INTENDED USE
The TB IgG/IgM Combo Rapid Test is a lateral flow chromato-immunodiagnosis for the simultaneous detection and differentiation of IgM anti-Mycobacterium Tuberculosis (M.TB) and IgG anti- M.TB in serum, plasma or whole blood. It is intended to be used as a screening test and as an aid in the diagnosis of infection with M. TB. Any reactive specimen with the TB IgG/IgM Combo Rapid Test must be confirmed with alternative testing method(s) and clinical findings.

SUMMARY AND EXPLANATION OF THE TEST
Tuberculosis is a chronic, communicable disease caused principally by M. TB hominis (Koch’s bacillus), occasionally by M. TB bovis. The lungs are the primary target, but any organ may be infected.

The risk of TB infection has exponentially declined in the 20th century. However, the recent emergence of drug-resistant strains, particularly among patients with AIDS, has rekindled interest in TB. The incidence of infection was reported around 8 million cases per year with a death rate of 3 million per year. The mortality exceeded 50% in some African countries with high HIV rates.

The initial clinical suspicion and radiographic findings, with subsequent laboratory confirmation by sputum examination and culture are the traditional method(s) in the diagnosis of active TB. However, these methods either lack sensitivity or are time consuming, in particular are not suitable for patients who are unable to produce adequate sputum, smear-negative, or suspected to have extra-pulmonary TB.

The TB IgG/IgM Combo Rapid Test is developed to alleviate these obstacles. The test detects IgM and IgG anti-M.TB in serum, plasma, or whole blood in 15 minutes. An IgM positive result indicates for a fresh M.TB infection, while an IgG positive response suggests a previous or chronic infection. Utilizing M.TB specific antigens, it also detects IgG anti-M.TB in patients vaccinated with BCG. In addition, the test can be performed by untrained or minimal skilled personnel without cumbersome laboratory equipment.

TEST PRINCIPLE
The TB IgG/IgM Combo Rapid Test is a lateral flow chromato-immunodiagnosis. The test cassette consists of: 1) a burgundy colored conjugate pad containing M.TB antigens conjugated with colloidal gold (M.TB conjugates) and rabbit IgG-gold conjugates, 2) a nitrocellulose membrane strip containing two test bands (T1 and T2 bands) and a control band (C band). The T1 band is pre-coated with monoclonal anti-human IgM for the detection of IgM anti-M.TB, the T2 band is pre-coated with reagents for the detection of IgG anti-M.TB, and the C band is pre-coated with goat anti-rabbit IgG.

When an adequate volume of test specimen is dispensed into the sample well of the cassette, the specimen migrates by capillary action across the cassette. IgM anti-M.TB if present in the specimen will bind to the M.TB conjugates. The immunocomplex is then captured on the membrane by the pre-coated anti-human IgM antibody, forming a burgundy colored T1 band, indicating a M.TB IgM positive test result.

IgG anti-M.TB, if present in the specimen, will bind to the M.TB conjugates. The immunocomplex is then captured by the pre-coated reagents on the membrane, forming a burgundy colored T2 band, indicating a M.TB IgG positive test result.

Absence of any T bands (T1 and T2) suggests a negative result. The test contains an internal control (C band) which should exhibit a burgundy colored band of the immunocomplex of goat anti-rabbit IgG/rabbit IgG-gold conjugates regardless of the color development on any of the T bands. Otherwise, the test result is invalid and the specimen must be retested with another device.

REAGENTS AND MATERIALS PROVIDED
1. Each kit contains 30 test devices, each sealed in a foil pouch with four items inside:
   a. One cassette device.
   b. One plastic dropper.
   c. One sealed plastic dropper containing sample diluent.
   d. One desiccant.
   e. One package insert (instruction for the use).
2. Positive Control (1 vial, red cap, 1 mL, Cat # R0053-P)
3. Negative Control (1 vial, green cap, 1 mL, Cat # R0053-N)

MATERIALS REQUIRED AND AVAILABLE FOR PURCHASE
1. Positive Control (1 vial, red cap, 1 mL, Cat # R0053-P)
2. Negative Control (1 vial, green cap, 1 mL, Cat # R0053-N)

MATERIALS REQUIRED BUT NOT PROVIDED
1. Clock or Timer
2. Lancing device for whole blood test

WARNINGS AND PRECAUTIONS
For In Vitro Diagnostic Use
1. This package insert must be read completely before performing the test. Failure to follow the insert gives inaccurate test results.
2. Do not open the sealed pouch, unless ready to conduct the assay.
3. Do not use expired devices.
4. Bring all reagents to room temperature (15°C-30°C) before use.
5. Do not use the components in any other type of test kit as a substitute for the components in this kit.
6. Do not use hemolized blood specimen for testing.
2. Clinical Performance For IgG Test

A total of 200 specimens from the non-TB patients and 35 specimens from the patients under anti TB treatment were tested by the TB IgG/IgM Combo Rapid Test and a commercial TB IgG ELISA kit. Comparison for all subjects is showed in the following table.

<table>
<thead>
<tr>
<th>TB IgG/IgM Combo Rapid Test</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG ELISA Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>31</td>
<td>7</td>
<td>38</td>
</tr>
<tr>
<td>Negative</td>
<td>193</td>
<td>200</td>
<td>393</td>
</tr>
<tr>
<td>Total</td>
<td>224</td>
<td>207</td>
<td>431</td>
</tr>
</tbody>
</table>

Relative Sensitivity: 85.6%, Relative Specificity: 96.5%, Overall Agreement: 95.3%

LIMITATIONS OF TEST

1. The Assay Procedure and the Assay Result Interpretation must be followed closely when testing the presence of antibodies to M.TB in serum or plasma from individual subjects. Failure to follow the procedure may give inaccurate results.

2. The TB IgG/IgM Combo Rapid Test is limited to the qualitative detection of IgG and IgM anti-M.TB in human serum or plasma. The intensity of the test band does not have linear correlation with the antibody titer in the specimen.

3. The test also recognizes antibodies to M. bovis and M. africanum.

4. An IgG positive response may be detected in BCG vaccinated personnel.

5. A negative result for an individual subject indicates absence of detectable antibodies to M.TB. However, a negative test result does not preclude the possibility of exposure to or infection with M.TB.

6. A negative result can occur if the quantity of the antibodies to M.TB present in the specimen is below the detection limits of the assay, or if the antibodies that are detected are not present during the stage of disease in which a sample is collected.

7. Immunocompromised condition such as HIV infection may reduce the test sensitivity. If HIV co-infection is highly suspected, the TB IgG/IgM Combo Rapid Test is highly recommended.

8. Some specimens containing unusually high titer of heterophile antibodies or rheumatoid factor may affect expected results.

9. If the symptom persists, while the result from TB IgG/IgM Combo Rapid Test is negative, it is recommended to re-test the specimen with an alternative test device.

10. The results obtained with this test should only be interpreted in conjunction with other diagnostic procedures and clinical findings.

REFERENCES


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