Health Update

KITSAP PUBLIC HEALTH DISTRICT

February 25, 2016

Adherence to sexual transmission prevention guidelines for Zika virus especially important in light of new reports; updates issued for caring for infants/children with possible Zika infection

Actions Requested

- **Advise patients at risk (i.e., travelers to or residents in affected areas) to adhere to current recommendations for preventing sexual transmission of Zika virus,** particularly men with pregnant partners.
- **Be aware that maternal-infant transmission during delivery is possible.** Suspect acute Zika virus disease in an infant <=2 weeks old with a clinically compatible illness if the mother was in an affected area within 2 weeks of delivery.
- **Read the attached CDC guidelines** on (1) sexual transmission and (2) caring for infants/children.
- **Contact our Communicable Disease staff to report any suspect cases and request Zika virus testing**. Please call us prior to collecting specimens and have relevant travel/exposure history and clinical information available.

For questions, please contact our Communicable Disease staff at 360-337-5235.

Background

The Centers for Disease Control and Prevention (CDC) recently issued a health alert strongly encouraging adherence to the current recommendations for protecting people against sexual transmission of Zika virus. Since the original interim guidelines were published (which discussed only 3 cases related to sexual transmission), there are now 14 additional reports of possible sexual transmission under investigation in the U.S. Several involve pregnant women. In all events for which information is available, travelers reported symptom onset within 2 weeks prior to their non-traveling female partner's symptom onset. Zika virus might persist in semen for longer than it is detectable in blood. Abstinence or condom use are recommended for the duration of pregnancy. If the female partner is not pregnant, couples still might consider abstaining or condoms. Sexual transmission from infected women to their sex partners has not been documented, nor has transmission from persons who are asymptomatically infected.

Acute Zika virus disease is thought to be mild in children as it generally is in adults. Acute infections should be suspected in children (aged 0-18 years) if the child has 2 or more of: fever, rash, conjunctivitis, or arthralgia AND either (a) traveled to a Zika affected area or (b) is an infant within the first 2 weeks of life born to a mother who was in a Zika affected area within 2 weeks of delivery. Congenital infections can result from intrauterine transmission during pregnancy; prior guidance on evaluating such potential infections remains essentially the same. Infants without microcephaly or intracranial calcifications whose mothers tested negative for Zika virus or were not tested for Zika virus should receive routine care.

It is important to rule-out dengue and chikungunya when considering Zika. Testing for Zika virus is currently limited to CDC and certain other public health labs; approval from our Communicable Disease staff must be obtained prior to submission.

Resources

(1) CDC Zika virus website for healthcare providers: www.cdc.gov/zika/hc-providers/index.html
(2) Previous Zika virus health alerts: http://www.kitsappublichealth.org/healthcare/provider_archives.php

Attachments: (1) CDC Health Advisory "Update: Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016" (Feb. 23, 2016).
(2) "Update: Interim Guidelines for Health Care Providers Caring for Infants and Children with Possible Zika Virus Infection — United States, February 2016" (MMWR, Feb. 19, 2016).

This is an official

CDC HEALTH ADVISORY

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Update: Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016

Summary: The Centers for Disease Control and Prevention (CDC) recently published recommendations for protecting people against sexual transmission of Zika virus (1). As stated in that report, information about possible sexual transmission of Zika virus was based on one published report of transmission from a man to a woman, one published report in which Zika virus was detected in semen of a man with hematospermia, and one case of possible sexual transmission then under investigation in Texas. An additional case of Zika virus detected in semen in a man was reported after the CDC recommendations were published (2). As of February 23, 2016, CDC and state public health departments are investigating 14 additional reports of possible sexual transmission of the virus, including several involving pregnant women. While additional investigations are being completed, CDC is issuing this HAN Advisory as a strong reminder to state, local, and US territorial public health departments, clinicians, and the public to be aware of and adhere to current recommendations for preventing sexual transmission of Zika virus, particularly for men with pregnant partners. These recommendations may change as more information becomes available.

