



**CDC Health Update:
Testing of Urine Specimens for Zika Virus Infection**

May 27, 2016

The CDC issued a Health Update on May 25, 2016 entitled “Diagnostic Testing of Urine Specimens for Suspected Zika Virus Infection”.

Los Angeles County Health Care Providers should continue to use the [Zika Virus Testing and Report Form](#) which includes instructions on specimen collection and submission, the indications for Zika virus testing, and how to report a suspect case. The form has been updated to emphasize the following points:

- **If within 7 days from onset of symptoms, BOTH URINE and SERUM specimens** should be submitted for rRT-PCR detection of Zika virus.
- Urine specimens should be collected within 14 days after symptom onset to improve the sensitivity for Zika virus detection. Urine specimens collected within 30 days will continue to be accepted at the LAC Public Health Laboratory.

The LAC Public Health **Zika Virus Testing and Report Form** can be accessed here: publichealth.lacounty.gov/acd/Diseases/EpiForms/ZikaInfoTestReq.pdf

The full CDC Health Update can be found on the next page.

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HAN HEALTH UPDATE

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Diagnostic Testing of Urine Specimens for Suspected Zika Virus Infection

Summary

On May 13, 2016, the Centers for Disease Control and Prevention (CDC) issued [interim guidance](http://www.cdc.gov/mmwr/volumes/65/wr/mm6518e1.htm) (<http://www.cdc.gov/mmwr/volumes/65/wr/mm6518e1.htm>) that recommends Zika virus rRT-PCR testing of urine collected less than 14 days after symptom onset, along with testing of patient-matched serum samples, for the diagnosis of suspected Zika virus infection (1). The purpose of this Health Alert Network (HAN) health update is to further disseminate information about the interim guidance to clinical and public health professionals.

Background

Zika virus is a mosquito-borne flavivirus. Zika virus infection during pregnancy can cause microcephaly and other severe fetal brain defects. Zika virus infection is also associated with Guillain-Barré syndrome. Transmission of Zika can occur through mosquito bite, from a pregnant woman to her fetus, through sexual contact with an infected male, and possibly through blood transfusion. The most common symptoms of Zika virus disease are fever, rash, joint pain, or conjunctivitis. Other common symptoms include muscle pain and headache. Evidence from case reports and experience from related flavivirus infections indicate that the incubation period for Zika is likely a few to 14 days.

Diagnostic testing for Zika virus infection can be accomplished using molecular and serologic methods. The U.S. Food and Drug Administration (FDA) has issued [Emergency Use Authorizations](http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm) (EUA) (<http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>) for several diagnostic assays to detect Zika virus infection (2). The EUAs authorize real-time reverse transcription-polymerase chain reaction (rRT-PCR) assays to detect Zika virus RNA in specified clinical sample types, and an immunoglobulin M (IgM) antibody capture enzyme-linked immunosorbent assay (ELISA) to detect anti-Zika virus IgM antibodies in serum and cerebrospinal fluid. The CDC Trioplex rRT-PCR assay is authorized by FDA for Zika virus testing of urine and serum. Anti-Zika IgM antibodies develop during the first week of illness and persist for approximately 12 weeks following infection. However, extensive cross-reactivity can occur in flavivirus serological assays, and therefore additional tests, such as the plaque reduction neutralization test (PRNT), are necessary to distinguish Zika virus infection from other flavivirus infections.

Although Zika virus RNA is unlikely to be detected in serum after the first week of illness, recent data suggest that Zika virus RNA can persist in urine for at least two weeks post symptom onset (3). Given this information, on May 13, 2016, CDC issued interim guidance on rRT-PCR testing for Zika virus RNA in urine (1). CDC now recommends that, for persons with suspected Zika virus disease, Zika virus rRT-PCR should be performed on both urine and serum specimens collected within 7 days after onset of symptoms. Zika virus rRT-PCR also should be performed on urine specimens collected within 14 days after onset of symptoms. A positive rRT-PCR result in either specimen confirms Zika virus infection. However, a negative rRT-PCR in a serum or urine sample collected at any time point after illness onset does not exclude Zika virus infection, and in these cases IgM antibody testing should be performed on serum.

CDC recommendations for Zika virus testing of serum and other clinical specimens remain unchanged at this time. Please contact your state or local health department to facilitate testing.

Recommendations for Health Care Providers and Public Health Practitioners

- Collect urine samples within 14 days post symptom onset along with patient-matched serum samples for those who match CDC Zika virus clinical and/or epidemiological testing criteria for Zika virus infection.
- Perform Zika virus rRT-PCR testing on urine, in conjunction with testing of serum using the appropriate molecular or serologic assay, based on days post symptom onset.

Additional Considerations

- Further investigation is needed to determine the sensitivity and utility of Zika virus rRT-PCR on urine specimens collected ≥ 14 days after onset of symptoms: limited data in pregnant women suggest that viremia in serum might be prolonged in pregnancy (4, 5).

References

1. CDC. Interim guidance for Zika virus testing of Urine – United States, 2016. MMWR Morb Mortal Wkly Rep 2016; 65. DOI: <http://dx.doi.org/10.15585/mmwr.mm6518e1>.
2. Food and Drug Administration. Emergency Use Authorizations. <http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm>
3. Comparison of Test Results for Zika Virus RNA in Urine, Serum, and Saliva Specimens from Persons with Travel-Associated Zika Virus Disease — Florida, 2016 <http://www.cdc.gov/mmwr/volumes/65/wr/mm6518e2.htm>
4. Driggers RW, Ho CY, Korhonen EM, et al. Zika virus infection with prolonged maternal viremia and fetal brain abnormalities. N Engl J Med. March 30, 2016. DOI: 10.1056/NEJMoa1601824
5. Bocanegra C. Zika virus infection in pregnant women in Barcelona, Spain. Clin Microbiol Infect. April 3, 2016. DOI: 10.1016/j.cmi.2016.03.025.

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>
- Memorandum – Revised diagnostic testing for Zika, chikungunya, and dengue viruses in US Public Health Laboratories (not updated with urine guidance): <http://www.cdc.gov/zika/state-labs/index.html>
- Diagnostic testing: <http://www.cdc.gov/zika/hc-providers/diagnostic.html>
- Collection and submission of body fluids for Zika virus testing: <http://www.cdc.gov/zika/hc-providers/body-fluids-collection-submission.html>

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