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# Diagnostic value of laboratory tests in the context of localized and disseminated Lyme disease

## English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

# SUMMARY

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### Introduction

Lyme disease, a vector-borne illness transmitted by the black-legged tick, is on the rise in Quebec. The number of confirmed or probable cases recorded in Québec's notifiable diseases (MADO) registry doubled between 2013 and 2017 (143 vs. 329 cases) and was 500 in 2019. While there seems to be unanimity in the medical and scientific community as to the definition and features of the localized stage of the disease, the situation is different for the early and late disseminated stages. Indeed, the distinction between the disseminated stages, post-treatment Lyme disease syndrome and so-called chronic Lyme disease is not clear either in medical practice or the scientific literature. To address the lack of clear guidance on the management of Lyme disease patients in Québec, the Direction générale adjointe de la protection de la santé publique (DGAPSP), in collaboration with the Direction de la biovigilance et de la biologie médicale (DBBM) and the Direction des affaires pharmaceutiques et du médicament (DAPM) of the Ministère de la Santé et des Services sociaux (MSSS), asked the Institut national d'excellence en santé et en services sociaux (INESSS) to develop recommendations and knowledge transfer tools on post-exposure prophylaxis (PEP) for the prevention of Lyme disease and on the recognition, diagnosis and treatment of this disease in those affected. This exercise was intended to equip Québec health professionals, particularly those on the front line, to deal with this growing disease. It was agreed with the requestor that the work would be carried out in two phases, the first dealing with PEP and the localized and disseminated stages of the disease, the second with so-called chronic Lyme disease.

### Methodology

For the purpose of carrying out that part of the task dealing specifically with diagnosis, INESSS collected and analyzed scientific data on the diagnostic value of the laboratory tests available in North America and best clinical practice recommendations published by learned societies and assessment agencies, to determine which ones contribute the most to the diagnostic process for Lyme disease and to support the scientific evidence for the purpose of developing clinical and implementation recommendations regarding the diagnosis of the disease. To this end, it conducted a systematic search of the scientific literature published in French, English and German, and of practice guidelines and guidance documents published in North America, Europe and Oceania. An additional search using the Google search engine was conducted for published reports, practice standards, regulations and guidance documents.

The scientific data were analyzed according to the continent where Lyme disease was contracted and to where the tests were performed, in order to take into account the distribution of the genospecies of bacteria in the *Borrelia burgdorferi sensu lato* (*B. burgdorferi s.l.*) complex in these territories. The tests' diagnostic value in the context of so-called chronic Lyme disease is discussed in a specific state-of-knowledge document.

## Results

The diagnostic value of twelve laboratory tests was investigated, four of which are methods for the direct detection of *B. burgdorferi s.l.* bacteria. Currently, no method for the direct detection of *B. burgdorferi s.l.* bacteria is sensitive and specific enough to make the diagnosis. Furthermore, most of the tests examined do not distinguish between an active infection and a past infection. In addition, the continent where Lyme disease is contracted has an influence on the diagnostic value of certain tests, including bacterial culture, immunoblotting and two-tiered serology.