Background

CDC is working with state, local, and US territorial public health departments, US Government agencies, and international partners in response to outbreaks of Zika virus disease (Zika) in multiple territories and countries in the Americas. Accumulating evidence links maternal Zika virus infection with congenital microcephaly, miscarriages, and other adverse fetal outcomes (3). In addition, there are reports of a possible association with Guillain-Barré syndrome (4). No vaccine or specific antiviral drug is currently available to prevent or treat Zika.

Zika virus is spread primarily by the bite of infected *Aedes* species mosquitoes (most commonly, *Aedes aegypti*). In areas where Zika virus transmission is ongoing, people should follow precautions to prevent mosquito bites (http://www.cdc.gov/zika/prevention/). Sexual transmission of Zika virus also can occur and is of particular concern during pregnancy. In early February 2016, the Dallas County Department of Health and Human Services announced an occurrence of sexually transmitted Zika infection (5). On February 5, 2016, following the confirmation of this Texas sexual transmission event, CDC published interim guidelines for preventing sexual transmission of Zika virus (1).

As of February 23, 2016, CDC and state public health departments are investigating 14 additional reports of possible sexual transmission of the virus, including several events involving possible transmission to pregnant women. In two of these new suspected sexual transmission events that have been investigated to date, Zika virus infection has been confirmed in women whose only known risk factor was sexual contact with an ill male partner who had recently travelled to an area with local Zika virus transmission; testing for the male partners is pending. For four additional suspected sexual transmission events, preliminary laboratory evidence (IgM antibody test) is available for the women, but confirmatory testing is still pending. For eight suspected events, the investigation is ongoing. In all events for which information is available, travelers reported symptom onset within 2 weeks prior to their non-traveling female partner's symptom onset.

Because these reports suggest sexual transmission may be a more likely means of transmission for Zika virus than previously considered, CDC is issuing this HAN Advisory to underscore the importance of adhering to the interim guidance published on February 5 and outlined below. The recommendations, which apply to men who reside in or have traveled to areas with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices/) and their sex partners, will be revised as more information becomes available.

Recommendations for men and their pregnant partners
Men who reside in or have traveled to an area of active Zika virus transmission who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex (i.e., vaginal intercourse, anal intercourse, or fellatio) for the duration of the pregnancy. Pregnant women should discuss their male partner's potential exposures to mosquitoes and history of Zika-like illness (http://www.cdc.gov/zika/symptoms) with their health care provider; providers can consult CDC's guidelines for evaluation and testing of pregnant women (6).

Recommendations for men and their nonpregnant sex partners
Men who reside in or have traveled to an area of active Zika virus transmission who are concerned about sexual transmission of Zika virus might consider abstaining from sexual activity or using condoms consistently and correctly during sex. Couples considering this personal decision should take several factors into account. Most infections are asymptomatic, and when illness does occur, it is usually mild with symptoms lasting from several days to a week; severe disease requiring hospitalization is uncommon. The risk for acquiring vector-borne Zika virus in areas of active transmission depends on the duration and extent of exposure to infected mosquitoes and the steps taken to prevent mosquito bites (http://www.cdc.gov/zika/prevention). After infection, Zika virus might persist in semen when it is no longer detectable in blood; studies to determine the duration of persistence in semen are not yet completed.

Accumulating evidence of sexual transmission suggests that exposure to Zika virus includes unprotected sexual contact with a symptomatic male partner who resides in or has traveled to an area of active Zika virus transmission. Zika virus testing is currently recommended to establish a diagnosis of infection in exposed persons with signs or symptoms consistent with Zika virus disease, and may be offered to asymptomatic pregnant women with possible exposure to Zika virus (6). However, interpretation of results is complex, and health care providers should contact their state, local, or territorial health department for assistance with arranging testing and interpreting results. At this time, testing of exposed, asymptomatic men for the purpose of assessing risk for sexual transmission is not recommended. Sexual transmission of Zika virus from infected women to their sex partners has not been documented, nor has transmission from persons who are asymptomatically infected. Sexual transmission of many infections, including those caused by other viruses, is reduced by consistent and correct use of latex condoms.

