Overview

Useful For
An aid in the diagnosis of dengue virus infection

Highlights
Detection of the dengue virus nonstructural protein 1 (NS1) antigen is suggestive of recent exposure and/or acute infection with dengue virus.

This test should be used for diagnostic purposes only.

Dengue NS1 antigenemia overlaps with dengue virus viremia and can be used as an acute phase marker for infection.

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>DENS1</td>
<td>Dengue NS1 Ag, S</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>DNAGI</td>
<td>Dengue Ag Interpretation</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Testing Algorithm
See Mosquito-borne Disease Laboratory Testing in Special Instructions.

Special Instructions
  - Mosquito-borne Disease Laboratory Testing

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.5 mL
Test Definition: DNSAG
Dengue Virus NS1 Ag, S

Forms
If not ordering electronically, complete, print, and send a Microbiology Test Request (T244) with the specimen.

Specimen Minimum Volume
0.4 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>Reject</td>
</tr>
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</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
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</table>

Clinical and Interpretive

Clinical Information
Dengue virus (DV) is a globally distributed flavivirus with 4 distinct serotypes (DV-1, -2, -3, -4) and is primarily transmitted by the *Aedes aegypti* mosquito, found throughout the tropical and subtropical regions of over 100 countries. DV poses a significant worldwide public health threat with approximately 2.5 to 3 billion people residing in DV endemic areas, among whom 100 to 200 million individuals will be infected and approximately 30,000 patients will succumb to the disease, annually.

Following dengue infection, the incubation period varies from 3 to 7 days and while some infections remain asymptomatic, the majority of individuals will develop classic dengue fever. Symptomatic patients become acutely febrile and present with severe musculoskeletal pain, headache, retro-orbital pain, and a transient macular rash, most often observed in children. Fever defervescence signals disease resolution in most individuals. However, children and young adults remain at increased risk for progression to dengue hemorrhagic fever and dengue shock syndrome, particularly during repeat infection with a new DV serotype.

Detection of the DV nonstructural protein 1 (NS1) has emerged as an alternative biomarker to both serologic and molecular based techniques for diagnosis of acute DV infection. NS1 antigenemia is detectable within 24 hours and up to 9 days following symptoms onset. This overlaps with the DV viremic phase and NS1 is often detectable prior to IgM seroconversion. Concurrent evaluation for the NS1 antigen alongside testing for IgM- and IgG-class antibodies to DV (DENG) provides optimal diagnostic potential for both early and late dengue disease.

Reference Values
Negative

Reference values apply to all ages.

Interpretation
Positive:

The presence of dengue nonstructural protein 1 (NS1) antigen is consistent with acute-phase infection with dengue virus.

The NS1 antigen is typically detectable within 1 to 2 days following infection and up to 9 days following symptom onset.

NS1 antigen may also be detectable during secondary dengue virus infection, but for a shorter duration of time (1-4 days following symptom onset).

Negative:

The absence of dengue NS1 antigen is consistent with the lack of acute-phase infection.

The NS1 antigen may be negative if specimen is collected immediately following dengue virus infection (<24-48 hours) and is rarely detectable following 9 to 10 days of symptoms.

Cautions

Results should be used in conjunction with clinical presentation and exposure history.

Though uncommon, false-positive nonstructural protein 1 (NS1) results may occur in individuals with active infection due to other flaviviruses, including West Nile virus and yellow fever virus.

Negative NS1 antigen results may occur if the specimen was collected greater than 7 days following symptom onset. Serologic testing for the presence of IgM and IgG antibodies to DV is recommended in such cases.

Supportive Data

The presence of nonstructural protein 1 (NS1) antigen overlaps with the dengue virus (DV) viremic phase for the first 4 to 5 days following infection and therefore, the performance characteristics of the InBios DV NS1 EIA were compared to the Focus Diagnostics DV real-time PCR (RT-PCR), which detects RNA from all 4 DV serotypes. Seventy-seven serum samples previously evaluated by the Focus Diagnostics RT-PCR assay were also tested by the InBios DV NS1 EIA and the results are compared in Table 1 below. Discordant samples were also tested by the PlateliaTM NS1 Ag EIA (BioRad Laboratories, Marnes-la-Coquette, France).

<table>
<thead>
<tr>
<th>Focus Diagnostics DV RT-PCR</th>
<th>InBios DV NS1 EIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive 24</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative 1(a)</td>
</tr>
<tr>
<td>Equivocal</td>
<td>Equivocal 0</td>
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</table>

a. This sample was negative by the Platelia NS1 EIA

b. Five samples were also positive by the Platelia NS1 EIA
Test Definition: DNSAG
Dengue Virus NS1 Ag, S

c. One sample was negative and one sample was indeterminate by the Platelia NS1 EIA

Sensitivity: 96% (24/25); 95% Confidence Intervals (CI): 79.1%-100%

Specificity: 82.7% (43/52); 95% CI: 70.1%-90.9%

Overall Agreement: 87.1% (67/77); 95% CI: 77.6%-93%

Clinical Reference

Performance

Method Description
The InBios NS1 enzyme-linked immunosorbent assay (ELISA) is a 2-step sandwich-format colorimetric immunoassay for qualitative detection of nonstructural protein 1 (NS1) antigen in serum. Testing is performed according to manufacturer’s instructions on the Triturus automated EIA analyzer (Grifols, Miami, FL). Diluted patient samples and controls incubated in wells coated with purified capture antibody, specific for the dengue NS1 antigen. Following incubation, wells are washed, incubated with a horseradish peroxidase-conjugated polyclonal antibody specific to NS1 antigen and reincubated. Wells are subsequently washed and 3,3′,5,5′-tetramethylbenzidine substrate is added and incubated in the dark at room temperature. Stop solution is added next and the optical density (OD) of the reaction is measured at 450/620 nm. The immune status ratio (ISR) for each sample is calculated from the ratio of the OD obtained with the test sample divided by the OD from the calculated cutoff value (determined by the cutoff control sample). (Package insert: InBios DENV DetectTM NS1 ELISA, Seattle, WA)

PDF Report
No

Day(s) and Time(s) Test Performed
Tuesday; 9 a.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
7 days

Performing Laboratory Location
Rochester
Test Definition: DNSAG
Dengue Virus NS1 Ag, S

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
86790-NS1 Ag

LOINC® Information

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<tbody>
<tr>
<td>DNSAG</td>
<td>Dengue Virus NS1 Ag, S</td>
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<table>
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