PE1662/P
Petitioner submission of 10 February 2020

Petitioner Response to Meeting on 12 September 2019

We were disappointed that, at the meeting on 12 September 2019, apart from brief mention of GP training, there was no discussion of how to improve treatment, the core focus of our petition. We wish to remind the committee that our petition is entitled "*Improve Treatment* for Patients with Lyme Disease and Associated Tick-borne Diseases". For those who continue to be so chronically ill for years and decades after a tick-bite that they are unable to work, unable to get out of the house, and sometimes even unable to get out of bed, it is crucial that treatment is improved.

An autopsy study gives a view on what many patients fear, including both petitioners [1]. A woman suffering from Lyme disease had 16 years of treatment for Lyme disease and subsequently died after antibiotics were withdrawn. Many patients in Scotland are being denied any treatment at all.

Sally Mavin mentioned scaremongering and that many patients believe they have Lyme but don't. She also said that including discussion of Borrelia miyamotoi is misleading. We wish to remind the committee that the petition is about all tick-borne diseases. Many patients are severely ill after a tick-bite and cannot get a diagnosis or treatment. Lyme Disease UK's patient forum now has over 11,000 members, many of whom are severely ill and unable to work after a tick bite. They may not have Lyme but they are unable to get testing, diagnosis or treatment for all the infections a tick can carry. Our petition covers so much more than Lyme disease. Studies have shown that in Scotland Anaplasma is in 73% of sheep [2], Babesia in 59.6% of badgers [3], Bartonella in at least 15% of cats [4], Babesia venatorum in 9% of sheep [2], and a Babesia odocoilei-like parasite is in 15% of wild red deer [2], and yet human illness is ignored.

[1] https://www.ncbi.nlm.nih.gov/pubmed/31614557
[2] http://theses.gla.ac.uk/8750/
[3] https://www.ncbi.nlm.nih.gov/pubmed/28696186
[4] https://www.ncbi.nlm.nih.gov/pubmed/21570883

Scottish Testing

There are **no ISO accredited tests for any of these co-infections** at the Lyme and Tick-borne Diseases Reference Laboratory. Unaccredited tests for Borrelia miyamotoi and Anaplasma are available within the first 4 weeks from the bite. However, there are no tests for those available after 4 weeks, and no tests at all for Bartonella henselae, Bartonella quintana, other Rickettsiae species, or Babesia.

Babesia testing is available at other labs in Scotland but patients find it difficult to get tested for all species. Sometimes only Babesia microti, the US strain, is tested for. It is difficult to get tested for Babesia divergens, the European strain, and tests are not available at all to our knowledge for Babesia venatorum and Babesia duncani, found by private consultants in European patients.

It was mentioned that there was now a test for Borrelia miyamotoi available. However, we wish to point out that this is not ISO accredited, often given as a reason for not accepting "German tests". There seems to be double standards in acceptance of testing.

It was also stated that there was no Q fever in Scotland. However, a study in 1970 showed that “approximately 1% of 4880 cattle had antibodies to the organism” [5]. There are a few human cases of Q fever in Scotland annually [7].

It was also stated that it was not known but that it was thought that Borrelia valaisiana causes few cases. There have been case reports in the literature of Borrelia valaisiana causing illness [8]. If testing does not include that strain, and if patients are complaining of severe illness that is not diagnosed with current tests, how do they know that it is not caused by Borrelia valaisiana? Also, if we cannot get tested, then there may be a good reason why there are few case studies in the literature.

Although Kathleen Robertson mentioned that even veterinary testing for Lyme disease is not accurate, it was not acknowledged that testing is unreliable in late illness in humans. One study found that “Using clinically representative LD test sensitivities, the two-tier test generated over 500 times more false-negative results than two-stage HIV testing” [9].

There was no mention of the fact that the antibody response varies after treatment, resulting in seronegativity. As an example, in the autopsy study above [1], serological testing was negative even though the woman was PCR-positive and culture-positive after treatment. In a study in monkeys, antibodies did not develop in one monkey, waned with antibiotic treatment, and waned without treatment in some [10]. We have been told by a Lyme testing specialist that the Mikrogen blot test used at Raigmore gives a negative result when people are only positive for VlsE (a Borrelia surface lipoprotein), which is a quite common profile.

It was also said that molecular assays pick up more strains than standard tests. That seems to imply that standard tests do not pick up all strains and so are unreliable. When such serological testing is relied on so heavily in Scotland, patients are denied treatment when there is continued ongoing infection.

The laboratory has a remit for all tick-borne infections in Scotland and yet they have said the lab is currently under strain with Lyme disease testing alone. We want them to be given the resources and funding to allow them to develop testing for all co-infections known to exist in Scotland and to develop testing which addresses the issues of seronegativity with current Lyme disease tests.

