSIBLE ZIKA EXPOSURE DURING PREGNANCY

Should occur at birth and at each well-visit:

• Comprehensive physical exam, including growth parameters
• Developmental monitoring and screening
• Vision screening
• Newborn hearing screen at birth, preferably with automated auditory brainstem response
KEY CHANGES BY GROUP
INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

• Monitor for an expanded list of potential problems including difficulty breathing or swallowing and hydrocephaly after birth
• Follow-up care no longer guided by Zika virus testing results
KEY CHANGES BY GROUP:
INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

• Coordinated care by a multidisciplinary team and an established medical home is recommended

• Consider consultation with following specialists:
  – Infectious disease specialist for evaluation of other congenital infections
  – Neurologist by age 1 month
  – Ophthalmologist by age 1 month
  – Clinical geneticist
  – Early intervention and developmental specialists
  – Family and supportive services

• Possible consultations based on clinical findings of infant:
  – Endocrinologist
  – Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist
  – Orthopedist, physiatrist, or physical therapist
  – Pulmonologist or otolaryngologist for concerns about aspiration
KEY CHANGES BY GROUP:

INFANTS WITH BIRTH DEFECTS CONSISTENT WITH CZS BORN TO MOTHERS WITH POSSIBLE ZIKA VIRUS EXPOSURE DURING PREGNANCY

• Infants in this group no longer need:
  – Thyroid testing unless clinical symptoms indicate an issue
  – Diagnostic ABR test at 4-6 months if they passed newborn screening using automated ABR
Infants should receive a comprehensive eye exam by an ophthalmologist by age 1 month (same as infants with indications of Zika)
KEY CHANGES BY GROUP:

Infants Without Clinical Findings Consistent with Zika Born to Mothers with Exposure to Zika but Without Lab Evidence of Exposure During Pregnancy

• Includes infants born to mothers who:
  – Were never tested during pregnancy
  – Tested negative but still had possible exposure to Zika
• These infants require no testing or clinical evaluation beyond standard evaluation and routine preventative care
• Laboratory testing of these infants not routinely recommended
• If at any time findings consistent with CZS are made, appropriate referrals and evaluation should follow
TESTING RECOMMENDATIONS FOR CONGENITAL ZIKA VIRUS INFECTION

- Testing is recommended for:
  - Infants with clinical findings consistent with CZS and
  - Infants without clinical findings consistent with CZS who were born to mothers with lab evidence of possible Zika virus exposure during pregnancy

- Concurrent Zika virus RNA nucleic acid testing (NAT) of serum and urine and Zika virus IgM testing of serum should be performed within a few days after birth, if possible
**INTERPRETING TEST RESULTS FOR CONGENITAL ZIKA VIRUS INFECTION**

**Infant test result (serum, urine or cerebrospinal fluid)**

<table>
<thead>
<tr>
<th>NAT</th>
<th>IgM</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>Positive</td>
<td>Any result</td>
<td>Confirmed congenital Zika virus infection(1)</td>
</tr>
<tr>
<td>Negative</td>
<td>Nonnegative*</td>
<td>Probable congenital Zika virus infection(2)(4)</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Congenital Zika virus infection unlikely(3)(4)</td>
</tr>
</tbody>
</table>

*Nonnegative serology terminology varies by assay and might include “positive,” “equivocal,” “presumptive positive,” or “possible positive”

- (1) Distinguishing between congenital and postnatal infection is difficult in infants who live in areas with ongoing Zika virus transmission and who are not tested soon after birth. If timing of infection cannot be determined, evaluate infants as if they have congenital Zika virus infection.
- (2) If Zika virus plaque reduction neutralization test is negative, this suggests infant’s IgM test is a false positive.
- (3) Congenital Zika virus infection is unlikely if specimens are collected within first few days after birth and clinical evaluation is normal, but providers should remain alert for any new findings.
- (4) Lab results should be interpreted in context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with CZS, and any confirmatory testing with plaque reduction neutralization testing.
Testing Recommendations for Postnatal Zika Virus Infection

• Guidance for testing and clinical management of infants and children with postnatal Zika virus infection is in line with recommendations for adults
  – Zika virus PCR and serologic testing is recommended during the first 2 weeks after symptom onset to diagnose postnatal Zika virus disease.
  – Serologic testing is recommended 2-12 weeks after symptom onset
AAP Call to Action

• In the wake of recent hurricanes, pediatricians may see displaced families from areas with Zika outbreaks who need additional care

• CDC is urging providers to be vigilant for these women and children from Puerto Rico and the US Virgin Islands

• AAP News article, October 24, 2017:
CDC RESOURCES

Health Care Providers Caring for Infants and Children.