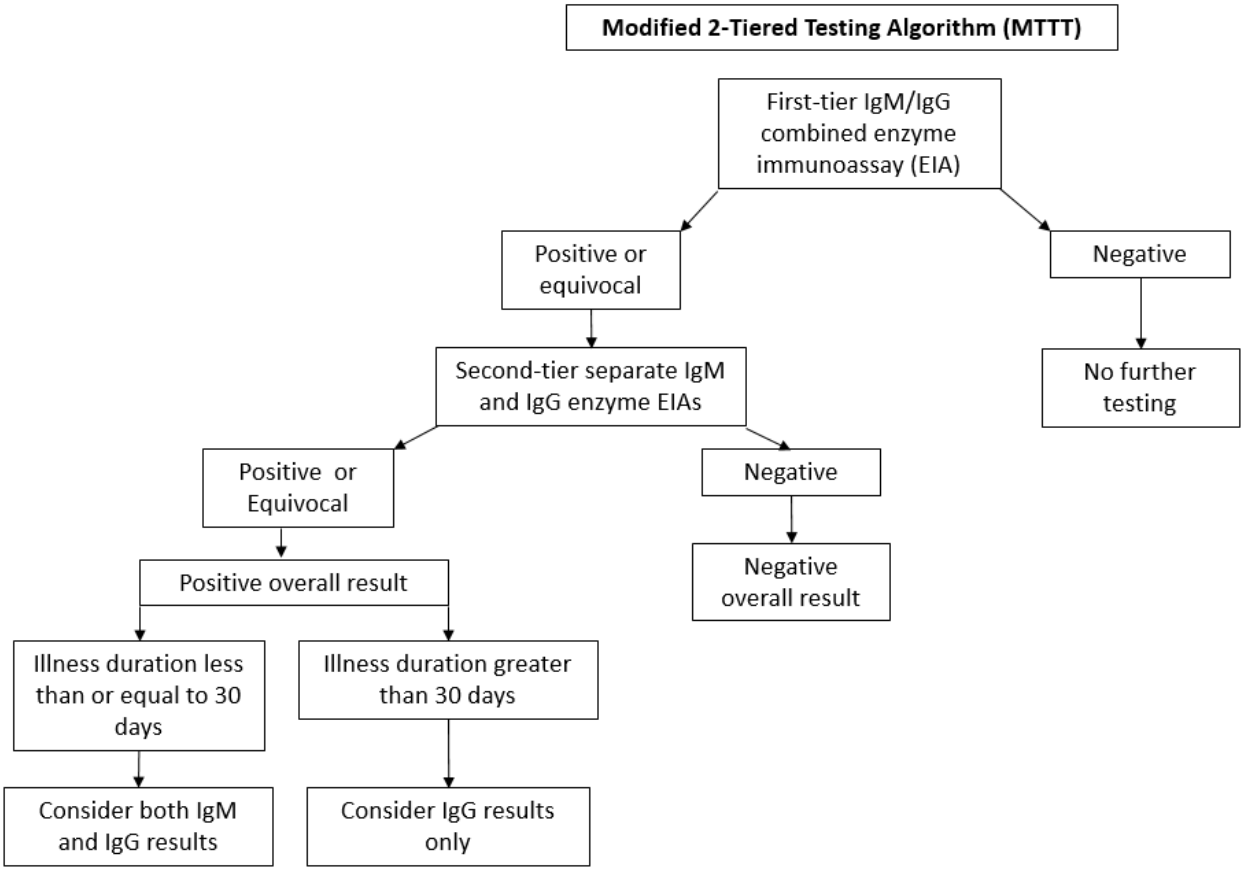
New Modified 2-Tiered Testing Algorithm (MTTT) to Support a Clinical Diagnosis of Lyme disease

In July 2019, the FDA cleared four previously-cleared tests with new indications to aid in the diagnosis of Lyme disease.[1] This clearance ushered in a paradigm shift in the diagnosis of Lyme disease, which has long relied on a two-tiered algorithm consisting of an initial screening IgM/IgG enzyme immunoassay (EIA) followed by separate confirmatory determinations of IgM and/or IgG with an immunoblot method. The new "modified" two-tiered testing algorithm (MTTT) uses two separate EIA assays sequentially (as pictured below) to assess for the presence of anti-*Borrelia burgorferi* antibodies in a patient's blood. This new approach was endorsed by the CDC soon after FDA approval.[2]



In both the traditional two-tiered testing algorithm and the MTTT, CDC recommends disregarding IgM test results if a patient has had symptoms greater than 30 days.[3]

This modification of the testing algorithm means 1) much more streamlined workflow in the laboratory and 2) results that should be LESS confusing to clinicians and patients. A move away from the immunoblot confirmatory test will end reporting of individual bands that do not rise to the level of overall test positivity.

The initial screening EIA used at DHMC remains the same as before. We run the *Borrelia* VlsE1/pepC10 IgG/IgM Test System (Zeus Scientific). This assay detects IgG and IgM class antibodies in human sera to the specific VlsE1 and pepC10 antigens. The new 2nd tier confirmatory EIA assays—the *Borrelia*

burgdorferi IgM Test System and the *Borrelia burgdorferi* IgG Test System (Zeus Scientific) each use whole cell antigens of *Borrelia burgdorferi*.

Lyme disease remains a particularly challenging area of clinical microbiology. A national biobank has been formed to help test developers create better tests.[4] Additional references are included for those who want to dive into the literature leading up to this change.[5-9]

References

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