As we learn more about the incidence and duration of seminal shedding from infected men and the utility and availability of testing in this context, recommendations to prevent sexual transmission of Zika virus will be updated.

References

1. Oster AM, Brooks JT, Stryker JE, et al. Interim Guidelines for prevention of sexual transmission of Zika virus — United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:120–121. http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e1.htm
2. Atkinson B, Hearn P, Afrough B, et al. Detection of Zika virus in semen [letter]. Emerg Infect Dis. 2016 May [*cited February 22, 2016*]. http://dx.doi.org/10.3201/eid2205.160107
3. Martines RB, Bhatnagar J, Keating MK, et al. Evidence of Zika virus infection in brain and placental tissues from two congenitally infected newborns and two fetal losses — Brazil, 2015. *MMWR Morb Mortal Wkly Rep*. 2016;65 (Early Release)(06):1-2. http://www.cdc.gov/mmwr/volumes/65/wr/mm6506e1.htm?s_cid=mm6506e1_e. Published February 19, 2016.
4. European Centre for Disease Prevention and Control. Rapid risk assessment: Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome – 10 December

2015. http://ecdc.europa.eu/en/publications/Publications/zika-virus-americas-association-with-microcephaly-rapid-risk-assessment.pdf. Published 2015. Accessed Feb 1, 2016.
5. Dallas County Health and Human Services. DCHHS reports first Zika virus case in Dallas County acquired through sexual transmission. February 2, 2016. http://www.dallascounty.org/department/hhs/press/documents/PR2-2-16DCHHSReportsFirstCaseofZikaVirusThroughSexualTransmission.pdf
6. Oduyebo T, Petersen EE, Rasmussen SA, et al. Update: interim guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65. http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2.htm?s_cid=mm6505e2_e

For More Information

- General information about Zika virus and disease: http://www.cdc.gov/zika/
- Zika virus information for clinicians: http://www.cdc.gov/zika/hc-providers/index.html
- Protection against mosquitoes: http://wwwnc.cdc.gov/travel/yellowbook/2016/the-pre-travel-consultation/protection-against-mosquitoes-ticks-other-arthropods
- Travel notices related to Zika virus: http://wwwnc.cdc.gov/travel/notices
- Information about Zika virus for travelers and travel health providers: http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/zika
- HAN Advisory: Recognizing, managing, and reporting Zika virus infections in travelers returning from Central America, South America, the Caribbean, and Mexico. January 15, 2016. http://emergency.cdc.gov/han/han00385.asp
- Pan American Health Organization PAHO): http://www.paho.org/hq/index.php?option=com_content&view=article&id=11585&Itemid=41688&lang=en
  Approximate distribution of *Aedes aegypti* and *Ae. albopictus* mosquitoes in the United States: http://www.cdc.gov/chikungunya/resources/vector-control.html

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Categories of Health Alert Network messages:

Health Alert	Requires immediate action or attention; highest level of importance
Health Advisory	May not require immediate action; provides important information for a specific incident or situation
Health Update	Unlikely to require immediate action; provides updated information regarding an incident or situation
HAN Info Service	Does not require immediate action; provides general public health information

##This message was distributed to state and local health officers, state and local epidemiologists, state and local laboratory directors, public information officers, HAN coordinators, and clinician organizations##

Centers for Disease Control and Prevention
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Update: Interim Guidelines for Health Care Providers Caring for Infants and Children with Possible Zika Virus Infection — United States, February 2016

