

Laboratory News

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Changes to Lyme Disease Serologic Testing

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Effective March 6th 2023, Marshfield Labs will transition from the standard two-tier test (STTT) algorithm to the modified two-tier test (MTTT) algorithm for Lyme disease (LD) serological testing.

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Modified Two-Tier Testing

When Marshfield Labs transitions to the modified two-tier test (MTTT) algorithm for Lyme disease (LD) serological testing, confirmatory immunoblots will not be performed, nor bands data reported; instead, final results will consist of a negative or positive report together with an interpretive comment.

Further Details

Our current LD antibody test follows the longstanding STTT algorithm that uses a screening enzyme immunoassay (EIA) and a confirmatory immunoblot (aka Western blot) for all samples that screen as Positive or Equivocal.

In the past decade studies have demonstrated that using a second, immunologically different, EIA to confirm screen EIA Positive or Equivocal results gives increased sensitivity for early LD with no loss in sensitivity in more advanced cases nor in specificity overall^{1, 2, 3, 4}.

In this so-called MTTT algorithm, immunoblots are not used, thus positive bands cannot be reported. Instead, a report of Negative, Positive for IgM, Positive for IgG, or Positive for IgM & IgG anti-*B. burgdorferi* antibodies together with an interpretive comment will be made.

Please see the Table below for reporting and interpretation examples. Note that the MTTT still suggests that IgM results in patients with ≥ 30 days of the infection be disregarded, since a detectable IgM titer after that time may be due to non-specific cross-reactions.

For any technical questions, please contact: Immunodiagnostics lab at 715-221-6290.
For any clinical consultations, please contact: Dr. Thomas Novicki at 715-221-6132.

Guidance for the Interpretation of LD MTTT Results

Test Sequence			Interpretation for Laboratories	Interpretation for Providers
Tier 1	Tier 2a	Tier 2b		
<i>VlsE/pepC10</i> <i>IgM/IgG Total</i> <i>Immunoassay</i>	<i>Whole Cell</i> <i>Antigen IgM</i> <i>Immunoassay</i>	<i>Whole Cell</i> <i>Antigen IgG</i> <i>Immunoassay</i>		
Negative	Testing Not Indicated	Testing Not Indicated	Negative for antibodies to <i>B. burgdorferi</i> (Lyme disease).	No laboratory evidence of infection with <i>B. burgdorferi</i> (Lyme disease).
Positive/ Equivocal	Negative	Negative	Antibodies to <i>B. burgdorferi</i> (Lyme disease) not confirmed.	No laboratory evidence of infection with <i>B. burgdorferi</i> (Lyme disease).
Positive/ Equivocal	Positive	Negative	IgM-class antibodies to <i>B. burgdorferi</i> (Lyme disease) detected.	Results are consistent with acute or recent infection with <i>B. burgdorferi</i> (Lyme disease).
Positive/ Equivocal	Negative	Positive	IgG-class antibodies to <i>B. burgdorferi</i> (Lyme disease) detected.	Results are consistent with <i>B. burgdorferi</i> (Lyme disease) infection in the recent or remote past. IgG-class antibodies may remain detectable for months to years following resolution of infection.
Positive/ Equivocal	Positive	Positive	IgM and IgG-class antibodies to <i>B. burgdorferi</i> (Lyme disease) detected.	Results are consistent with <i>B. burgdorferi</i> infection (Lyme disease) in the recent or remote past. Antibodies may remain detectable for months to years following resolution of infection.

(Excerpted from APHL [Suggested Reporting Language, Interpretation and Guidance Regarding Lyme disease Serologic Test Results](https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf). <https://www.aphl.org/aboutAPHL/publications/Documents/ID-2021-Lyme-Disease-Serologic-Testing-Reporting.pdf>. Accessed 12/10/2022

References

1. Branda JA, Linskey K, Kim YA *et al.* Two-Tiered Antibody Testing for Lyme disease with Use of 2 Enzyme Immunoassays, a whole-Cell Sonicate Enzyme Immunoassay Followed by a VlsE C6 Peptide Enzyme Immunoassay. *Clin Infect Dis* 2011; 53:541–547.
2. Mollins CR, Delorey MJ, Sexton C *et al.* Lyme Borreliosis Serology: Performance of Several Commonly Used Laboratory Diagnostic Tests and a Large Resource Panel of well-characterized patient specimens. *J Clin Microbiol* 2016; 54:2726-2734.
3. Branda JA, Body BA, Boyle J *et al.* Advances in Serodiagnostic Testing for Lyme disease Are at Hand. *Clin Infect Dis* 2018 Mar 19; 66(7):1133-1139.
4. Sfeir, MM, Meece JK, Theel ES, *et al.* Multicenter Clinical Evaluation of Modified Two-Tiered Testing Algorithms for Lyme Disease Using Zeus Scientific Commercial Assays. *J Clin Microbiol* 2022; 60:1-11