MAYO CLINIC LABORATORIES

Test Definition: DENVP

Dengue Virus Antibody/Antigen Panel, Serum

Overview

Useful For

Aiding in the diagnosis of dengue virus infection by detection of IgM and IgG antibodies and the nonstructural protein 1 (NS1)

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
DENG	Dengue Virus Ab, IgG, S	No	Yes
DENM	Dengue Virus Ab, IgM, S	No	Yes
DENS1	Dengue NS1 Ag, S	Yes, (DNSAG)	Yes
INT69	Dengue Interpretation	No	Yes

Testing Algorithm

For more information see Mosquito-borne Disease Laboratory Testing.

Special Instructions

- Mosquito-borne Disease Laboratory Testing

Highlights

Detection of the dengue virus nonstructural protein 1 (NS1) antigen and/or antidengue virus IgM 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.

Infection with other flaviviruses, including West Nile virus, can lead to false-positive antibody results.

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions: Centrifuge and aliquot serum into plastic vial.

Forms

If not ordering electronically, complete, print, and send Infectious Disease Serology Test Request (T916) with the specimen.

Specimen Minimum Volume

0.8 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Heat-inactivated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	

Clinical & Interpretive

Clinical Information

Dengue virus (DV) is a globally distributed flavivirus with 4 distinct serotypes (DV-1, -2, -3, -4). It is primarily transmitted by the *Aedes aegypti* mosquito, which is 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 dengue-specific IgM and IgG-class antibodies remains the most commonly utilized diagnostic method. Seroconversion occurs approximately 3 to 7 days following exposure, and therefore, testing of acute and convalescent sera may be necessary to make the diagnosis. 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 (as performed in this profile) for the NS1 antigen alongside testing for IgM- and IgG-class antibodies to DV provides optimal diagnostic potential for both early and late dengue disease.

Reference Values

IgG: Negative
IgM: Negative
NS1: Negative
Reference values apply to all ages.

Interpretation

The presence of IgG-class antibodies to dengue virus (DV) is consistent with exposure to this virus sometime in the past. By 3 weeks following exposure, nearly all immunocompetent individuals should have developed IgG antibodies to DV.

The presence of IgM-class antibodies to DV is consistent with acute-phase infection.

IgM antibodies become detectable 3 to 7 days following infection and may remain detectable for up to 6 months or longer following disease resolution.

The absence of IgM-class antibodies to DV is consistent with lack of infection. However, specimens collected too soon following exposure may be negative for IgM antibodies to DV. If DV remains suspected, a second specimen, collected approximately 10 to 12 days following exposure should be tested.

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).

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

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

Cautions

Test results should be used in conjunction with clinical evaluation, including exposure history and clinical presentation.

False-positive results, particularly with the dengue virus (DV) IgG enzyme-linked immunosorbent assay, may occur in persons infected with other flaviviruses, including Zika virus, West Nile virus, and St. Louis encephalitis virus. Obtaining a detailed exposure history and additional laboratory testing may be necessary to determine the infecting virus.

Positive test results may not be valid in persons who have received blood transfusions or other blood products within the last several months.

The significance of a negative result in an immunosuppressed patient is unclear.

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 more 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

A total of 200 prospective serum samples submitted for dengue virus (DV) IgM and IgG testing by the Focus Diagnostics DV IgM and IgG enzyme immunoassays (EIA) were also tested by the InBios IgM and IgG DV assays. The results were compared and the data summarized in Tables 1 and 2.

Table 1. Comparison of the InBios and Focus (Quest) Diagnostics DV IgM EIA

InBios DV IgM EIA	**Focus (Quest) Diagnostics DV IgM EIA**	
	Positive	Negative
Positive	14	0
Negative	1	184
Equivocal	1	0

Sensitivity: 87.5% (14/16); 95% CI 62.7%-97.7%
Specificity: 100% (184/184); 95% CI 97.5%-100%
Agreement: 99% (198/200); 95% CI 96.1%-99.9%

Table 2. Comparison of the InBios and Focus (Quest) Diagnostics DV IgG EIA

InBios DV IgG EIA	**Focus (Quest) Diagnostics DV IgG EIA**	
	Positive	Negative
Positive	34	0
Negative	0	164
Equivocal	2	0

Sensitivity: 94.4% (34/36); 95% CI 80.9%-99.4%
Specificity: 100% (164/164); 95% CI 97.2%-100%

Agreement: 99% (198/200); 95% CI 96.1%-99.9%

An additional 42 serum samples positive for IgG-class antibodies to West Nile virus (n=24), St. Louis encephalitis virus (n=9) and California (LaCrosse) virus (n=9) were also tested by the InBios DV IgG EIA and the data are summarized below in Table 3.

