TN Department of Health

Current as of 02/26/19

Considerations and Instructions for Zika Virus Testing

1. **Who should I test for Zika virus?**
   - Zika virus testing is currently recommended by TDH and CDC for:
     - Anyone with possible recent ZIKV exposure who has experienced symptoms consistent with ZIKV
     - Symptomatic pregnant women with possible Zika virus exposure
     - Asymptomatic pregnant women with ongoing possible Zika virus exposure
     - Pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus infection
     - Symptomatic infants born to a mother with a travel history to an area with Zika virus transmission within two weeks of delivery.
     - Infants born to mothers with positive, pending, or inconclusive test results for Zika virus infection.
     - Infants with microcephaly or intracranial calcifications whose mother traveled to an area with Zika virus transmission during the pregnancy.
       - It is important to note — clinical management of the patient will not change based on test results.
   - Zika virus may be considered for:
     - Asymptomatic pregnant women with recent possible but no ongoing exposure to Zika virus (i.e., travelers)
   - Zika virus testing is not recommended for:
     - Non-pregnant asymptomatic individuals
     - Preconception screening

2. **What specimens are needed for Zika virus testing?**
   - **Serum/Plasma**
     - 2.0 mL
     - Whole blood should be centrifuged. If performed in a biological safety cabinet, plasma can be decanted prior to shipment to avoid hemolysis. Ship serum in a sterile plastic tube with a tightly-sealing screw cap. If a sterile plastic tube with a tightly-sealing screw cap is not available, a red-top vacutainer can be used.
   - **Urine**
     - 10.0 mL
     - Must be submitted with a patient-matched serum specimen.
   - **Cerebrospinal fluid** (CSF)
     - Only if collected for other studies & only when submitted alongside a patient-matched serum specimen.
     - 1.0–2.0 mL
     - Store in a sterile, tightly-sealing screw cap tube. Ship CSF in a sterile plastic tube with. If a sterile plastic tube with a tightly-sealing screw cap is not available, a red-top vacutainer can be used.
   - **Fetal or Infant Tissues**
     - At birth, collect placenta and umbilical cord for histopathological testing.
     - Within 2 days of birth, collect cord blood sample or serum.
     - CSF if collected for other studies & only when submitted alongside a patient-matched serum specimen.
     - Note — if eligible infant is identified >2 more than two days after birth, contact Regional Health Officer for guidance.

3. **What tests are available for Zika virus?**
   - **rRT-PCR** (molecular) testing should be performed for patients possibly exposed to Zika virus who have symptoms consistent with Zika virus infection. Appropriate samples for molecular testing are serum and urine samples collected <14 days after symptom onset. Urine should always be collected with a patient-matched serum specimen.
   - **IgM ELISA** (serology) testing is used for the qualitative detection of Zika virus IgM antibodies in serum. Appropriate samples for IgM ELISA testing are serum samples collected >4 days after symptom onset (or at least 2 weeks after return from travel in asymptomatic pregnant women).
   - **PRNT** (plaque reduction neutralization assay) is used to confirm or rule out Zika virus infection following a positive, equivocal or inconclusive Zika IgM ELISA result.

4. Which laboratories can test for Zika virus?

Multiple commercial laboratories throughout Tennessee now offer testing appropriate for assessing persons who may have had recent ZIKV infection 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. State public health laboratories and TDH can conduct confirmatory Zika virus testing as necessary to accurately diagnose and monitor the incidence of Zika virus disease in Tennessee.

Laboratory	rRT-PCR		IgM ELISA
	Urine specimen	*Serum specimen*	*Serum specimen*
Commercial Laboratories			
ARUP	✓	✓	✓
LabCorp	✓	✓	✓
Quest Diagnostics	✓	✓	✓
Public Health Laboratories			
Tennessee Department of Health Laboratory Services – Nashville	✓	✓	✓
Tennessee Department of Health Laboratory Services – Knoxville	✓	✓	
Shelby County Department of Health Lab	✓	✓	

5. How can I submit a specimen for Zika virus testing to the Tennessee Department of Health?

Providers should use commercial laboratories to order Zika tests for their patients and pre-approval for testing by the local/regional health department is not needed in the commercial sector. However, providers should notify the local/regional health department as soon as Zika virus infection is suspected.

The Tennessee Department of Health will continue to provide Zika virus testing and providers should call the local/regional health department to request testing at the state lab.

Testing at the state lab is available in specific situations such as:

- Pregnant females with abnormal ultrasound and history of exposure to Zika virus as requested by the health care provider
- Infant born with suspected Zika congenital syndrome or an infant born to a mother with laboratory evidence of possible Zika virus infection during pregnancy
- As determined on a case by case basis

If health care providers have a question on who should be testing or what tests to requests, please contact your Local/Regional Health Department using the information provided here. There is no charge for Zika testing conducted at the Tennessee Department of Health, though shipping or transport to the laboratory is the responsibility of the provider.