[5] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(70)92829-1/fulltext
[6] https://www.ncbi.nlm.nih.gov/pubmed/19912614
[7] https://hpspubsrepo.blob.core.windows.net/hps-website/nss/1764/documents/1_qfever.pdf
[8] https://www.ncbi.nlm.nih.gov/pubmed/15503409

[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5602438/
[10] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189071

Education

We agree that public education should be a government responsibility. It is really important that the public understand how to prevent tick-bites, recognize ticks, know how to remove ticks, and know the symptoms of multiple tick-borne diseases to look out for even when a rash is not present.

It is also really important that GPs understand how to diagnose tick-borne illnesses, not just Lyme disease but all infections present in Scotland, and understand that multiple infections can be transmitted from a single tick bite and cause more severe illness. We therefore ask that the experts who developed the Royal College of GPs "Lyme Disease Toolkit" are invited to provide training for all GPs in Scotland [11].

Our main concern is that even consultants are not equipped to diagnose tick-borne illnesses. Rupert Shaw mentioned red water disease, which is caused by Babesia. It seems it is much more acknowledged in animals than it is in humans. Studies in humans have shown that co-infection with Borrelia and Babesia causes more severe symptoms than with Borrelia infection alone [12]. Other studies have shown that multiple infections from a single tick-bite are the rule not the exception, with some ticks carrying 5 pathogens [13]. However, in general, consultants in Scotland do not seem willing to acknowledge chronic Lyme disease or contemplate the possibility of polymicrobial infection from a single tick bite. We therefore request that consultants are trained on the ILADEF Physician Training Program [14].

[11] https://www.rcgp.org.uk/clinical-and-research/our-programmes/clinical-priorities/spotlight-projects-2019-to-2020/lyme-disease.aspx
[12] https://www.ncbi.nlm.nih.gov/pubmed/8637139
[13] https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004539
[14] https://iladef.org/physician-training-program

Tick Attachment Times

Kathleen Robertson mentioned that there is an 18-24 hour window after being bitten before you are infected because the bacteria lie in the midgut of the tick and need time to migrate to the salivary glands. However, this seems to apply only to the US strain and has been found to be different for different strains. A study showed that "all European B. burgdorferi sl strains studied were detected in female salivary glands before blood meal and infected mice within 24 h of tick bite. Moreover, Borrelia-infected nymphs were able to infect mice as early as 12 h of tick attachment. Our study shows the need to remove ticks as early as possible after attachment." [15]. We therefore believe that, although there is higher risk with longer attachment, it is misleading to reassure the public by quoting the 18-24 hour window.

[15] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6079464/

Treatment

Kathleen Robertson mentioned she has had Lyme disease. We are pleased that she has recovered. However, we want to make it clear that many patients are treated with standard treatment and still go on to develop chronic debilitating symptoms. Both petitioners are severely ill many years after a tick bite, and there are many more patients in a similar position. A study in the Western Isles found that 2/3 of those who were diagnosed and treated with recommended treatment had ongoing long-term symptoms after treatment. She mentioned that doxycycline is the treatment of choice for Lyme disease in animals, and this is the main form of treatment in the NICE guidelines. However, other antibiotics have been found to be more effective [16]. We want further studies on the most effective early treatment which avoids the issues apparent with doxycycline. And although it is often stated that long-term antibiotics are not effective, there has not been a single controlled randomized study to evaluate the efficacy of prolonged anti-infectious treatment (longer than 3 months) on the chronic form of the disease, so that is also needed.

Sally Mavin also mentioned that the NICE Guidelines are based on good evidence. We believe that this is misleading. We wish to point out that the NICE guidelines [17] state:

- They do not know "What are the incidence, presenting features, management and outcome of Lyme disease in the UK?"
- They do not know "What is the current seroprevalence of Lyme disease-specific antibodies and other tick-borne infections in people in the UK?
- They do not know "What is the most clinically and cost-effective serological antibody-based test, biomarker or other test for diagnosing Lyme disease in the UK at all stages, including re-infection?" and "published evidence is of either low or very low quality and is not UK based."
- They do not know "What are the most clinically and cost-effective treatment options for different clinical presentations of Lyme disease in the UK
- "The evidence on the effectiveness of antimicrobial treatment regimens used in different presentations of Lyme diseases is of poor quality, out-dated and often based on small studies." and "There is currently insufficient quality evidence on the most effective drug and dose, and the effectiveness of extended treatment or retreatment regimens in those with continuing symptoms remains uncertain, leading to multiple referrals in search of alternative diagnoses."

[16] https://www.ncbi.nlm.nih.gov/pubmed/8387966
[17] https://www.nice.org.uk/guidance/ng95

National Strategy

We are in strong favour of the development of a national strategy for tackling tick-borne diseases. However, the core focus must be on developing treatment strategies for those who are chronically ill to improve outcomes for patients. We have suggested development of a fluid multi-agency National Plan similar to that in France. Setting up one or more specialist treatment centres with consultants trained on the ILADEF Physician Training Program [14] would be a core objective within

that. This would address the needs of patients who are severely and chronically ill after a tick bite and currently abandoned without help.