

State of the Globe: What's the Right Test for Diagnosing Rickettsial Diseases

The differential diagnosis of fever in the tropical world has to include Rickettsial diseases, apart from usual malaria, dengue, enteric fever, leptospirosis, and viral hemorrhagic fevers. Diagnostic tests play an essential role in stratifying, ruling out, and monitoring infectious diseases.

Multiple studies have been done to evaluate various types of diagnostic tests. Multiple investigations have been done to define the specificity and sensitivity of each of these tests. There are also a large number of comparative studies to establish the advantages and disadvantages and strengths and weaknesses of one test over the other.

When searched in PubMed, there was a little paucity of research regards studies on diagnostic tests in Rickettsial Diseases. Shivalli states in her article that there is a rising frequency of scrub typhus outbreaks and because it has overlapping clinical symptoms with malaria, leptospirosis, dengue fever, etc., the diagnosis of scrub typhus is based on laboratory tests or even the presence of a classical “eschar” could be quite convincing, but the major drawback is missing one as the native population has dark skin.^[1]

In 2015, the Department of Health Research and Indian Council for Medical Research published Guidelines for Management of Rickettsial diseases in India.^[2]

In these guidelines, four major diagnostic tests were highlighted namely:

1. Weil–Felix
2. IgM and IgG ELISA
3. Polymerase chain reaction (PCR)
4. Immunofluorescence assay (IFA).

All the four tests are valuable in diagnosing Rickettsial diseases.

The current literature suggests that IFA is the gold standard test, but the most commonly used test in diagnosing scrub

typhus in India is IgM ELISA.^[2,3] Although Weil–Felix is a heterophile antibody test that is easily available, inexpensive, and useful for diagnosing Rickettsial diseases, the only challenge is that it has to be carried out after 5–7 days of onset of fever. There is also baseline variability across regions, and standardization studies are needed to decide on titers for disease identification. IgM and IgG ELISA suffer from the same challenge of regional variability but offer two-step diagnostic benefit because the IgM is positive at the end of the 1st week while the IgG becomes positive by the end of the 2nd week. PCR is positive within the 1st week, but the gold standard is the IFA. Cost is the major factor.^[2]

A study done by Paris and Dumler concluded that the ELISA and the Nucleic Acid Amplification Assays are now replacing the indirect IFA. This will help to recognize early infection, thus helping early intervention.^[4]

In 2015, a PLoS One article evaluated the Scrub Typhus Infection Criteria (STIC). STIC included a combination of culture, PCR assays, and IFA. Lim *et al.* evaluated these criteria using Bayesian latent class models. They effectively concluded that STIC had very low specificity and they inferred that the IFA IgM was the main cause of the same due to its own virtue of being a very weak specific test. This study highlighted the need for increased volume of research in scrub typhus diagnostics.^[5] The main drawback of IFA method is the inaccessibility to fluorescent microscopes in underprivileged setups where the disease is often endemic. Indirect immunoperoxidase, a variation of the standard IFA method, can be used with a light microscope, and the results of these tests are equivalent to those from IFA.^[6,7]

Another study concluded that the Weil–Felix test had a poor sensitivity hence lacked the capability to be a routine diagnostic test. It was found that IgM ELISA was a better substitute for IFA.^[8] Rapid bedside kits have been described

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that give results within 1 h, but the availability of these tests is severely limited by their cost.^[9]

Duration of illness, type of tests available in the community, affordability, and ruling out malaria typhoid dengue, and other causes of acute undifferentiated febrile illness are factors which play into the capability of interpreting tests results when it comes to scrub typhus.

The era of point of care test for diagnosing scrub typhus is yet to come. Until then, clinical medicine and the art of exclusion of differential diagnoses will play an important role in diagnosis and management of scrub typhus.

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