

“Chronic” Lyme disease: current state
of knowledge and overview of the
different perspectives
English summary

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SUMMARY

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Introduction

The diagnosis of Lyme disease is complex, and the information circulating about this disease on various websites and social media platforms is not always consistent with the scientific data. The medical community is fundamentally divided over the possibility that Lyme disease may cause persistent, general systemic symptoms. In addition, there are still many concerns and uncertainties regarding the reliability of laboratory tests and the efficacy of antibiotic treatments. Regardless of these uncertainties, the presence of such persistent and often significant symptoms is a reality for many people and is the reason for a large number of medical visits and requests for laboratory tests or specialized examinations. Furthermore, some people struggling with such symptoms and looking for their cause step outside Québec’s conventional healthcare system. They turn to clinicians who specialize in managing such patients, or they resort to tests performed by certain private laboratories and to treatments, both pharmacological and nonpharmacological.

In May 2019, at the request of three branches of the Ministère de la Santé et des Services sociaux (MSSS), INESSS published clinical and implementation recommendations for the diagnosis, treatment and management of patients with localized or disseminated Lyme disease to equip health professionals, especially front-liners, given the increase in this illness. As a continuation of this work, MSSS asked INESSS to shed scientific light on the plausibility that Lyme disease can cause persistent, general systemic symptoms, to provide a portrait of the experience of patients who struggle with such symptoms, and to make recommendations for managing patients with suspected or confirmed Lyme disease. The purpose of this document is to take a detailed look at the data gathered during this work on:

- The plausibility that Lyme disease can cause persistent, general systemic symptoms;
- The contribution of laboratory approaches and tests to the diagnostic process;
- The benefits and risks of prolonged single or combined treatments and those of other therapeutic options, both pharmacological and nonpharmacological, that are suggested in this context.

The gathering of this information helped in preparing the report and in developing the recommendations stemming from this work.

Methodology

To prepare this state-of-knowledge document, INESSS gathered scientific data, best clinical practice recommendations published by learned societies and assessment agencies, and the perspectives of various stakeholders, including patients and clinicians with varied practice in dealing with Lyme disease. To this end, it conducted a systematic search of the scientific literature published in French and English on the different aspects to be documented, and of practice guidelines and guidance documents published in North America and Europe. An additional search, using the Google search engine, was carried out for published reports, practice standards, regulations and guidance documents. This search was extended to the government websites of public health agencies and ministries and departments of health in Canada, the United States, France, the United Kingdom, New Zealand and Australia. The websites and public documents of the Association québécoise de la maladie de Lyme and Enfance Lyme Québec were consulted as well.

To gather the different perspectives, INESSS created an advisory committee consisting of clinicians, including medical specialists; experts in laboratory tests, acarological surveillance and public health; and patient partners with Lyme disease. In addition, clinicians with expertise in managing patients with persistent, general systemic symptoms attributed to Lyme disease were consulted through interviews or a survey to obtain the perspectives of clinicians with differing viewpoints. Further consultations were held with representatives from the Association québécoise de la maladie de Lyme and Enfance Lyme Québec, and interviews were conducted with patients with persistent, general systemic symptoms attributed to Lyme disease and with parents of children with such symptoms. The patient perspective was supplemented with case histories described in documents provided by patient associations and those mentioned by the various persons consulted.

Results

The condition of certain patients with persistent, general systemic symptoms, which are constant or cyclical, is attributed to Lyme disease. Some of these patients have a history of confirmed Lyme disease (i.e., diagnosis established with a high degree of certainty), while others do not.

Although the terms "chronic Lyme disease" and "Post-treatment Lyme disease syndrome" are widely used in the literature to describe individuals who have persistent, general systemic symptoms attributed to Lyme disease, there is no consensus regarding these terms either among learned societies and technology assessment agencies or among clinicians. The analysis of the data gathered indicates that these terms actually refer to poorly defined conditions where the etiology of the persistent symptoms is attributed to different causes and even different pathogens. Moreover, the available scientific data concerning the various hypotheses put forth to explain how infection with bacteria from the *B. burgdorferi* s.l. complex could cause persistent, general systemic symptoms are limited, especially with respect to studies conducted in humans. Therefore, the current state of scientific knowledge does not enable ruling on the plausibility that *B.*

burgdorferi s.l. bacteria cause, directly or indirectly, symptoms that persist in patients with a history of confirmed Lyme disease. Nor does it enable ruling on the plausibility that the infection was not diagnosed because of a negative serology result, the non-tick transmission of the bacterium or the presence of concomitant infections that affect the course of the illness in patients without a history of confirmed Lyme disease.

