State of California—Health and Human Services Agency
California Department of Public Health

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Date: December 21, 2017

To: California Health Care Providers

From: California Department of Public Health

Updated Guidance for Health Care Providers: Assessment and Testing for Zika Virus Infection in Pregnant Women and their Newborns

I. **Background:** The impact of Zika virus infection in pregnancy remains a great concern. Pregnant women should have access to Zika virus testing, including testing of asymptomatic pregnant women when appropriate.

Nearly half of all California Zika cases to date have reported travel to Mexico and many others have reported travel to other Central and South American countries. In 2017, Mexico has reported declining numbers of cases and the incidence of new Zika infections in California has substantially declined. These factors together lead to a lower pre-test probability of infection when considering testing pregnant women and their newborns. As of November 24, 2017, 162 pregnant women with travel-associated Zika infection have been reported in California since 2015. Of these, 136 women have had completed pregnancies and 9 infants have been born with microcephaly and other Zika-associated anomalies. More than half of the infants born in California with Zika-associated birth defects were born to Zika-exposed mothers who were asymptomatic for Zika infection.

Based on the changing epidemiology of Zika virus infections in California since 2015, together with input from specialty organizations, CDPH is updating recommendations for the assessment and testing of pregnant women and their newborns for Zika virus infection. These updates align CDPH recommendations with current CDC interim guidance[a,b]. See the CDPH Zika webpage for tools and resources to implement this guidance in California.

Zika virus testing by detection of viral RNA (nucleic acid testing, NAT) or serology (IgM antibody testing) is available in commercial clinical laboratories throughout California and, as is typical of screening for other infectious diseases, can be directed to traditional commercial laboratory resources. Please submit your specimens to commercial laboratories for processing using your regular clinical testing protocol. Local public health laboratories and CDPH conduct confirmatory Zika virus testing as necessary to accurately diagnose and monitor the incidence of Zika virus disease in California.

For questions regarding the application of this updated interim CDPH Zika Guidance in your area, please contact your local health department. CDPH is available to your local health department for consultation as needed.

II. **Zika Virus Testing for Pregnant Patients: CDPH, CDC, ACOG and the Society for Maternal Fetal Medicine recommend that all pregnant women should be evaluated for possible Zika virus exposure during each prenatal care visit.** This evaluation should include an assessment[1] of signs and symptoms of Zika virus disease, a travel history to an area with risk of Zika virus transmission[2], and a woman's sexual partner's potential exposure.

A. **Symptomatic Pregnant Women** with possible Zika virus exposure[2] and symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) of Zika virus disease should be tested for Zika virus as soon as possible:

   i. Concurrent Zika virus NAT in serum and urine and IgM antibody testing if 12 weeks or less since symptom onset. If non-negative IgM and Zika virus NAT negative, confirm with plaque reduction neutralization test (PRNT).

B. **Asymptomatic Pregnant Women** *with ongoing*[3] possible Zika virus exposure[2] should be offered:

   i. NAT testing on serum and urine three times during pregnancy starting with the initiation of prenatal care and coinciding with prenatal visits. Testing each trimester may be considered.

   ii. IgM antibody testing during the first and second trimester may be considered for those with an appropriate exposure history (e.g., exposure limited to current pregnancy), but is not routinely recommended. Prolonged IgM persistence may make it challenging to determine whether the infection occurred during the current pregnancy or prior to the current pregnancy.

   iii. Testing should be performed unless woman has prior evidence of laboratory-confirmed Zika virus infection.

C. **Asymptomatic Pregnant Women** with recent *but without ongoing* exposure are not routinely tested but instead should be assessed carefully for factors that increase the likelihood of Zika infection. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection.

   i. Risk factors that may prompt testing include:

      a) Locally-transmitted Zika infections reported in the region of travel at the time of the possible exposure

      b) Sexual partner with travel to a Zika-risk area and unprotected (e.g., without use of male or female condom or dental dam) sexual exposure

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[1] *Screening Pregnant Women for ZIka Testing*, https://www.cdc.gov/zika/pdfs/ZikaPreg_ScreeningTool.pdf

[2] For symptomatic pregnant women/persons, refer to the CDC Areas with Risk of Zika (https://wwwnc.cdc.gov/travel/page/zika-information)

For asymptomatic pregnant women, use the WHO Zika Virus Classification Table (http://www.who.int/emergencies/zika-virus/classification-tables/en/) WHO risk classification "Category 1" countries to help limit the risk of false positive test results.

