One Step Dengue IgG/IgM Rapid Test

Cat.No.: DNG 431

1. Explanation of the test

[INTRODUCTION] Dengue viruses, transmitted by the mosquito, *Aedes aegypti* and *Aedes albopictus* mosquitoes, are widely distributed throughout the tropical and subtropical areas of the world. There are four known distinct serotypes (dengue virus 1,2,3 and 4). In children, infection is often subclinical or causes a self-limited febrile disease. However, if the patient is infected second times with a different serotype, a more severe disease, dengue hemorrhagic fever or dengue shock syndrome, is more likely to occur. Dengue is considered to be the most important arthropod-borne viral disease due to the human morbidity and mortality it causes.

Traditionally, the serological diagnosis of an acute dengue virus infection has relied on showing a 4-fold or greater rise in anti-dengue virus antibody between paired acute- and convalescent-phase sera from a patient. The haemagglutination-inhibition test has been the most commonly used serological assay for dengue diagnosis.

Rapid and reliable tests for primary and secondary infections of dengue are essential for patient management. Primary Dengue infection is associated with mild to high fever, headache, muscle pain and skin rash. Immune response includes IgM antibodies produced by 5th day of symptoms and persist for 30—60 days. IgGs appear the 14th day and persist for life. Secondary infections often result in high fever and in many cases with haemorrhagic events and circulatory failure. Secondary infections show that IgGs rise within 1-2 days after the onset of symptoms and induce IgM response after 20 days of infection.

[INTENDED USE] Dengue IgG / IgM Rapid Test is *a* solid phase immunochromatographic assay for the rapid, qualitative and differential detection of IgG and IgM antibodies to dengue virus in human serum, plasma or whole blood. This test is intended for professional use to aid in the presumptive diagnosis between primary and secondary dengue infection. This test provides only a preliminary test result. Therefore, isolation of virus, antigen detection in fixed tissues, RT-PCR and serological test like haemagglutination-inhibition test, more specific alternative diagnosis method must be used in order to obtain a confirmation of dengue virus infection.

[PRINCIPLE] Dengue IgG / IgM Rapid Test is designed to simultaneously detect and differentiate IgG and IgM antibodies to dengue virus in human serum, plasma or whole blood. This test also can detect all 4 Dengue serotypes by using a mixture of recombinant Dengue envelope proteins.

Dengue IgG / IgM test device has 3 pre-coated line, "1" (Dengue IgG Test Line), "2" (Dengue IgM Test Line) and "C" (Control Line) on the surface of the device. All three lines in result window are not visible before applying any samples. The "Control Line" is used for procedural control. Control line should always appear if the test procedure is performed properly and the test reagents of control line are working. A purple "1" and "2" lines will be visible in the result window if there are enough IgG and/or IgM antibodies to Dengue virus in the sample. If IgG and/or IgM antibodies to Dengue virus arc not present in the sample, there is no color appearance in "1" and/or "2".

When a specimen is added to the sample well, IgG or IgM in specimen sample bind to anti-human IgG or IgM antibodies immobilized in two lines across the test membrane. If dengue specific immunoglobulins of the IgG or IgM are present in the sample, colloidal gold complexes containing dengue antigen captured by the bound patient's IgG or IgM give visible colored lines.

2. Materials provided

1) 25 Test devices individually foil pouched with a desiccant

Each test device contains anti-human IgG (G), anti-human IgM (M) and anti-Dengue IgG (C) as capture materials. Also device contain a gold conjugate pad with recombinant dengue virus envelope proteins.

2) Assay diluent (4ml/dropping bottle)

3) 10$\mu\ell$ capillary pipette

4) Package insert

3. Precautions

1) For best results, strict adherence to these instructions is required.

2) All specimens should be handled as being potentially infectious.

3) Do not open or remove test devices from their individually sealed pouches before their use

4) Do not reuse test devices.

5) All reagents must be at room temperature before running the assay.

6) Do not use reagents beyond the stated expiration date marked on the package label.

7) The components in this kit have been quality control tested as standard batch unit. Do not mix components from different lot numbers.

8) The assay diluent contains low concentration of sodium azide as a preservative. Sodium azide is toxic and should be handled carefully to avoid ingestion and skin contact.

4. Kit Storage and stability

The kit can be stored at room temperature (2~30°C) or refrigerated. The test kit is stable through the expiration date marked on the package label. DO NOT FREEZE. Do not store the test kit in direct sunlight.

5. Specimen Collection and Preparation

1) Specimen to be tested should be obtained and handled by standard methods for their collections.

A. Serum: allow the blood to clot, then centrifuge to separate the serum.

B. Plasma: collect the whole blood into the tube contained anticoagulants such as heparin, citrate, or EDTA. Centrifuge the blood and separate the plasma.

C. Whole blood: collect the whole blood into the collection tube containing anti-coaggulants such as heparin, EDTA, and sodium citrate.

2) All specimens should be tested as soon as early they are prepared. If necessary, they may be stored at 2-8℃ for up to 24 hours or at -20℃ for longer periods.

3) Precaution

A. Anti-coagulants such as heparin, EDTA, and citrate do not affect the test result.

B. Use separately disposable capillary tubes or pipette tips for each sample in order to avoid cross-contamination of either samples which could cause erroneous results.