Table 3. Cross-reactivity of the InBios DV IgG EIA with antibodies to West Nile virus, St. Louis encephalitis virus, and California (LaCrosse) virus

InBios DV IgG EIA	West Nile virus IgG positive	St. Louis encephalitis virus positive	California (LaCrosse) virus positive
Positive	18	7	1
Negative	2	0	8
Equivocal	4	2	0

Note that the InBios DV IgG EIA shows significant cross-reactivity with antibodies to West Nile virus and St. Louis encephalitis virus.

The presence of nonstructural protein 1 (NS1) antigen overlaps with the 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 4 below. Discordant samples were also tested by the Platelia NS1 Ag EIA (BioRad Laboratories, Marnes-la-Coquette, France).

Table 4. Comparison of the InBios NS1 EIA to RT-PCR for DV detection

InBios DV NS1 EIA	**Focus Diagnostics DV RT-PCR**	
	Positive	Negative
Positive	24	7(b)
Negative	1(a)	43
Equivocal	0	2(c)

a. This sample was negative by the Platelia NS1 EIA
b. Five samples were also positive by the Platelia NS1 EIA
c. One sample was negative and 1 sample was indeterminate by the Platelia NS1 EIA

Sensitivity: 96% (24/25); 95% 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

1. Centers for Disease Control and Prevention (CDC). Clinical Testing Guidance for Dengue. Updated August 26, 2024. Accessed December 11, 2024, Available at www.cdc.gov/dengue/hcp/diagnosis-testing/index.html
2. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. Geneva: World Health Organization; 2009
3. Khan MB, Yang ZS, Lin CY, et al. Dengue overview: An updated systemic review. J Infect Public Health. 2023;16(10):1625-1642. doi:10.1016/j.jiph.2023.08.001

Performance

Method Description

Dengue virus IgM:
In this enzyme-linked immunosorbent assay (ELISA), samples and controls are diluted in sample dilution buffer and incubated in microtiter wells coated with antihuman IgM antibodies. This incubation is followed by incubation with dengue-derived recombinant antigens (DENRA) and normal cell antigen (NCA) separately. After incubation and washing, the wells are treated with a DEN-specific monoclonal antibody labeled with horseradish peroxidase (HRP). After a second incubation and washing step, the wells are incubated with tetramethylbenzidine (TMB) substrate. Acid stop is added and absorbance at 450 nm is read. The ratio of absorbencies of the DENRA and the control antigen wells determine whether the result is positive or negative.(Package insert: InBiOS DENV Detect IgM CAPTURE ELISA. InBios International, Inc; Revision 10/01/2019)

Dengue virus IgG:
In this enzyme-linked immunosorbent assay, controls and diluted samples are incubated in microtiter wells coated with monoclonal antibody bound to dengue-derived recombinant antigens (DENRA). After incubation and washing, wells are treated with IgG antibody labeled with horseradish peroxidase. After a second incubation and washing, wells are incubated with tetramethylbenzidine substrate. Acid stop is added, and absorbance at 450 nm is measured. The ratio of the absorbencies of the DENRA and the control wells determines whether a result is positive or negative.(Package insert: InBiOS DENV Detect IgG ELISA. InBios International, Inc; Revision 05/01/2018)

Nonstructural protein 1:
The InBios nonstructural protein 1 (NS1) ELISA is a 2-step sandwich-format colorimetric immunoassay for qualitative detection of NS1 antigen in serum. Diluted patient samples and controls are incubated in wells coated with purified capture antibody, specific for the dengue NS1 antigen. Following incubation, wells are washed, incubated with HRP-conjugated polyclonal antibody specific to NS1 antigen and reincubated. Wells are subsequently washed and TMB substrate is added and incubated at room temperature in the dark. Stop solution is added next and the optical density (OD) of the reaction is measured at 450/620 nm. The immune status ratio 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 Detect NS1 ELISA.InBios International, Inc; Revision 01/18/2019)

PDF Report

No

Day(s) Performed

Tuesday

Report Available

Same day/1 to 7 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & 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 account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

86790 x 3

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
DENVP	Dengue Virus Ab/Ag Panel, S	104595-4

Result ID	Test Result Name	Result LOINC® Value
DENG	Dengue Virus Ab, IgG, S	29661-6
DENM	Dengue Virus Ab, IgM, S	29663-2
DENS1	Dengue NS1 Ag, S	75377-2
INT69	Dengue Interpretation	69048-7