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CDC has updated its interim guidelines for U.S. health care providers caring for infants born to mothers who traveled to or resided in areas with Zika virus transmission during pregnancy and expanded guidelines to include infants and children with possible acute Zika virus disease (*1*). This update contains a new recommendation for routine care for infants born to mothers who traveled to or resided in areas with Zika virus transmission during pregnancy but did not receive Zika virus testing, when the infant has a normal head circumference, normal prenatal and postnatal ultrasounds (if performed), and normal physical examination. Acute Zika virus disease should be suspected in an infant or child aged <18 years who 1) traveled to or resided in an affected area within the past 2 weeks and 2) has ≥2 of the following manifestations: fever, rash, conjunctivitis, or arthralgia. Because maternal-infant transmission of Zika virus during delivery is possible, acute Zika virus disease should also be suspected in an infant during the first 2 weeks of life 1) whose mother traveled to or resided in an affected area within 2 weeks of delivery and 2) who has ≥2 of the following manifestations: fever, rash, conjunctivitis, or arthralgia. Evidence suggests that Zika virus illness in children is usually mild (*2*). As an arboviral disease, Zika virus disease is nationally notifiable. Health care providers should report suspected cases of Zika virus disease to their local, state, or territorial health departments to arrange testing and so that action can be taken to reduce the risk for local Zika virus transmission. As new information becomes available, these guidelines will be updated: http://www.cdc.gov/zika/.

Zika virus is primarily transmitted to humans through the bite of *Aedes* species mosquitoes, most commonly *Aedes aegypti* and possibly *Aedes albopictus* (*3*). Zika virus was first detected in the Region of the Americas (Americas) in Brazil in the spring of 2015 (*4*) and had spread to 26 countries and territories in the Americas as of February 17, 2016 (http://www.cdc.gov/zika/geo/active-countries.html). In October 2015, a marked increase in the number of infants with microcephaly was reported in Brazil (*5*). Because of the temporal and geographic occurrence of Zika virus infection in pregnant women before the reported increase in microcephaly, a possible association with prenatal Zika virus infection was postulated (*5*). Laboratory evidence from a limited number of cases with microcephaly has supported this potential association (*6*,*7*). Other documented modes of Zika virus transmission include intrapartum transmission from a mother with viremia to her infant, sexual transmission, and laboratory exposures (*8*–*11*). Additionally, blood transfusion (*10*) and organ or tissue transplantation pose theoretical risks for transmission. There is no reported evidence of transmission through breastfeeding, although Zika virus RNA has been found in breast milk (*9*).

Although the exact incubation period of Zika virus disease has yet to be determined, evidence from case reports and experience from related flavivirus infections indicate that the incubation period likely is 3 days to 2 weeks (*12*). Symptomatic disease is generally mild and characterized by two or more of the following: acute onset of fever, rash, arthralgia, or nonpurulent conjunctivitis (*2*,*13*). The rash associated with Zika virus disease has been described as pruritic (*13*) and maculopapular (*14*).

The spectrum of Zika virus disease in neonates infected in the perinatal period is unknown. Perinatal transmission of Zika virus infection to infants from mothers infected near the time of delivery has been reported in two cases; one of these infants was asymptomatic, and the other had thrombocytopenia and a diffuse rash (*9*). Mother-to-infant transmission of dengue virus, a related flavivirus, during the perinatal period has resulted in findings in the newborn ranging from no symptoms to severe illness (including fever, thrombocytopenia, and hemorrhage), most often with fever onset during the first week of life (*15*).

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Similarly West Nile virus, another mosquito-borne flavivirus, has been transmitted during the perinatal period from three mothers to their infants, with each infant having one of the following manifestations: rash, viral encephalitis, and viral meningitis (*16*). The clinical features that might be observed in infants who acquire Zika virus during the perinatal period are currently unknown.

