Testing Guidance and Interpretation of Results for Healthcare Providers

Dengue and Zika Virus Testing Guidance: Symptomatic Non-Pregnant People with a Clinically Compatible Illness and Risk for Infection with Both Viruses*

Specimen collected ≤7 days postsymptom onset

- Perform dengue and Zika virus NAATs
  - Positive dengue virus NAAT
    - Acute dengue virus infection
  - Positive Zika virus NAAT
    - Acute Zika virus infection
  - Negative dengue and Zika virus NAATs

Specimen collected >7 days postsymptom onset

- Perform dengue and Zika virus IgM serology
  - Positive dengue or Zika virus IgM
    - Perform dengue and Zika virus PRNTs
      - Dengue virus PRNT ≥10 and Zika virus PRNT <10
        - Recent dengue virus infection
      - Dengue virus PRNT <10 and Zika virus PRNT ≥10
        - Recent Zika virus infection
      - Dengue virus PRNT ≥10 and Zika virus PRNT ≥10
        - Recent flavivirus infection
      - Dengue virus PRNT <10 and Zika virus PRNT <10
        - No evidence of dengue or Zika virus infection

- Perform dengue and Zika virus NAATs
  - Positive dengue and Zika virus NAATs

* Specimen and test selection: Dengue and Zika virus NAATs, IgM antibody testing, and PRNTs should be performed on serum. Some NAATs also can be performed on plasma, whole blood, cerebrospinal fluid, or urine, and some antibody tests can be performed on plasma, whole blood, or cerebrospinal fluid. Laboratories might choose to perform dengue and Zika virus NAATs and IgM antibody testing simultaneously rather than sequentially, or to perform dengue virus nonstructural protein-1 testing instead of dengue virus NAAT.

Indications to repeat assay(s): If the patient’s illness has epidemiologic or clinical significance (e.g., first case of local transmission in area, new transmission mode, or unusual clinical syndrome), repeat a positive NAAT on newly extracted RNA from the same specimen. For indeterminate IgM antibody test results, repeat IgM antibody testing or perform PRNT on the same specimen. In areas where PRNTs are not performed, report the indeterminate results and request a second serum specimen for IgM antibody testing.

Interpretation of results: Dengue and Zika virus IgM antibodies can be detected in serum for months following infection. The specific timing of infection cannot be determined. Data on the epidemiology of viruses known to be circulating at the location of exposure and clinical findings should be considered when interpreting the results of serologic diagnostic testing.

Abbreviations: IgM = immunoglobulin M; NAAT = nucleic acid amplification test; PRNT = plaque reduction neutralization test
### TABLE 1. Interpretation of dengue and Zika virus diagnostic test results for patients with a clinically compatible illness and risk for infection with both viruses

<table>
<thead>
<tr>
<th>Dengue and Zika virus IgM antibodies</th>
<th>Dengue virus PRNT</th>
<th>Zika virus PRNT</th>
<th>Nonpregnant patients</th>
<th>Pregnant women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive (either assay)† ⊕‡</td>
<td>≥10</td>
<td>&lt;10</td>
<td>Recent dengue virus infection</td>
<td>Dengue virus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Positive (either assay)† ⊕‡</td>
<td>&lt;10</td>
<td>≥10</td>
<td>Recent Zika virus infection</td>
<td>Zika virus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Positive (either assay)†</td>
<td>≥10</td>
<td>≥10</td>
<td>Recent flavivirus infection¶</td>
<td>Flavivirus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Any result</td>
<td>&lt;10</td>
<td>&lt;10</td>
<td>No evidence of dengue or Zika virus infection**</td>
<td>No evidence of dengue or Zika virus infection**</td>
</tr>
<tr>
<td>Positive dengue virus assay, negative Zika virus assay</td>
<td></td>
<td></td>
<td>Presumptive recent dengue virus infection</td>
<td>Presumptive dengue virus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Positive Zika virus assay, negative dengue virus assay</td>
<td></td>
<td></td>
<td>Presumptive recent Zika virus infection</td>
<td>Presumptive Zika virus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Positive (both assays)</td>
<td></td>
<td></td>
<td>Presumptive recent flavivirus infection¶</td>
<td>Presumptive flavivirus infection, timing cannot be determined</td>
</tr>
<tr>
<td>Positive dengue virus assay, Zika virus assay not performed</td>
<td></td>
<td></td>
<td>Presumptive recent flavivirus infection¶</td>
<td>Presumptive flavivirus infection, timing cannot be determined</td>
</tr>
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<td>Positive Zika virus assay, dengue virus assay not performed</td>
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<td>Presumptive flavivirus infection, timing cannot be determined</td>
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<tr>
<td>Negative (both assays)</td>
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<td>No evidence of dengue or Zika virus infection**</td>
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<td>Negative Zika virus assay, dengue virus assay not performed</td>
<td></td>
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<td>No evidence of Zika virus infection**</td>
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</tr>
</tbody>
</table>

**Abbreviations:** IgM=immunoglobulin M antibody testing; NAATs=nucleic acid amplification tests; PRNT=plaque reduction neutralization test.

* In the absence of testing to detect IgM antibodies, negative NAAT results might reflect collection after clearance of detectable viral RNA and does not rule out infection.

† Includes presumptive positive, indeterminate, and equivocal IgM antibody results that are not resolved by retesting.

‡ IgM and PRNT antibody testing infrequently provide discordant results (e.g., dengue virus IgM positive, Zika virus IgM negative with dengue virus PRNT titer <10, Zika virus PRNT titer ≥10; or dengue virus IgM negative, Zika virus IgM positive with dengue virus PRNT titer ≥10, Zika virus PRNT titer <10). In such cases, report results as “presumptive flavivirus infection” and request a second specimen for retesting.

¶ In the absence of NAAT, negative IgM or neutralizing antibody testing in specimens collected ≤7 days after illness onset might reflect collection before the development of a detectable antibody response and does not rule out infection.