The British Society of Immunology is the largest immunology society in Europe. We represent over 6000 immunologists working in academia, clinical medicine, and industry. Our main objective is to promote and support excellence in research, scholarship, and clinical practice in immunology for the benefit of human and animal health.

Immunology plays a key role in understanding the progression, diagnosis, and treatment of Lyme disease.

Key points

- Lyme disease is the most common vector-borne infectious disease in the UK, with around 2000 to 3000 new cases every year in England and Wales. Enhanced monitoring and improved public awareness are thought to be the primary drivers behind increased incidence in recent years.
- Early diagnosis of Lyme disease, made primarily on the basis of observable clinical features (e.g. rash) and the patient’s history of exposure to Lyme infected areas, is key to prevent the disease progressing to the more serious later stages of infection.
- Laboratory testing, which involves immunological analysis of the patient’s blood, can be used to support a diagnosis. However, existing diagnostic techniques are not without significant problems, and further research is required to improve the accuracy of diagnostic testing.
- Patients treated appropriately with antibiotics can expect to fully recover, although this may take some time. The existence of “chronic” Lyme disease due to lingering Borrelia infection and its use as an explanation for long-standing poor health is controversial. The long-term use of antibiotics to treat those with residual symptoms can be harmful and should only be considered in the context of ongoing clinical research.

Lyme disease

Lyme disease, or Lyme borreliosis, is a disease caused by the bacterium *Borrelia* that is transmitted to humans through the bite of infected hard bodied ticks, commonly known as deer or sheep ticks. In North America the disease is caused exclusively by *Borrelia burgdorferi* though in Europe other species of *Borrelia* are involved. The disease is not transmitted directly from person to person, nor from other insects or animals. Ticks acquire the bacteria by feeding on birds or small mammals that carry the organism in their blood.

Lyme disease is most prevalent in rural areas where the animal vectors for *Borrelia* are commonly found, though it can occur throughout the UK and recent investigations have even found infected ticks in London parks. Areas inhabited by deer are particularly suitable habitats, however deer do not carry Lyme disease themselves and rather play a key role in supporting tick populations as an important feeding host for adult ticks. Specific locations where the disease is often transmitted include areas of woodland or heathland such as the New Forest, Norfolk (Thetford Forest) and parts of the Lake District and Scottish Highlands.

Health risks

The clinical progression of Lyme disease infection in humans can be arbitrarily divided into early and late stage manifestations.

Early stage symptoms include the classic erythema migrans rash that develops as concentric rings in a "bull’s eye" around the site of the bite. The rash, which appears in around 80% of cases, is a hallmark of *Borrelia* infection and is the only clinical feature which can enable a reliable diagnosis. Other symptoms that may also develop in the early stage include fatigue, muscle pain, headache, fever, and neck stiffness.

If left untreated the bacteria can in some cases spread to other sites in the body. Patients with late stage infection may display neurological symptoms (such as numbness and pain in the limbs) or problems with the heart (including inflammation of the heart muscle, known as myocarditis). Lyme arthritis, a painful swelling of the joints, particularly in the knee, is also a rare complication in the UK.

Diagnosis

Early diagnosis is important to ensure the disease does not progress to the more serious later stages of infection. The majority of Lyme cases are diagnosed based on the patient’s clinical features, in particular erythema migrans, in combination with their history of exposure to an environment where ticks are likely to be present.

Where Lyme disease is suspected laboratory investigations may be ordered to confirm a diagnosis. These tests involve immunological analysis of the patient’s blood for the presence of antibodies produced against *Borrelia* as part of the body’s normal immune response to encountering the bacterium. Diagnostic testing for Lyme disease is carried out at Public Health England’s rare and imported pathogens laboratory (RIPL) at Porton Down. Centralising laboratory services and clinical support in this manner plays an important role in ensuring a timely and effective diagnostic service that is able to offer the best scientific analysis and clinical advice available.

However, testing for antibodies is not without its challenges. For example, there is a propensity for false positives due to cross-reactions with other bacterial or viral antibodies. It also takes a number of weeks for the body to produce enough antibodies – a process known as seroconversion – to allow for detection, meaning that tests in the immediate period following exposure often produce a negative result. Moreover, if treatment is given during these initial stages, as is recommended, seroconversion may not occur, making it impossible to confirm a diagnosis. Another issue is that immunological testing in this way does not confirm the actual presence of the bacteria, but rather the body’s immune reaction to having encountered that bacterium at some previous time. Importantly, once seroconversion has been accomplished, the antibodies remain elevated in the blood for a prolonged period of time, even after treatment. This means that a positive result is not confirmatory of current infection but indicative of exposure to *Borrelia* that may or may not have been recent. It is therefore difficult to confirm an acute infection. Moreover, those who live in Lyme endemic areas may have persistently high levels of antibodies in their blood.

To improve the reliability of testing a “two-tier” approach is recommended, utilising two different methods of immunological analysis. However, the problems described above remain, and for these reasons serological testing is not suitable on its own to confirm a diagnosis but instead plays an important role in supporting clinicians in their decision making. The challenges associated with these tests mean that further research to investigate more accurate diagnostic tests should be a priority in Lyme disease research.
Treatment

Antibiotics are an effective treatment for Lyme disease at all stages of infection. Patients treated at the early stages of disease, especially when the rash is present, will usually recover quickly and completely, although some patients may require a longer period to convalesce. In those patients where symptoms prove refractory a further course of antibiotics is usually required.iii

Surveillance

Lyme borreliosis is the most common vector-borne (transmitted to humans by another living organism, primarily bloodsucking insects) infectious disease in England and Wales. Public Health England estimates there to be around 2000 to 3000 new cases of Lyme disease in England and Wales every year, with 15% of these contracted while abroad.iv

Laboratory confirmed cases of Lyme disease have risen steadily since reporting began in 1986. Much of this rise is likely down to increased awareness amongst GPs and the general public as well as the introduction of an enhanced surveillance program in 1996 to improve reporting levels. Laboratory confirmed cases of the disease represent a minority of cases as most are diagnosed and treated in primary care on the basis of clinical features, such as erythema migrans, without the need for blood testing.iv

"Chronic" or post-treatment Lyme disease syndrome

Lyme disease is a complex infection and it can take a number of weeks or even months for the symptoms to resolve following treatment. However a very small percentage of patients continue to report chronic problems after this period, such as fatigue, pain, and muscle aches. This can be labelled as post-treatment Lyme disease syndrome or by some as “chronic” Lyme disease. Chronic Lyme disease has also been offered as an explanation for groups of patients with long-standing subjective symptoms which are as yet medically unexplained, similar to “ME”.vii

Certain advocates believe that the persistence of these symptoms can be explained by residual *Borrelia* infection which has managed to survive treatment. This has provoked interest in the long-term prescription of antibiotics for periods up to 1 year as a possible course of treatment. However, research in this area has not found any evidence to support this theory and those that do receive prolonged courses of antibiotics have not been shown to do any better than patients treated with placebo.viii It is also important to remember that long-term use of antibiotics is associated with serious and harmful complications.viii Current evidence suggests that these symptoms are more likely caused by neurological damage as a result of previously untreated or inadequately treated infection.ix

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3. PHE (2013). *PHE publishes new tick leaflets to remind people to be tick aware*.