

## **Tick Borne Infections in the EU: A New Epidemic in the Face of Global Warming**

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While ticks are known to be seasonal with peaks in the autumn and spring, global warming has extended the season for these vectors, facilitating their range and geographic footprint. Ticks carry many different organisms, not just *Borrelia burgdorferi*, the bacteria of Lyme disease. Lyme disease was first officially recognised in 1975 in Old Lyme Connecticut USA, based on an investigation by the CDC into an unusual outbreak of 'juvenile arthritis'. Studies of the affected children identified bacterial infections, later identified as *Borrelia*, a spirochete bacteria, similar to other spirochetes known to infect humans, including syphilis and leptospirosis<sup>1</sup>.

Besides *Borrelia*, ticks can carry many other pathogens, including *Anaplasma/Rickettsiae* bacteria, *Babesia*, and many other bacteria and viruses. Studies of ticks in Ireland demonstrate a presence of such pathogens<sup>2</sup>. Clinical syndromes are generally well understood in animals but tend to be poorly understood in humans. While deer are known to host ticks, some carrying Lyme and other infectious agents, many smaller animals and birds are vessels for ticks also. The migratory patterns of birds enable ticks to transfer with ease from one region to another. Tick borne encephalitis (TBE) is endemic in Eastern Europe, and recently cases of TBE have been identified in the UK in Devon, New Forest, and Norfolk.

The diagnosis of Lyme disease, as a prototype of vector borne disease, is imperfect. As bacteria circulate in such small numbers, it is not possible, as a rule, to develop a PCR test or antigen test sensitive enough to detect replicating organisms. Thus we are dependent on inadequate immunological tests (antibody, elispot assays) to measure the host immune systems response to an infection. A positive test indicates previous or active infection however many patients have a negative antibody test but active replicating infection that cannot be identified because of the lack of an antigen specific test.

In one study sensitivities have shown the current antibody tests are between 34-59%<sup>3</sup>. Therefore Lyme disease needs to be a clinical diagnosis, as one cannot wait to initiate treatment based solely on testing. Following a tick bite, there is an incubation period where the bacteria replicates in the skin and then spreads by hematogenous means to most tissues of the body. Patients may experience a classic ECM rash (erythema chronicum migrans), migratory arthritis or Bell's palsy, but many may have atypical neurological, rheumatological or cardiological symptoms. They may consult with different specialists but, without multisystem involvement, they may not entertain Lyme as a possible diagnosis.

Treatment should be initiated immediately when a rash occurs following a tick bite, or indeed even in cases where the patient is symptomatic without a rash. Whilst textbooks say Lyme is easy to diagnose and treat, and most patients are cured with short course antibiotics, this is not always the case. USA guidelines state that after two weeks of antibiotic treatment, commonly doxycycline 100mg twice daily, infection is eradicated. However, it is documented in the medical literature that failures can occur with shorter term treatment<sup>4-7</sup>. The Infectious Disease Society of America (IDSA) state short term antibiotic treatment resolves infection but some patients with persisting symptoms experience 'Post Treatment Lyme Disease Syndrome', a condition characterised by chronic neurological and/or rheumatological complications. However, it is not clear if the infection is eradicated, and some studies have shown patients do better with longer or repeated courses of treatment.

The International Lyme and Associated Diseases Society (ILADS) advocate that treatment should be based on patient symptoms and continue until symptoms resolve<sup>8</sup>. Revised UK NICE guidelines now recommend initial treatment consisting of doxycycline 100mg twice, daily for three weeks, and then if symptoms persist switching to amoxicillin 1g three times daily for three weeks. However, these guidelines only address 'early' infection, following a tick bite and do not allow for symptoms that develop later (chronic Lyme)<sup>9</sup>. However, once again a PubMed search provides easily accessible evidence of persistent infection, or infection despite antibiotic treatment<sup>10</sup>. There is no current mechanism to test for co-infections; the only infection addressed in the UK and Ireland is Lyme disease. As ticks carry many pathogens, it is likely that other tick borne infections are contributing to patients' symptoms.

While treatment is important, prevention and early recognition is the best way for those on the 'coal face', to thwart the consequences of chronic Lyme/co-infections. Educating the public on the importance of tick prevention, covering exposed body parts, using insect repellent, and checking for ticks upon return from the outdoors, are key messages that should be reinforced. In addition, medical professionals should recognise the ECM rash, and initiate treatment empirically as waiting for a positive Lyme test result leads to poor health outcomes for patients.

Global warming has precipitated the spread of ticks which host an increasing number of pathogens. The changes in our ecosystem are pushing us, as humans, into closer contact with ticks. Apart from *Borrelia*, multiple other bacteria are likely infecting humans, and the reported cases to public health authorities are likely to be grossly under-estimated. Many patients are diagnosed with other conditions (chronic fatigue syndrome, ME, FND, fibromyalgia, chronic headaches, etc.) without Lyme disease being part of the differential.

In Ireland, only cases of neuroborreliosis are reported. This represents only 10 cases annually although, the relevant health authority concedes that there 'may be' up to 200 cases per year, which conflicts with modelling that estimates 2,500 annual infections. While there are parts of Ireland where Lyme is well recognised, no part of the country is immune. Lyme disease does not just affect rural dwellers - dogs may bring home ticks and infect those living in urban settings also. Therefore Lyme disease will continue to be the 'great imitator'. It is not easy to diagnose and not easy to treat. It has been reported in one study that only 14% of patients recalled a tick bite<sup>11</sup>, only 50% get the classic bullseye rash<sup>12</sup>, and only about 50% have a positive standard Lyme antibody test<sup>13</sup>. In some patients the infection does not clear, and it triggers a cascade of infection, inflammation and dysimmunity that may cause ongoing and long-term complications.

We are increasingly learning more about 'long covid' because of the investment of research monies into this condition. Sadly, no research monies have been put into better understanding 'long Lyme'. Studies from Johns Hopkins looking at brain PET scans of patients with PTLDS<sup>14</sup> have found similar abnormalities in the brain as those with 'long COVID'<sup>15</sup>. Ireland is an agricultural country, and many are picking up Lyme locally. The Irish travel all over the world and are bringing vector borne diseases acquired abroad home with them. Many of them continue for years with these 'mystery' illnesses. Until we have better education for GPs and consultants alike in Ireland on the complexities of tickborne infections, until we have better diagnostics and until we have investment in research funding to improve our understanding of these conditions, patients will continue to be left undiagnosed and untreated.

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