[3] "Ongoing risk of Zika virus exposure" is defined as follows: Currently living in or frequently (daily or weekly) traveling to an area with Zika virus transmission or having ongoing unprotected exposure to a potentially infected sexual partner.

c) Longer duration of travel (e.g., over four weeks) or multiple sexual exposures

d) Engagement in higher risk activities (e.g., outdoor recreation as opposed to indoor activities) while in an area with risk of Zika transmission

e) Known mosquito bites in an area with risk of Zika transmission

f) Lack of use of protective clothing and insect repellent on a regular basis in an area with risk of Zika transmission

g) Compromised integrity of housing in an area with risk of Zika transmission (e.g., lack of window screens or air conditioning)

h) Other household members diagnosed with Zika virus infection

i) High risk patient occupation, e.g., potential laboratory or needle stick exposure

j) Patient is recipient of recent transfusions or transplants, especially in an area with risk of Zika transmission and there is not reliable testing of blood supply for Zika virus

ii. When indicated, testing high risk asymptomatic pregnant patients without ongoing exposure should include:

a) Concurrent Zika virus NAT and IgM antibody testing if 12 weeks or less since exposure. If non-negative IgM and Zika NAT negative, confirm with PRNT. Prolonged IgM persistence may make it challenging to determine whether the infection occurred during the current pregnancy or prior to the current pregnancy.

D. Pregnant women **who have recent possible Zika virus exposure and who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome should receive Zika virus testing to assist in establishing the etiology of the birth defects. Testing should include both NAT and IgM tests.**

i. If amniocentesis is being performed as part of clinical care, NAT testing of amniocentesis specimens should also be performed.

E. **Pathology testing of placental tissues for Zika virus infection may be considered to aid in maternal diagnosis for women with an exposure history/epidemiologic link to an area with risk of Zika infection, as appropriate.**

i. Placental Zika virus testing may be considered on a case-by-case basis in consultation with public health and is prioritized for: 1) symptomatic mothers with probable (unspecified flavivirus) Zika virus infection; and 2) mothers with an infant or fetus with possible Zika virus-associated birth defects but no definitive diagnosis of Zika virus infection during pregnancy.

III. Zika Virus Testing for Pregnant Women at Antenatal and Delivery Hospitalizations

A. **Pregnant women with an exposure history who meet the criteria in II. above and have not yet been tested since last exposure should be evaluated for testing for Zika virus as described.**

IV. Zika Virus Testing for Newborn Infants

A. **Laboratory testing for congenital Zika virus infection is recommended for the following infants:**

i. Infants born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.

ii. Infants with clinical findings suggestive of congenital Zika syndrome and possible maternal Zika virus exposure during pregnancy, regardless of maternal testing results.

B. **Newborn specimen collection** should occur *ideally* within the first two days of life.

i. Zika virus NAT testing should be performed on both infant serum and urine and Zika virus IgM antibody testing should concurrently be performed on infant serum. If non-negative IgM and negative Zika virus NAT, confirm with PRNT.

Note: Birth hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done.

ii. If CSF is collected for other purposes, NAT and IgM antibody testing should be performed on CSF.

iii. For infants with clinical findings consistent with congenital Zika syndrome, testing CSF for Zika virus NAT and IgM antibodies should be considered, especially if serum and urine testing are negative and another etiology has not been identified.

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[a] Adebanjo T, Godfred-Cato S, Viens L, et al. Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017. MMWR Morb Mortal Wkly Rep 2017;66:1089–1099. DOI: http://dx.doi.org/10.15585/mmwr.mm6641a1

[b] Oduyebo T, Polen KD, Walke HT, et al. Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure—United States (including U.S. territories), July 2017. MMWR Morb Mortal Wkly Rep 2017;66:781–93 DOI: http://dx.doi.org/10.15585/mmwr.mm6629e1