

## **HOLISTIC OR DEDICATED APPROACH IN LYME DISEASE?**

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Dear Editor,

Further to the paper by Haddad et al [1] describing a retrospective monocentric observation of patients presenting with suspected Lyme borreliosis we would like to make the following comments. Patients were classified as confirmed Lyme borreliosis (LB) case when they met the following criteria: tick bite, characteristic clinical signs, positive serology (ELISA and Western blot), and clinical recovery after antibiotic treatment. We would like to pinpoint that the majority of patients with tick-borne illnesses have no memory of tick bite, because of the small size of the tick (nymph) or the location of the bite. Many have no erythema migrans. Many signs and symptoms of LB are often found in other conditions, so differential diagnosis is often difficult. Published data demonstrate the lack of reliable serologic tests to reach the diagnosis of LB. The ECDC reported a sensitivity of the enzyme immunoassay / immunoblot of 0.77 (95% CI 0.67–0.85) in the diagnosis of neuroborreliosis, and warned that the results of serologies for LB should be interpreted with caution [2]. The reason is the great difficulty to define populations of patients and controls, in the frequent absence of specific clinical criteria [3] and in the absence of a reliable biological gold standard. Furthermore, a meta-analysis of LB test accuracy published in 2016 reported a sensitivity of only 59.5% (30.6-86.2%) [4]. The possibility of co-infections due to other bacteria or parasites is mentioned but has not been systematically investigated with reliable tests. Thus, the diagnostic approach of the authors was based on a subjective evaluation. In case of negative Lyme serology, the only mean to distinguish between an unclear medical condition mimicking, for example, an auto-immune disease and a true auto-immune disease is the response to an empiric antibiotic treatment, which can be used as a diagnostic tool. This strategy was first mentioned in 2007 for the management of seronegative cases of neuroborreliosis [5] and, since 2011, is included in the reporting criteria of the US CDC of probable Lyme disease cases. In France, empiric antibiotic treatment has been recommended in the 2014 report of the French High Council of Public Health (Haut Conseil de la Santé Publique) and now fully recommended in the 2018 French recommendations of the High Authority for Health (Haute Autorité de Santé). In Haddad et al's article, treatment failure was considered when patients still presented persistent symptoms despite 4 weeks of antibiotic therapy. May we put forward that this is a major bias of the study. Patients experiencing a worsening of symptoms during the first weeks of treatment, a frequent event due to the Jarisch-Herxheimer reaction [6], are classified as failure or side-effect of treatment. The authors of this article therefore may exclude the diagnosis of LB on the basis of the unreliability of the tests, and on a very questionable therapeutic failure. Research in

microbiology, immunology and genetics will help in the future to improve the diagnosis and management of LB, which is a major healthcare issue.

**Conflict of Interest : none**

## Références :

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