6. How does public health determine who is approved for Zika virus testing at the Tennessee Department of Health?

- Regional Health Officers determine if individuals meet criteria for testing using current CDC guidance.
- In summary, ZIKV testing is currently recommended by TDH and CDC for:
  - Anyone with possible recent ZIKV exposure who has experienced symptoms consistent with ZIKV
  - Symptomatic pregnant women with possible ZIKV exposure
  - Asymptomatic pregnant women with ongoing possible ZIKV exposure (ongoing exposure is defined as residence in or frequent travel to an area with risk of ZIKV transmission)
  - Pregnant women with possible ZIKV exposure who have a fetus with prenatal ultrasound findings consistent with congenital ZIKV infection
  - Infants with clinical findings consistent with congenital ZIKV syndrome and possible maternal ZIKV exposure during pregnancy, regardless of maternal testing results
  - Infants without clinical findings consistent with congenital ZIKV syndrome born to mothers with laboratory evidence of definitive or possible ZIKV infection during pregnancy

7. How do I ship specimens to the Tennessee Department of Health?

- If approved for testing by a Regional Health Officer, submit specimens along with the PH-4182 form (Tennessee Department of Health Division of Laboratory Services Clinical Submission Requisition form).
  - Required fields are marked with an asterisk
  - Under the "TEST REQUESTED" section, check "Other" and write in "Zika virus"
  - Health Departments that create a lab order online through PTBMIS do not need to include PH-4182.
- Specimens should be placed in an insulated container with blue ice packs (2-6°C). Additional blue ice packs should be used during hot weather to ensure specimen integrity.
- Ship the specimens along with the PH-4182 form to the Tennessee Department of Health:

Nashville Laboratory **FedEx or UPS or hand delivery:** State Laboratory Services 630 Hart Lane Nashville, TN 37216 615-262-6300 **USPS:** State Laboratory Services P.O. Box 305130 Nashville, TN 37230-5130	**Knoxville Laboratory** **FedEx or UPS or hand delivery:** Knoxville Regional Laboratory 2102 Medical Center Way Knoxville, TN 37920 865-549-5201 **USPS:** Knoxville Regional Laboratory P.O. Box 59019 Knoxville, TN 37950	**Memphis Laboratory** **FedEx or UPS or hand delivery:** Shelby County Health Department 814 Jefferson Avenue Room 258 Memphis, TN 38105 901-222-9477 phone

8. How long does it take to get results from the Tennessee Department of Health?

- rRT-PCR results are usually available within one week.
- IgM ELISA results are usually available within 2 weeks.
- PRNT confirmation of positive, equivocal, or inconclusive IgM ELISA can only be completed at CDC and may take several weeks.

9. How are results reported from the Tennessee Department of Health to healthcare providers?

Tennessee Department of Health sends laboratory results to the provider listed on the specimen submission form (PH-4182) by U.S. Postal Service.

10. How do I interpret Zika virus test results?

- **rRT-PCR**
  - A positive rRT-PCR result confirms Zika virus infection, and no IgM ELISA testing is needed.
  - A negative rRT-PCR result does not exclude recent infection. Therefore, IgM ELISA testing should be performed. More information about subsequent IgM ELISA testing for rRT-PCR negative patients is available here: http://emergency.cdc.gov/han/han00392.asp
- **IgM ELISA**
  - A positive, equivocal, or inconclusive IgM ELISA test requires further testing to confirm a diagnosis. Please consult with your Regional Health Officer, the Tennessee Department of Health, or the latest interim guidance for interpreting test results from the CDC, available here: https://www.cdc.gov/zika/hc-providers/testresults.html
  - A negative IgM ELISA test might reflect specimen collection before development of detectable antibodies and does not exclude Zika virus infection.
  - A negative IgM ELISA test on a specimen collected <7 days after onset of symptoms and a negative rRT-PCR result rules out recent infection.
  - A negative IgM ELISA result on a specimen collected from 7 days to 12 weeks after onset of symptoms rules out recent infection.
- **PRNT**
  - A PRNT using a 90% cutoff value with a titer ≥10 against Zika virus, together with negative PRNTs (i.e., <10) against other flaviviruses is confirmatory for recent infection with Zika virus.
  - For additional guidance on interpreting IgM ELISA and PRNT results, please see the MMWR "Interim Guidance for Interpretation of Zika Virus Antibody Test Results", available here: http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm.

11. Should I test for Zika for couples or persons who are trying to get pregnant?

- Testing for Zika virus is ***not*** recommended for asymptomatic couples or persons interested in conceiving in which one or both partner has had possible exposure to Zika because:
    - A negative test result does not necessarily rule out recent Zika infection and may give false reassurance if:
        - Test was done after the virus was no longer present in the blood but may still be found in other bodily fluids (urine, semen, etc.)
        - Test was done too early and the antibody levels were not detectable in the blood.
        - Test was done too late and the antibody levels fell to levels that were not detectable.
- Test results can sometimes be negative even though there may be a true infection, as no test is 100% accurate.
- We are still learning about Zika virus shedding in genital secretions and how to interpret test results done on semen or vaginal fluids.
- For additional guidance and recommendations please visit: https://www.cdc.gov/pregnancy/zika/women-and-their-partners.html
    - Couples or persons trying to get pregnant should wait the recommended time after Zika exposure to conceive.