Available evidence regarding the spectrum of Zika virus disease in infants and children who are infected through mosquito bites indicates that most children are asymptomatic or have mild illness, similar to the findings seen in adults infected with Zika virus disease. In the outbreak in Yap Island, Micronesia, in 2007, among persons with clinical illness (age range = 1–76 years), fever, macular or papular rash, arthralgia, and conjunctivitis were the most common signs and symptoms (*2*). In that outbreak, children aged 0–19 years had lower attack rates of confirmed and probable Zika virus disease than did adults aged 20–59 years (*2*). Additional published data are available for 10 children, aged 3–16 years (*17*–*22*) with Zika virus disease in Africa, Asia, South America, and the Pacific. All 10 children had fever, but none had rash, two had conjunctivitis, and three had arthralgia. Vomiting was reported in two children (*17*,*22*), and diarrhea was reported in two children (*22*). Among eight recent travel-related cases among children in the United States, all had rash and at least one other sign or symptom (fever, arthralgia, nonpurulent conjunctivitis) (CDC, unpublished data, 2016).

Deaths from Zika virus infection appear to be rare in persons of all ages. One death was reported in a female aged 15 years with sickle cell disease (hemoglobin SC), who experienced 4 days of fever, myalgia, abdominal pain and jaundice (*18*). A blood sample collected 5 days after illness onset was positive by reverse transcription–polymerase chain reaction (RT-PCR) for Zika virus RNA and negative for dengue, chikungunya, and yellow fever viruses (*18*). This patient died from complications of sickle cell disease after developing severe acute respiratory distress syndrome, hemothorax, and splenic sequestration (*18*). An additional death was reported in a female aged 16 years whose symptoms included headache, nausea, and petechiae; blood samples obtained 7 days after illness onset were positive by RT-PCR for Zika virus RNA (*23*). No further information was reported (*23*).

Guillain-Barré syndrome has been reported following Zika virus infection, although a causal link has not been established. Overall Guillain-Barré syndrome incidence appears to increase with increasing age (*24*). However, it is unclear how often Guillian-Barré syndrome after Zika virus infection has occurred in children (*10*). In French Polynesia, among 38 reported cases of Guillian-Barré syndrome after Zika virus infection, none occurred among children (*25*). One report from Brazil refers to six patients, aged 2–57 years, with neurologic syndromes (four with Guillain-Barré and two with acute disseminated encephalomyelitis) after laboratory-confirmed Zika virus infection; however, no further data were reported (*13*).