6. Procedure of the test

1) Allow the sealed test cassette and the specimen come to room temperature.

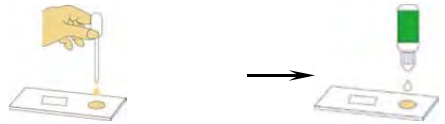
2) Remove the test device from foil pouch, place it on a flat, dry surface.

3) Use the provided capillary pipette, add 10$\mu\ell$ of serum/plasma or whole blood into the sample well, as shown in the following picture. (Micropipette use is recommended to add specimen accurately and efficiently.)

4) Then add 2 drops (about 80-100μL) of **sample diluent** into the sample well.

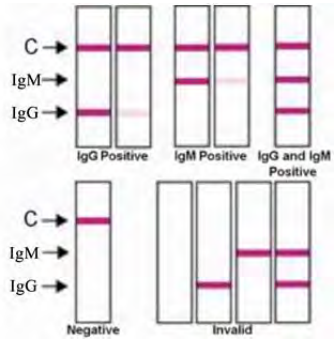
5) Interpret test results at 15-20 minutes.

6) Please do not read the results after 20 minutes of this testing.



10 μL of specimen　　2 drops of sample diluent

7. Interpretation of the test



IgM Positive
The control line (C) and IgM line (2) are visible on the test device. This is positive for IgM antibodies to Dengue virus. This is indicative of a primary dengue infection.

IgG Positive
The control line (C) and IgG line (1) are visible on the test device. This is positive for IgG antibodies. This is indicative of secondary or past dengue infection.

IgG and IgM Positive
The control line (C), IgM (2) and IgG line (1) are visible on the test device. This is positive for both IgM and IgG antibodies. This is indicative of a late primary or early secondary dengue infection.

Negative
The control line is only visible on the test device. No IgG and IgM antibodies were detected. Retest in 3-5 days if dengue infection is suspected.

Invalid
The control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Repeat the test using a new test device.

8. Limitation of the test

1) This test is for in vitro diagnostic use only.

2) This test detects the presence of antibodies to dengue in the specimen and should not be used as the sole criterion for the diagnosis of Dengue virus infection.

3) In early infections and some secondary infections, detectable levels of IgM antibodies may be low. Some patients may not produce detectable levels of antibody within the first seven to ten days after infection. If symptoms persist, the test should be repeated after 1~3 days with the first specimen of patient.

4) Serological cross-reactivity with the Flavivirus group (Dengue virus, St. Louis encephalitis, Japanese encephalitis. West Nile and yellow fever virus) is common.

5) As the result of all diagnostic tests, results must be considered with other clinical information available to the physician.

6) If the test result is negative and clinical symptoms persist, additional follow-up test using other clinical methods is recommended. A negative result does not preclude the possibility of an early infection of Dengue

9. Expected value

Primary dengue is characterized by the presence of detectable IgM 3-5 days after the onset of infection. Secondary dengue is characterized by the elevation of specific IgG 1-2 days after the onset of infection and in the majority of cases this is generally accompanied by an elevation of IgM.

Dengue IgG / IgM Rapid Test has been compared with a leading commercial Dengue IgM and IgG rapid test. The correlation between these two systems is 99.5 %

10. Performance Characteristics

1) Comparison of Dengue IgG / IgM Rapid Test with HI Test

Dengue IgG / IgM Rapid Test with HI Test showed good correlation with haemagglutination-inhibition (HI) test

Titer of HI Test	Dengue IgG/IgM	
	Dengue IgM Positive	Dengue IgG Positive
Primary infection		
1:10	+/-	-
1:20	+	-
>1:40	+	-
Secondary infection		
1:320	+	+
1:640	+	+
1:1280	+	+
>1:2560	+	+

2) Sensitivity

To assess sensitivity, 15 paired specimen from patients with primary infection and 20 paired specimen with secondary infection were tested. In this test, Dengue IgG / IgM Rapid Test showed that it could diagnose the majority of dengue virus effectively.

	IgM positive/ Total 1st collection	IgM Positive /Total 2nd collection	IgG Positive /Total 1st collection	IgG Positive /Total 2nd collection
Primary	14/15	15/15	0/15	3/15
Secondary	4/20	18/20	20/20	20/20

3) Cross-reactivity test with other FIavivirus mediated and mosquitoes-borne disease

Dengue IgG / IgM Rapid Test showed no cross-reactivity with other FIavivirus mediated disease and mosquitoes-borne disease like Malaria

Disease	Dengue IgM Negative/Total	Dengue IgG Negative/Total
Japanese Encephalitis	25/25	25/25
Yellow Fever	25/25	25/25
Malaria P. falcifarum	25/25	25/25
Malaria P. vivax	25/25	25/25
Total	100/100	100/100

11. Bibliography of suggested reading

1) Dengue haemorrhaic fever : Diagnosis, treatment, prevention and control. WHO 2nd Edition 1997

2) Songee L. ranch and Paul N. Levett. Evaluation of four methods for detection of immunogloulin M antibodies to dengue virus. Clin. Diagn. Lab. Immunol. Vol 6(4) p 555-557,1999

3) Jan Groen et al. Evaluation of six immunoassays for detection of dengue-virus specific immunoglobulin M and G Antibodies. Clin. Diagn. Lab. Immunol. Vol 7(6) p 867-871,2000

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