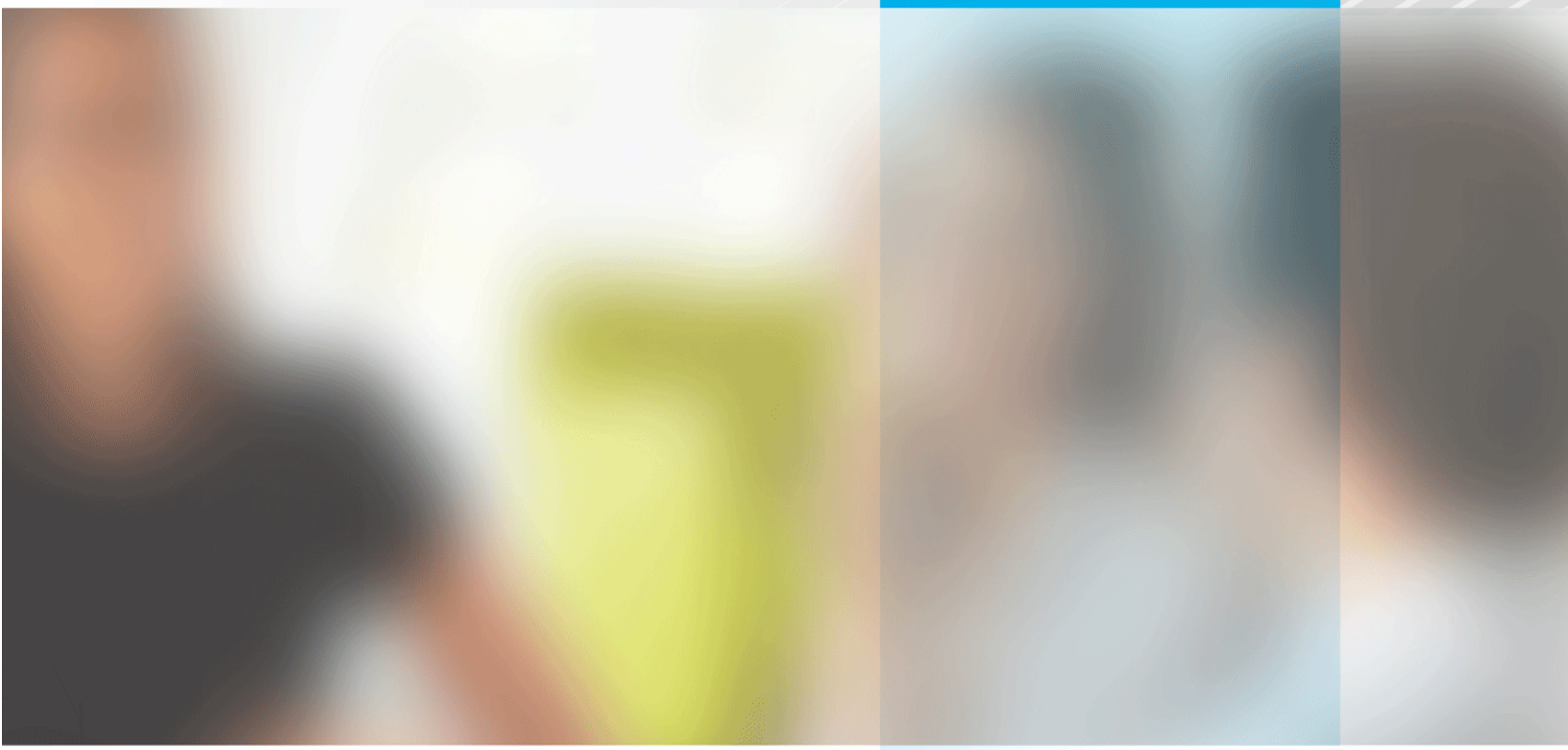
None of the tests studied in the context of erythema migrans attributable to Lyme disease has sufficient diagnostic value for use as a first-line test.

Two-tiered serology is the test that offers the best sensitivity and specificity in patients with a disseminated stage of the disease, especially those with Lyme arthritis. The various two-tiered serological methods studied yield similar results, but the combination of a VlsE ELISA test and immunoblotting provides the best specificity. While combining two types of ELISA may offer better sensitivity at the onset of the infection, the number of patients included in the selected studies was small.

The sensitivity of PCR and bacterial culture varies and is influenced by the methods used and the bacterial genospecies, among other things. In addition, the amount of CXCL13 present in cerebrospinal fluid may indicate a subpopulation of individuals with neuroborreliosis who have pleocytosis and anti-*Borrelia* antibodies in their cerebrospinal fluid or serum. Lastly, few or no studies were selected for the purpose of examining the diagnostic value of the anti-*Borrelia* antibody index (cerebrospinal fluid/serum ratio), detecting *B. burgdorferi s.l.* bacteria antigens, microscopy and histology, the lymphocyte transformation test, and the activated CD57+/CD3- NK lymphocyte count in the context of localized and disseminated Lyme disease.

## Conclusions

The systematic review of laboratory tests did not find one better than two-tiered serology for assisting in the diagnosis of disseminated Lyme disease. It did, however, reveal this test's low diagnostic value in the presence of erythema migrans and the need to document the continent(s) where Lyme disease may have been contracted to ensure that the appropriate immunoblotting tests are performed. Research should continue for the purpose of developing better-performing tests, particularly to facilitate diagnosis at the onset of the infection.

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