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LYME RESOURCE CENTRE

Lyme Disease in Scotland

A Position Paper by

Lyme Resource Centre

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Executive Summary

Lyme Disease and other tick-borne infections are increasingly common. We welcome recent direction from the Chief Medical Officer on responsibilities for early diagnosis. However, most people who are infected miss the early treatment window. Action is needed to address the suffering of those who are chronically ill. The burden of untreated infections is harmful, both to the individual and to the Scottish economy in terms of lost productivity and disability.

Background

- Lyme Disease testing is imperfect and generates too many false negatives.
- The current NICE guidelines on Lyme Disease address only acute infection and do not recognise chronic illness: their narrow evidence base did not take into account research demonstrating persistence of *Borrelia*, the Lyme Disease bacteria.
- Treatment for acute Lyme Disease fails 10-20% of patients: for those who are not given an early diagnosis, and go on to develop disseminated disease, there is no current guidance or pathway for care.
- Treatment for acute Lyme Disease is not sufficient for chronic infection: research shows that current recommended treatment fails to eradicate chronic infection.
- Patients with chronic Lyme Disease are currently being denied curative treatment: they are currently misdiagnosed or left undiagnosed, untreated and suffering without any NHS support and often in economic hardship as a consequence.
- It is very common that patients are infected with polymicrobial infections; such infections are not recognised or treated and comprehensive testing is not available.
- Clinical experience and the medical literature shows that, with appropriate diagnosis and treatment, longer treatment benefits chronically ill patients with such infections.
- French guidelines recognise chronic illness and provide a platform for improvements.

Actions and Recommendations

We recommend:

- **Implement a Scottish National Action Plan to Combat Tick-borne Diseases**
Scotland should take a lead by developing a fluid, multi-agency approach including testing, treatment, education and tick control, similar to that being implemented in France.
- **Develop SIGN Guidelines for Tick-borne Diseases**
With broader scope than the NICE guidelines on Lyme Disease, taking account of international research, including in-vitro studies, and covering not just Lyme Disease but all other tick-borne infections, including the complexities which arise when patients suffer from polymicrobial infections.
- **Commission an External Review**
A fresh look at the current situation regarding tick-borne diseases is required to combat the current suffering of many patients. Lyme Resource Centre is willing to conduct an independent review to give recommendations of next steps to support Scottish patients with these 'undiagnosed' and treatable infections.

Introduction

The letter from the Chief Medical Officer "Identification and Management of Lyme Disease – Educational Resources" issued on 13th June 2019 shows that Lyme Disease has been identified as an issue in Scotland and gives clear direction on the responsibilities of health boards and practitioners regarding Lyme Disease. As such, it is a big step forward. However, information is missing which results in patients being failed by current NHS Scotland protocols and treatment.

Work is currently being done on public awareness in Scotland by the Lyme Borreliosis Group of Health Protection Scotland. However, to date this has really only focused on producing limited public education materials. There has been no obvious public education campaign, no obvious campaign to educate doctors prior to the above letter, no help for those who have chronic and persistent Lyme infection, limited research into tick-borne diseases, and no concerted effort to tackle tick-borne diseases in general.

At a recent conference (International Crypto-Infections Conference, Dublin, May 2019) it was stated that, by 2050, 35% of the global human population will be infected with one or more tick-borne diseases. While this is a prediction, it is prudent to develop a comprehensive policy to address the issues, to avoid economic devastation when a vast percentage of the population will be so ill they are unable to work.

Addressing this issue needs so much more than public awareness. It involves the wider society and not just the medical community. A comprehensive strategy is required to tackle it. We propose:

- A National Action Plan to Combat Tick-borne Diseases
- Development of SIGN Guidelines for Tick-Borne Diseases
- An External Review

Background

Scotland is increasingly recognising the presence of tick-borne infections. Ticks are being found throughout the country, in urban as well as rural areas. With a rural economy of agriculture, forestry and tourism, our inhabitants work and are recreationally active in areas at high risk from tick exposure and bites, and we have a large tourist population going to similar regions who are at risk. Veterinarians are aware of the burden of disease of *Borrelia* (the Lyme bacteria) and other tick-borne infections (*Babesia*, *Rickettsiae/Anaplasma*) on their livestock. However, humans in the same environment are also at risk of getting bitten by the same ticks and developing the same or similar diseases. Medical doctors have little awareness of these infections or the risk to human populations.

The current public message is "avoid ticks, check for ticks, remove them correctly if you find them, and watch for the rash". If a rash is seen (which is the exception rather than the rule) and they get sick following such exposure, then patients are often appropriately treated.