The present work therefore shows that the condition of patients with persistent, general systemic symptoms attributed to Lyme disease is poorly defined and that further research is needed to better understand the etiology of these symptoms in both treated and untreated individuals. Since *B. burgdorferi s.l.* bacteria are apparently not the only possible etiological agents in this context and that other noninfectious mechanisms, as well as other clinical conditions, might also be involved, the data collected on these individuals should be analyzed separately from those collected in the context of localized and disseminated Lyme disease. This distinction does not preclude the possibility that some patients having persistent, general systemic symptoms may have Lyme disease or a history of confirmed Lyme disease. It simply reflects the scientific uncertainty surrounding the condition of patients in this group and their heterogeneity.

Different laboratory tests are recommended to help diagnose patients with persistent, general systemic symptoms attributed to Lyme disease. The tests for which a systematic review of the scientific literature was conducted are not specific to *B. burgdorferi s.l.* bacteria, and no studies were found that have evaluated their contribution to the diagnosis of patients with persistent symptoms, whether they have a history of confirmed Lyme disease or not. While it is not possible, with the body of data gathered, to rule on the contribution of these tests to diagnosis, it does suggest a limited contribution and the need for further research to develop more suitable laboratory tests.

The currently available scientific data suggest that prolonged single and combined anti-infective treatments have little or no efficacy for resolving persistent symptoms or improving quality of life. However, methodological limitations and the fact that all studies involved a heterogeneous population of individuals affect the level of certainty regarding these results. In addition, only studies conducted in patients with a history of confirmed Lyme disease were identified during the systematic search of the scientific literature. Their conclusions are therefore difficult to generalize to all those with persistent symptoms attributed to Lyme disease, since some of these patients do not have a history of confirmed disease. In addition, some clinicians prescribe this type of treatment on an empirical basis and interpret the decrease in symptoms or the occurrence of a Jarisch-Herxheimer-like reaction as evidence of active infection. However, there is no scientific data for assessing the contribution of this approach to diagnosis. Although it is not possible, with the data gathered, to rule on the efficacy or safety of prolonged anti-infective treatments, there appears to be some interest in conducting better-designed studies and collecting data in the real-world care settings.

Different therapeutic approaches, both pharmacological and nonpharmacological, for relieving symptoms, preventing recurrences, boosting the immune system or treating an active infection are proposed in the literature, on special interest group websites and on various social media platforms. However, the available scientific data on these

approaches is very scant, and rarely is more than one case reported in a given publication. As in the case of prolonged anti-infective treatments, the data gathered is insufficient for ruling on the efficacy and safety of these treatment options in patients with persistent, general systemic symptoms attributed to Lyme disease, whether they have a history of confirmed Lyme disease or not. However, it would be useful to collect data on certain approaches, particularly those that have already been shown to be effective and safe in other complex diseases.

Conclusion

The review of the current state of scientific knowledge did not enable confirmation or ruling out that infection by *B. burgdorferi s.l.* bacteria can, directly or indirectly, cause persistent, general systemic symptoms, whether the patient has a history of confirmed Lyme disease or not. Nor did it enable ruling on the contribution of new laboratory approaches and tests to diagnosis or on the benefits and risks of prolonged single and combined anti-infective therapies in this context. Furthermore, this work shows that the condition of patients with such symptoms is not circumscribed and that it goes beyond infection with *B. burgdorferi s.l.* bacteria. The areas of uncertainty mentioned point to the need for research to be conducted to better understand the etiology of these symptoms, develop diagnostic tools and identify effective and safe treatment regimens. Pending the publication of studies of good methodological quality, courses of action to improve the management of these patients are presented in the report published concurrently with this state-of-knowledge document.

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