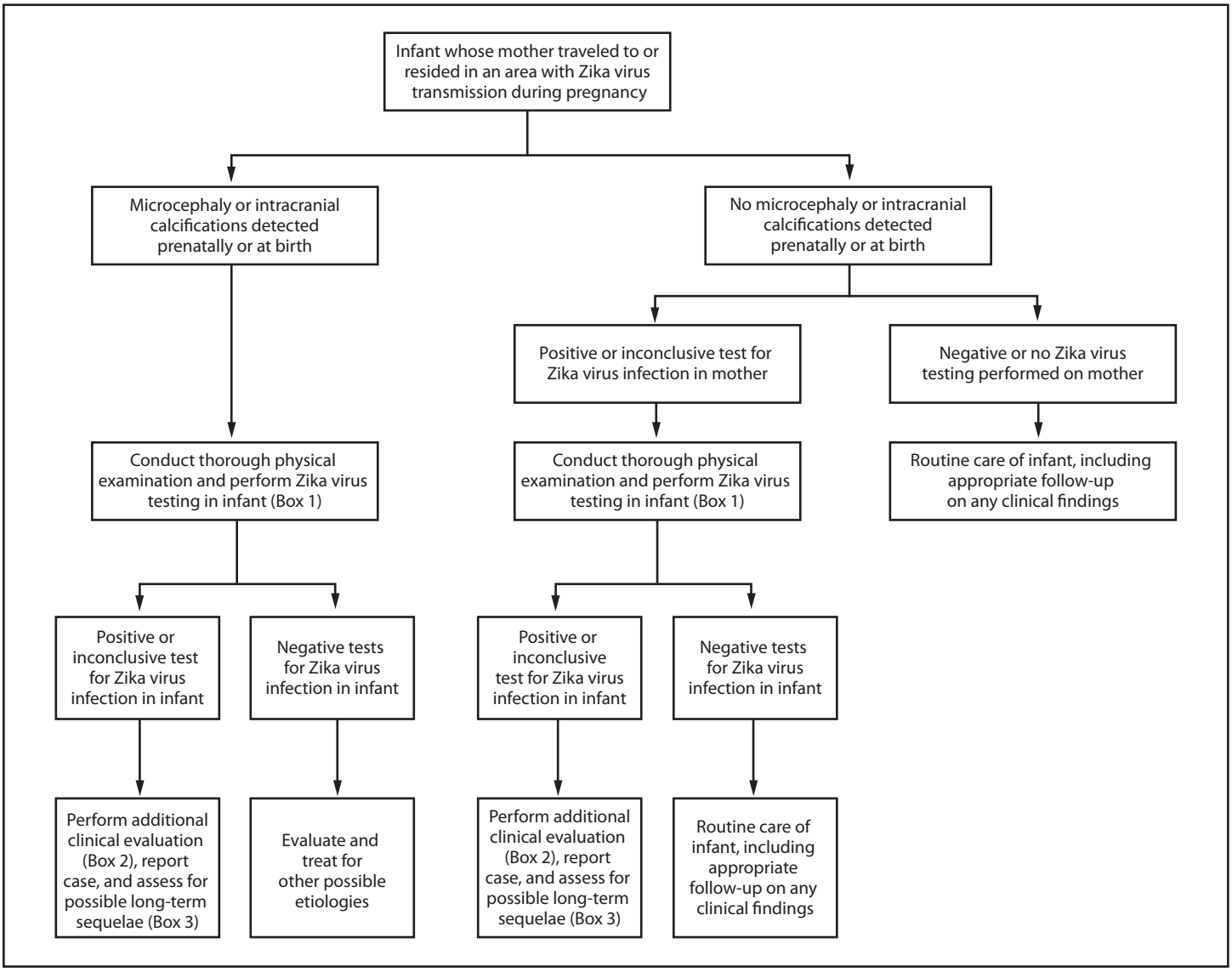
Updated Recommendations for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection

Congenital infections result from intrauterine transmission from mother to fetus during pregnancy. Testing of infants with possible congenital Zika virus infection who were born to mothers who traveled to or resided in areas affected by Zika virus during pregnancy should be guided by 1) whether the infant had microcephaly or intracranial calcifications detected prenatally or at birth and 2) the mother's Zika virus testing results. The results of previous prenatal ultrasounds and maternal Zika virus testing should be reviewed, and a thorough newborn physical examination, with assessment of head (occipitofrontal) circumference, length, and weight, should be performed (*26*,*27*). The evaluation of infants with microcephaly or intracranial calcifications or infants whose mothers have positive or inconclusive test results for Zika virus infection remains the same as described in the recommendations released on January 26 (Figure) (Box 1,2,3) (*1*). Infants without microcephaly or intracranial calcifications whose mothers have negative Zika virus test results or who were not tested for Zika virus should receive routine care (Figure). Because information on the effects of congenital Zika virus infection is limited, health care providers should exercise clinical judgment in the assessment of newborns with abnormalities other than microcephaly or intracranial calcifications who were born to mothers who traveled to or resided in an area with active Zika virus transmission during pregnancy. For these infants, health care providers should consider testing the mother before testing the infant. These guidelines will be updated as additional information becomes available.

Guidelines for Evaluation and Management of Infants and Children Aged <18 Years with Possible Acute Zika Virus Disease

Acute Zika virus disease should be suspected in an infant or child aged <18 years who 1) traveled to or resided in an affected area within the past 2 weeks and 2) has two or more of the following manifestations: fever, rash, conjunctivitis, or arthralgia. Acute Zika virus disease should also be suspected in an infant in the first 2 weeks of life 1) whose mother traveled to or resided in an affected area within 2 weeks of delivery and 2) who has two or more of the following manifestations: fever, rash, conjunctivitis, or arthralgia. Arthralgia can be difficult to detect in infants and young children and can manifest as irritability, walking with a limp (for ambulatory children),

FIGURE. Interim guidelines for the evaluation and testing of infants whose mothers traveled to or resided in an area with ongoing Zika virus transmission* during pregnancy†,§,¶



Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–7.