Such a message is absolutely necessary, and certainly welcomed, but only partly addresses the issues. It misses the majority of patients who are bitten by a tick, as most tick bites are not noted, less than 50% get a rash, and often the rash, if noted, is mis-diagnosed.

Some pertinent issues to tick-borne infections and its impact on the Scottish population include the following:

- Tick numbers are increasing with global warming
- Many people will not see a tick (they are the size of a pin head) or a rash
- Lyme Disease testing is unreliable, an immunological test which misses many cases
- Lyme Disease is often misdiagnosed as other syndromes
- There is a short treatment window when *Borrelia*, the Lyme bacteria, is easy to treat
- Long standing *Borrelia* infection leading to 'Chronic Lyme' is much harder to treat
- Ticks carry multiple different infections, not just *Borrelia*; people bitten are at risk of acquiring multiple infections simultaneously.

Raising public awareness may reduce:

- the number of people who are bitten;
- the length of time that ticks are attached; and
- the number of people who miss the treatment window.

But it will not reduce:

- the increasing number of ticks;
- the percentage of people missing the treatment window because they fail to see a tick bite or rash;
- the percentage who are treated within that treatment window but still develop chronic persistent infection;
- the percentage of people denied accurate diagnosis and treatment because of unreliable or incomplete testing; or
- the severity of symptoms for those who suffer with chronic infection.

Issues

Tick Numbers are Increasing

Moredun Research Institute (1) and others report that ticks in Scotland are spreading geographically and increasing in numbers, most likely because of climate change.

Tick Bite or Rash not Seen

According to a recent review (2) "a major obstacle is that only 30% of the patients report a history of tick bite and only 70–80% present with a primary erythema migrans, the pathognomonic [diagnostic] initial lesion [of Lyme Disease]. This lesion may go unrecognized, or may be mistaken for an 'insect bite' or an 'allergic rash'. Mini-erythema migrans are less likely to be diagnosed". The situation is more complex in Scotland as in a recent study (3), "the low number of patients with erythema migrans (48%) was surprising

and is much lower than that documented in other studies (69.1 to 89.3%)." and "only 61% of patients could recall having a tick bite". A recent study in monkeys (4) found that only 10% infected by a tick bite "produced a bona fide erythema migrans rash".

The public health message to watch out for ticks and rashes therefore covers only a limited portion of those infected. Because chronic Lyme Disease is so devastating, something must be done to address those people who do not identify a tick bite or rash, or where the rash is misdiagnosed as ringworm, cellulitis, or another condition.

Unreliable Lyme Disease Testing

With current two-tier testing, more than 50% of people who are infected with Lyme Disease will have negative serology (5 at 9 mins 20 secs in). In one study (6), "using clinically representative Lyme Disease test sensitivities, the two-tier test generated over 500 times more false-negative results than two-stage HIV testing". Would that be acceptable for an HIV test? It should therefore not be acceptable for Lyme Disease testing.

However, although the Scottish Government has acknowledged the unreliability of Lyme Disease serology testing, it is reported widely on social media forums that many Infectious Disease consultants in Scotland are of the opinion that the tests are 100% reliable and that false negatives do not exist. Many doctors will not treat unless the test is positive. When patients with Lyme Disease do not have a rash, obtaining a diagnosis and subsequent treatment can therefore be very difficult and valuable time is lost.

Also, current tests do not cover all species present in Scotland. The original test for Lyme was developed for the *Borrelia* strain in the USA, *Borrelia burgdorferi sensu strictu*. These are not the strains that exist in Scotland and the rest of the EU. We are aware that the National Reference Laboratory at Raigmore is developing a test for *Borrelia miyamotoi* (26). However, other species may exist in Scotland which have not yet been discovered. Currently we have inadequate 'indirect measures' of infection, namely antibody tests, which are missing the disease in many patients. We welcome recent investigation into PCR testing, but this is still investigational and many years away from being available to Scottish patients.

Misdiagnosis of Lyme Disease

At best we may currently identify and treat 20-50% of patients who remember a tick bite or rash. But what about the many patients who do not remember a tick, and do not have a rash, or they have a rash and it is misdiagnosed as ringworm, cellulitis, or another condition? This large majority of patients do not even appear to be on the radar of NHS Scotland. In many cases, a diagnosis of Lyme Disease is not even entertained, or sometimes when patients suggest such a possible diagnosis, their opinions are discounted or even ridiculed. These people often find themselves with a missed diagnosis yet find themselves referred to cardiologists, pain specialists, rheumatologists, and neurologists, or sometimes even infectious disease specialists. Ironically, they find themselves undergoing differential diagnosis for all sorts of rare and exotic diseases, while Lyme Disease is not being seriously considered or is even dismissed. Patients have been told: "Lyme is rare"; "This can't be

Lyme”; “Lyme can’t persist for years and years”. When a diagnosis cannot be made, they are often discharged without diagnosis, follow-up or treatment; and, even worse, their continued suffering is neither acknowledged nor understood. We need to focus on better understanding chronic persistent Lyme Disease in these patients, and the impact it has on people who receive no diagnosis, no treatment and no acknowledgement of their life-altering condition by NHS Scotland. Such chronic illness is alluded to but not covered in the NICE Guidelines. These guidelines only deal with ‘early Lyme’ which may only represent 20% of the total population of patients infected with *Borrelia*.

