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MEMORANDUM

**TO: Medical Officers of Health and Associate Medical Officers of Health
Public Health Units**

**FROM: Dr. S. Wajid Ahmed
Associate Chief Medical Officer of Health, Public Health**

**RE: Testing protocol changes for *Borrelia burgdorferi* (agent of Lyme
Disease) IgM/IgG antibodies – Modified Two-Tier Testing**

Dear Colleagues,

As you know, the current testing protocol for testing clinical samples for Lyme disease utilizes a standard two-tier testing (STTT) algorithm. Initially in the STTT algorithm, samples are tested for total IgM/IgG antibodies by enzyme-linked immunosorbent assay (ELISA). Samples that are reactive/indeterminate are further tested using a separate IgM/IgG Western blot assay. Public Health Ontario Laboratory (PHOL) communicates overall interpretation of the results to the submitting health care providers. The STTT algorithm has been in use for many years in Canada, including at PHOL.

During early-localized Lyme disease, sensitivity of the STTT ranges from 29-40% and therefore a negative test result during this stage does not rule out Lyme disease.

Because of poor sensitivity in the early stages of infection, Lyme disease cases are primarily diagnosed based on a clinical presentation consistent with Lyme disease along with tick exposure risk.

As the disease progresses from early-localized to early-disseminated to late-disseminated disease, the sensitivity of STTT increase significantly and negative STTT results essentially rules out Lyme disease.

Modified Two-Tier Testing (MTTT) Protocol for *Borrelia burgdorferi* (agent of Lyme Disease) IgM/IgG antibodies:

There have been several studies evaluating the use of Modified Two-Tier Testing (MTTT) approach in which a second ELISA is performed instead of traditional Western blot assay. Studies have shown that MTTT algorithm provides 15-25% higher sensitivity during early-localized disease, and comparable sensitivity during early-disseminated and late-disseminated disease compared to STTT. The MTTT algorithm has also shown comparable specificity to STTT.

Based on numerous studies, the Canadian Public Health Laboratory Network (CPHLN) and US Centers for Disease Control and Prevention (CDC) have endorsed the MTTT algorithm as an acceptable alternative method to STTT.

PHOL has evaluated the MTTT algorithm and found that MTTT-based approach is comparable, if not better, to the STTT approach in the detection of Lyme disease antibodies.

Adoption of Modified Two-Tier Testing Protocol:

As of April 1, 2023, PHOL will begin testing patient samples for Lyme disease antibodies using the MTTT algorithm. In this algorithm, initial screening (Tier 1) will be performed by IgG/IgM ELISA on whole cell lysates. Samples that are reactive or indeterminate will be further tested (Tier 2) on a second IgG/IgM ELISA targeting specifically VlsE1 and pepC10 antigens.

PHOL will revise and finalize the Test information sheet, Lyme disease investigation tool kit and will also communicate the changes more broadly prior to April 1, 2023. The Lyme disease-specific appendix under the Ontario Public Health Standards will also be updated and posted on our website. We are also exploring the opportunity to organize educational opportunities for clinicians on these changes.

Implication for practise:

The changes in testing algorithm will help to improve Lyme Disease diagnosis in early localized disease (by reducing the chances of a false negative result) and help to increase the turnaround time for Lyme Disease testing, leading to earlier intervention. The testing algorithm doesn't replace clinical decision making and is intended to support clinical decision making by increasing the sensitivity of the test and improved turnaround time for test results.

Please note that there are no changes to public health follow-up for Lyme disease and every case requires follow-up according to the Lyme disease-specific appendix.

Please share these updates locally with all your area healthcare providers for awareness.

Please reach out to Samir Patel (Samir.patel@oahpp.ca) if you have further technical questions about these changes.

Sincerely,



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