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## Borrelia genus

*Borrelia* is a genus of spirochete bacteria and the causative agent of the vectorborne Lyme disease. Depending on the bacterial species, infection is transmitted via bites from ticks of the *Ixodus* genus or lice. Of the 52 known species of *Borrelia*, 12 are known to cause Lyme disease or borreliosis and are transmitted by ticks. The major *Borrelia* species causing Lyme disease are *Borrelia burgdorferi*, *Borrelia afzelii*, and *Borrelia garinii*. In North America, *B. burgdorferi* sensu stricto and *B. mayonii* species cause Lyme, whereas in Europe and Asia *B. afzelii* and *B. garinii*, also referred to as *B. burgdorferi* sensu lato, are the major causes of Lyme disease. The sheep tick, *L. ricinius*, is the primary vector of the disease in Europe.

It is estimated that there are 2000-3000 new cases of Lyme disease in England and Wales each year with around 15% cases contracted abroad. Cases are more commonly diagnosed in the summer season relative to tick numbers.

Infection with *B. burgdorferi*, (including *B. garinii* and *B. afzelii*), can manifest itself in a range of dermatological, neurological, cardiac, and musculoskeletal disorders. Early infection with *Borrelia* can present as a classical 'bulls eye' rash known as erythema migrans. Subsequently the infection can disseminate to the skin, central nervous system (CNS) and heart. *Borrelia burgdorferi* is known to invade the CNS and be neurotropic, leaving the cerebrospinal fluid (CSF) to adhere to glial cells or other brain tissue<sup>1</sup>. Once in the CNS, *B. burgdorferi*, may remain latent, only to re-activate and cause illness months later. Chronic, infection is associated with high morbidity and may cause impairment of motor or sensory functions, resulting in reduced cognitive abilities. Early diagnosis and treatment is effective in preventing long lasting irreversible symptoms.

The early serodiagnosis of *Borrelia* infection is difficult because the antibody response in the first weeks of infection is absent/exhibits limited detectability<sup>2</sup>.

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Furthermore, there is little diagnostic value of antibody assays in distinguishing active and inactive infection as antibodies persist after therapy. *Borrelia burgdorferi* can be recovered from CSF, skin and blood by culture, however culture is not the gold standard method for *Borrelia* detection due to its lack of sensitivity<sup>3</sup>. The spirochaetes grow slowly and cultures need to be monitored for up to 12 weeks, with results confirmed by microscopy, PCR or staining by specific monoclonal antibodies<sup>3</sup>.

Molecular amplification has the advantage of being a highly sensitive and rapid technique. In blood, the bacteraemia is transient and high detection rates can be expected only during a short period of the primary infection<sup>4</sup>. A high correlation has been found between the detection of *B. burgdorferi* by PCR and the presence of erythema migrans<sup>5,6</sup>. In 2010, the European Federation of Neurological Sciences published guidelines stating that although PCR on CSF samples demonstrates low sensitivity, it may be useful for the identification of very early Lyme neuroborreliosis where there are no detectable antibodies or in patients who are immunodeficient<sup>3</sup>.

## Our assay:

At Micropathology Ltd, we use a nested PCR targeting the *flagellin* gene for the qualitative detection of *Borrelia* genus DNA. *Borrelia* species including (but not limited to) *B. burgdorferi*, *B. afzelii*, *B. garinii*, *B. lonestari*, and *B. andersonii* are detected by this assay. UKAS accredited specimen types for this assay include EDTA whole blood, CSF and tissue. Sample volume required for liquids is 200  $\mu$ L with tissues required about the size of a matchstick head. Other samples may be tested and are reported along with an appropriate caveat stating the assay is not UKAS accredited for testing such sample types. Moreover, we have previously extracted and detected *Borrelia burgdorferi* DNA from tick specimens.

This assay is included in annual external quality assurance schemes.

Turnaround times are stated in the user manual (<u>http://www.micropathology.com/customer-downloads-handbooks.php</u>) 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.

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