* Areas with Zika virus transmission are listed on the CDC website at http://wwwnc.cdc.gov/travel/page/zika-travel-information.

† Microcephaly defined as occipitofrontal circumference less than the third percentile for gestational age and sex based on standard growth curves (*26,27*), not explained by other etiologies.

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

¶ For infants, perform reverse transcription–polymerase chain reaction (RT-PCR) testing for Zika virus RNA and Zika virus and dengue virus IgM and neutralizing antibodies on serum collected from the umbilical cord or directly from infant within 2 days of birth, if possible. If cerebrospinal fluid is obtained for other reasons, 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. More information on laboratory testing for Zika virus infection is available at http://www.cdc.gov/zika/state-labs/index.html.

difficulty moving or refusing to move an extremity, pain on palpation, or pain with active or passive movement of the affected joint. Infants and older children can acquire Zika virus through mosquito-borne transmission. Infants can also be infected perinatally if the mother became infected with Zika virus during travel to or residence in an area with Zika virus transmission within 2 weeks of delivery. Infants whose mothers reported illness consistent with Zika virus disease near the time of delivery should be monitored for signs and symptoms of Zika virus disease. If an infant shows signs and

symptoms of acute Zika virus disease within the first 2 weeks of life, both the mother and infant should be tested for Zika virus infection. Persons might be exposed to Zika virus infection through sexual contact with a person who has traveled to or resided in an area affected by Zika virus (*11*).

BOX 1. Recommended Zika virus laboratory testing for infants and children when indicated*,†,§

For possible congenital Zika virus infection

- Test infant serum for Zika virus RNA, Zika virus immunoglobulin M (IgM) 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 reverse transcription-polymerase chain reaction (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.

For possible acute Zika virus disease

- If symptoms have been present for <7 days, test serum (and, if obtained for other reasons, cerebrospinal fluid) for Zika virus RNA by RT-PCR
- If Zika virus RNA is not detected and symptoms have been present for ≥4 days, test serum (and, if obtained for other reasons, cerebrospinal fluid) for Zika virus IgM and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–7.

* Indications for testing for congenital infection include 1) an infant with microcephaly or intracranial calcifications born to a woman who traveled to or resided in an area with Zika virus transmission while she was pregnant, or 2) an infant born to a mother with a positive or inconclusive test result for Zika virus infection.

† Indications for testing during acute disease include: Infants and children aged <18 years who 1) traveled to or resided in an affected area within the past 2 weeks and 2) have ≥2 of the following manifestations: fever, rash, conjunctivitis, or arthralgia. Infants in the first 2 weeks of life 1) whose mothers have traveled to or resided in an affected area within 2 weeks of delivery and 2) have ≥2 of the following manifestations: fever, rash, conjunctivitis, or arthralgia.

§ More information on laboratory testing for Zika virus infection is available at http://www.cdc.gov/zika/state-labs/index.html.

BOX 2. 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 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 photographic documentation of any rash, skin lesions, or dysmorphic features should be performed. 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 with 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.

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–7.

BOX 3. Recommended long-term follow-up for infants with possible congenital Zika virus infection

For all infants with possible congenital Zika virus infection, recommended long-term follow-up:

- Report case to state, territorial, or local health department and monitor for additional guidance as it is released.
- Consider conducting additional hearing screen at age 6 months. Refer any child with developmental delay for an audiologic evaluation. Ensure that appropriate follow-up of abnormal newborn hearing screening has occurred.
- Carefully evaluate occipitofrontal circumference and developmental characteristics and milestones throughout the first year of life, in consultation with appropriate medical specialists (e.g., pediatric neurology, developmental and behavioral pediatrics, physical and speech therapy).

