Additional Considerations for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection

Infant Zika Evaluation and Management

Based on previous CDC interim guidance (1), all infants born to mothers with laboratory evidence of Zika virus infection* during pregnancy should receive

- Comprehensive physical exam
- Head ultrasound
- Standard newborn hearing assessment
- Zika virus laboratory testing†

In addition, Zika virus laboratory testing is recommended for infants who have abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a maternal epidemiologic link§ suggesting possible exposure during pregnancy, regardless of maternal Zika virus test results.

Further evaluation, based on the results of the clinical evaluation and laboratory testing, should be performed in accordance with CDC Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm).

Possible Limitations of Infant Laboratory Testing

The optimal methods to test for congenital Zika virus infection are unknown. Because data on testing for congenital Zika virus infection are limited, current CDC infant testing guidance is based on experience with other congenital infections. Two recent studies describe a small number of infants with clinical findings consistent with congenital Zika syndrome in whom results of laboratory testing for Zika virus infection were negative (2, 3). Negative test results might occur in an infant with clinical findings of possible congenital Zika virus syndrome for several reasons:

- The clinical findings are due to another cause
- Testing was incomplete (e.g., RNA testing without antibody testing), performed on suboptimal specimens (e.g., cord blood rather than blood obtained from the infant), or performed too late (e.g., after RNA and IgM antibodies had cleared or waned) (4)
- The fetus failed to mount an IgM antibody response; it is unknown if some fetuses infected early in gestation might not mount an IgM antibody response (5)

New Considerations for Evaluation of Infants with Possible Congenital Zika Virus Infection

For infants who meet one or more of the criteria for testing for Zika virus infection, healthcare providers should test† and evaluate them in accordance with the updated CDC interim infant testing guidance (https://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w). However, there are some additional considerations to take into account:

Testing of cerebrospinal fluid (CSF)

CDC interim infant testing guidance recommends that Zika virus testing should be performed on CSF if it is/was collected for other reasons. However, there are limited reports of congenital Zika virus infection in which CSF was the only sample testing positive (3). Therefore, healthcare providers should consider obtaining CSF for Zika virus RNA and IgM antibody testing in infants with clinical findings of possible congenital Zika syndrome but whose initial laboratory tests are negative on serum and urine.

Testing of infants whose mothers have possible Zika virus exposure during pregnancy but were not tested or were tested more than 12 weeks after maternal exposure or symptoms

- Infants born to mothers with an epidemiologic link[§] to an area with risk of Zika and a CDC travel notice (https://wwwnc.cdc.gov/travel/page/zika-information) and for whom maternal testing was not performed before delivery or was performed more than 12 weeks after maternal exposure should have a comprehensive physical examination, including standardized measurement of head circumference.
    - Maternal diagnostic testing should be performed if exposure is within the last 12 weeks[¶], and testing of the placenta for Zika virus PCR should be considered (https://www.cdc.gov/zika/hc-providers/test-specimens-at-time-of-birth.html).
- Infant testing should be performed if maternal testing is consistent with laboratory evidence of Zika virus infection.
    - If an infant appears clinically well, further evaluation, including head ultrasound and infant laboratory Zika virus testing, can be deferred until maternal test results are available.
- If there is concern about infant follow-up or maternal testing is not performed or negative in the setting of an exposure that occurred more than 12 weeks earlier, head ultrasound, ophthalmologic assessment, and infant Zika virus testing should be considered before hospital discharge.

Testing beyond 2 days of life

CDC interim guidance for infants with possible congenital Zika virus infection recommends testing specimens collected from infants within 2 days after birth. If specimens are collected later, it may be difficult to distinguish congenital from postnatally acquired infection in areas with risk of Zika. Despite this limitation, testing specimens collected within the first few weeks to months after birth may still be useful in the evaluation for possible congenital Zika virus infection, especially among infants born in areas without risk of Zika.

Imaging

A head ultrasound is recommended before hospital discharge or within one month of birth for infants with possible Zika virus infection. For infants with a small or absent anterior fontanelle and poor visualization of the intracranial anatomy on ultrasound, other imaging (i.e., magnetic resonance imaging or computed tomography) should be considered.

Maintain a level of suspicion

For infants without laboratory evidence of Zika virus infection but for whom suspicion for congenital Zika virus infection remains, healthcare providers should

- Evaluate for other causes of congenital infection
- Consider an ophthalmology exam and auditory brainstem response (ABR) hearing test before hospital discharge or within 1 month of birth
- Consider performing other evaluation and follow up in accordance with CDC interim guidance for the evaluation and management of infants with possible congenital Zika virus infection (https://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w)

*Laboratory evidence of maternal Zika virus infection includes 1) Zika virus RNA detected by nucleic acid testing (NAT) (e.g., rRT-PCR) in any clinical specimen; or 2) positive Zika virus IgM antibodies with confirmatory neutralizing antibody titers obtained via plaque reduction neutralization testing (PRNT). Confirmatory neutralizing antibody titers are needed in addition to IgM antibodies for laboratory evidence of maternal Zika virus infection.

† Infant serum and urine should be tested for Zika virus by Zika NAT, and infant serum for Zika virus IgM antibodies. If CSF is obtained, it can also be tested. If the mother has not been tested, infant specimens that are IgM positive should be confirmed by PRNT. Specimen collection should ideally be performed within the first 2 days after birth.

§ An epidemiologic link includes travel to or residence in an area with risk of Zika (https://www.cdc.gov/zika/geo/index.html) or sex without a condom with a partner who traveled to or lived in such an area.

¶For pregnant women with possible Zika virus exposure who seek care >12 weeks after symptom onset or possible exposure, IgM antibody testing might be considered. However, a negative IgM antibody test or rRT-PCR result >12 weeks after symptom onset or possible exposure does not rule out recent Zika virus infection because IgM antibody and viral RNA levels decline over time.

References

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