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Borrelia genus

Borrelia is a genus of microaerophilic, slow-growing, Gram negative, spirochaete bacteria, of which many species have been associated with human disease. Depending on the species, *Borrelia* are transmitted through the bite of infected ticks and lice. They are the causative agents of Lyme disease (LD), also referred to as Lyme borreliosis (LB), and tick/louse-borne relapsing fever (TBRF/LBRF). Broadly, the genus is phylogenetically split into three major clades: the Lyme disease (LD) group, the relapsing fever (RF) group, and the 'reptile/echidna-associated' group, with each named after the disease/hosts they are typically associated with (Margos G *et a*l., 2018).

Worldwide, many species of *Borrelia* have been identified, however those which cause LD are referred to as '*Borrelia burgdorferi sensu lato (s.l.)'*, and are transmitted by hard ticks of the Ixodidae family. This group encompasses over 20 genospecies, including *B. burgdorferi sensu stricto (s.s.), B. afzelii, B. americana, B. bavariensis, B. bissettiae, B. californiensis, B. carolinensis, B. chilensis, B. garinii, B. japonica, B. kurtenbachii, B. lanei, B. lusitaniae, B. maritima, B. mayonii, B. sinica, B. spielmanii, B. tanuki, B. turdi, B. valaisiana* and *B. yangtzensis*, among others. Other clinically relevant *Borrelia* species not included in the *B. burgdorferi s.l.* complex include those associated with human RF, and are primarily transmitted by soft ticks of the family Argasidae, such as *B. hermsii,* with the exception of louse-borne *B. recurrentis* and hard tick-borne *B. miyamotoi* and *B. lonestari* (Guiqing Wang, 2015).

In the Northern hemisphere, LD is the most prevalent vector-borne disease, with an estimated 200,000 cases reported each year in Europe alone (Marques *et al*., 2021). In England and Wales, it is estimated that 2000-3000 new cases each year with around 15% cases contracted abroad. Cases are more commonly diagnosed in the summer season relative to tick numbers. In Europe and Asia, LD is primarily caused by two genospecies of the *B. burgdorferi s.l.* complex (*B. afzelii and B. garinii*), in addition to *B. burgdorferi s.s.,* whereas in the United States*, B. burgdorferi s.s.* and more rarely, *B. mayonii* are the predominant causes (Guiqing Wang, 2015).

There are multiple stages to LD, with early-localised infection at the site of the bite (sometimes characterised by a 'bull's-eye'/erythema migrans rash'), followed by early-disseminated infection where spirochaetes spread into the bloodstream. If left untreated,

infection may cause neurological complications with risk of meningitis in some patients. After several months, the disease becomes chronic, referred to as the late disseminated stage, causing high morbidity such as motor or sensory dysfunction and cognitive impairment.

Early diagnosis and treatment with antibiotics are usually effective in preventing long-lasting and irreversible symptoms. Typically, patients may be diagnosed upon presentation with erythema migrans, however, where this clinical presentation is absent, serological tests may be used for diagnosis. Serological testing for LD in the UK and much of the world typically follows a two-tier approach: first using a sensitive screening enzyme linked immunosorbent assay and second, a more specific confirmatory test to confirm the presence of *Borrelia*-specific IgG/IgM antibodies. However, as serological testing is most valuable after several weeks of infection once antibodies have reached detectable levels, molecular diagnosis using polymerase chain reaction targeting *Borrelia* DNA in blood, tissue and cerebrospinal fluid (CSF) may be considered a useful alternative during the early stages of disease (UKHSA, 2018).

Thus, service users may wish to send samples of EDTA whole blood, CSF and tissue from patients where LD is suspected.

Our assay:

At Micropathology Ltd, we use a nested PCR targeting the *flagellin* gene for the qualitative detection of *Borrelia* DNA. *Borrelia species including (but not limited to) B. burgdorferi s.l. (e.g. B. burgdorferi s.s., B. afzelii, B. bavariensis, B. bissettiae, B. garinii, B. mayonii) are detected with this assay. Borrelia* species associated with relapsing fever such as *B. lonestari* and *B. persica* may potentially be amplified with this assay. *B. miyamotoi* is not detectable using this assay.

UKAS accredited specimen types for this assay include EDTA whole blood, CSF and tissue specimens, however other clinically relevant sample types may be tested (e.g. ocular specimens such as aqueous humour or vitreous samples), and are reported alongside a caveat to state that the assay is not UKAS accredited for testing alternate sample types. Sample volumes required for this assay include: at least 200 µL for liquid specimens, and tissue specimens approximately the size of a matchstick head.

Please note, we have previously extracted and detected *Borrelia burgdorferi* DNA from tick specimens.

Turnaround times are stated in the laboratory user handbook with results usually available in practice much sooner than the given time frame. Where there is a delay, we are usually confirming a result and addressing clinical data given with the specimen.

References

Guiqing Wang, Chapter 104 - Borrelia burgdorferi and Other Borrelia Species, Editor(s): Yi-Wei Tang, Max Sussman, Dongyou Liu, Ian Poxton, Joseph Schwartzman, Molecular Medical Microbiology (Second Edition), Academic Press, 2015, Pages 1867-1909, ISBN 9780123971692, https://doi.org/10.1016/B978-0-12-397169-2.00104-9. (https://www.sciencedirect.com/science/article/pii/B9780123971692001049)

Margos G, Gofton A, Wibberg D, Dangel A, Marosevic D, Loh SM, Oskam C, Fingerle V. The genus Borrelia reloaded. PLoS One. 2018 Dec 26;13(12):e0208432. doi: 10.1371/journal.pone.0208432. PMID: 30586413; PMCID: PMC6306154.

Marques AR, Strle F, Wormser GP. Comparison of Lyme Disease in the United States and Europe. Emerg Infect Dis. 2021 Aug;27(8):2017-2024. doi: 10.3201/eid2708.204763. PMID: 34286689; PMCID: PMC8314816.

UK Health Security Agency (UKHSA). “Lyme Disease: Sample Testing Advice.” GOV.UK, 31 July 2018, www.gov.uk/guidance/lyme-disease-sample-testing-advice. Last updated: 20/04/2022