Adapted from: Staples, JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–7.

Evaluation of infants and children for acute (symptom onset within the past 7 days) Zika virus infection should include testing of serum and, if obtained for other reasons, cerebrospinal fluid (CSF) specimens for evidence of Zika virus RNA using RT-PCR. If Zika virus RNA is not detected and symptoms have been present for ≥4 days, serum may be tested for Zika virus immunoglobulin M (IgM) and neutralizing antibodies, and dengue virus IgM and neutralizing antibodies (Box 1). Laboratory evidence of Zika virus infection in an infant or child would include, in any clinical specimen, detectable Zika virus in culture, Zika virus RNA or antigen, or a clinical specimen positive for Zika virus IgM with confirmatory neutralizing antibody titers ≥4-fold higher than dengue virus neutralizing antibody titers (*1*). If Zika virus antibody titers <4-fold higher than dengue virus neutralizing antibody titers, test results for Zika virus are considered inconclusive (*1*). More information on laboratory testing can be found at http://www.cdc.gov/zika/state-labs/index.html. Health care providers should notify their local, state or territorial health department of suspected Zika cases to arrange testing and so that action can be taken to decrease the risk for local transmission in areas with *Aedes* species mosquitoes.

Illness associated with Zika virus is usually mild in children, and treatment of Zika virus infection involves supportive care. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue virus is ruled out as the cause of illness, because of the potential for hemorrhagic complications of dengue fever, and should be avoided in all children aged <6 months (*28*,*29*). Aspirin should not be used in children with acute viral illnesses because of its association with Reye's syndrome (*30*). The decision to obtain additional laboratory tests, diagnostic studies, and infectious disease consultation should be based on clinical judgment as guided by findings from a complete history and physical examination. Information on long-term outcomes among infants and children with acute Zika virus disease is limited (*10*); until more evidence is available to inform recommendations, routine pediatric care is advised for these infants and children.

Guidelines for Breastfeeding for Mothers with Zika Virus Infection

Zika virus RNA has been identified in breast milk, but attempts to culture the virus have been unsuccessful (*9*). No cases of Zika virus infection associated with breastfeeding have been reported. CDC encourages mothers with Zika virus infection and living in areas with ongoing Zika virus transmission to breastfeed their infants. Current evidence suggests that the benefits of breastfeeding outweigh the theoretical risks of Zika virus transmission through breast milk.

Prevention of Zika Virus Infection in Infants and Children

Prevention of mosquito bites is the primary means of preventing Zika virus infection in persosns of all ages traveling to or residing in areas with local Zika virus transmission. Mosquito bite prevention includes using air conditioning or window and door screens when indoors, wearing long-sleeved shirts and long pants, using permethrin-treated clothing and gear, and using insect repellents. When used as directed on the product label, most Environmental Protection Agency–registered insect repellents can be used to protect children aged ≥2 months against mosquito bites. Oil of lemon eucalyptus should not be used in children aged <3 years (http://wwwnc.cdc.gov/travel/yellowbook/2016/the-pre-travel-consultation/protection-against-mosquitoes-ticks-other-arthropods). Mosquito netting can be used to cover infants in carriers, strollers, or cribs to protect them from mosquito bites. Information on the safe use of insect repellents in children is available at http://www.epa.gov/insect-repellents/using-insect-repellents-safely-and-effectively.

Persons with Zika virus infection should take steps to prevent mosquito bites for at least the first week of illness to decrease the risk for human-to-mosquito-to-human transmission. Health care providers should educate parents and caregivers about mosquito bite prevention in infants and children if they are traveling to or residing in areas affected by Zika virus; mosquitoes also carry other viruses in addition to Zika. More information about prevention of Zika virus infection can be found at http://www.cdc.gov/zika/prevention/index.html.

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