Without reliable testing, many patients are misdiagnosed with other illnesses such as ME/CFS, fibromyalgia, functional neurological disorders, psychological conditions and sometimes even Multiple Sclerosis (MS), Alzheimer’s disease, or Parkinson’s disease.

In one study, it was found that 38.5% of patients with Multiple Sclerosis were positive for *Borrelia* (7). If even a portion of those could be identified and given correct treatment, it could make a huge difference to thousands of lives devastatingly impacted by Lyme Disease. Antibiotics given to these patients reverse and cure their disease. While not all MS patients have Lyme, most neurologists do not seriously entertain this as a potential differential diagnosis, even though it is clearly better for an individual patient to have a reversible infectious disease than a chronic progressive poorly responsive neurological condition such as MS.

Spirochaetes such as *Borrelia* are also heavily implicated in Alzheimer’s disease. A recent meta-analysis showed “a strongly positive association between bacterial infection and Alzheimer’s disease” (8). Studies to further pursue this observation need further investment in research.

Co-infections complicate the diagnosis. If animals are getting bitten by ticks and infected with *Borrelia*, *Babesia* and *Rickettsiae*, it is likely that they are biting humans as well. One private practice doctor has stated that 25% of patients coming to him with chronic fatigue were infected with *Anaplasma*, and many responded to antibiotic therapy with reversal of their condition.

Lyme Treatment Failures

A video by many eminent Lyme researchers gives a good overview of the state of knowledge on Lyme Disease (5). Recent research makes it very clear that Lyme Disease is very hard to treat if not caught early. Scientists state that, for mice and primates, there is a treatment window of only 56 days within which the standard recommended treatment works (5 at 31 mins 08 secs in). For 10-20% of people, standard treatment within the early treatment window fails (9). Many people do not remember a bite and do not get the rash or the rash is misdiagnosed, meaning they miss the 56-day treatment window. There are no guidelines to cover those patients with longer standing disease, and so many patients are denied further treatment. There are clear studies in the medical literature that demonstrate Lyme arthritis and Lyme Bell’s Palsy can develop years after a tick bite; and research studies demonstrate evidence of *Borrelia* as the cause of these syndromes. These studies

appear to have been ignored during development of the NICE guidelines and the Infectious Diseases Specialists 'fund of knowledge'. They deny the existence of chronic, persistent infection, and describe it as an 'immunological' or 'post-infectious' condition.

Although it is acknowledged that Lyme Disease is a complex infection which is difficult to diagnose, there is no guidance whatsoever on treatment for non-acute infection. The standard treatment defined in the NICE guidelines only addresses acute Lyme; current recommended treatments fail to work when Lyme Disease is recognised as the cause of long-standing illness. The NICE Guidelines do not give clear advice on what to do when standard treatment fails. For other infections, healthcare practitioners extend the treatment or change the treatment. This is standard practice for most infectious diseases, but not for Lyme Disease. If patients have not recovered, it is classed as 'post-infectious' Lyme Disease. As a result, patients are left alone to deal with persistent chronic infection and without help, treatment or understanding.

Treatment for Chronic Infection

The TV documentary "Disclosure: Under the Skin" on BBC One at 8:30pm on 17th June 2019 made it clear that many patients are suffering debilitating long-term symptoms and feel let down by the government and the NHS in Scotland.

New data on persisters (bacteria that persist inside cells despite treatment), chronic infection, and the benefits of combination therapies, both in vitro and in vivo models, have shown in recent studies, that combination therapy and longer therapies provide benefit for such patients. None of these data are covered by the NICE guidelines, or even considered by most Infectious Diseases specialists and others within NHS Scotland.

Some recent advances published in the medical literature found:

- In 2014, differences between *Borrelia burgdorferi* persister and growing cells was discussed, and a model was proposed for bacterial transition between the two states (10).
- In 2015, it was found that gene expression changes were related to the survival of persister bacteria (11). It was found that *Borrelia burgdorferi* forms drug-tolerant persister cells (12), and that *Borrelia afzelii* and *Borrelia garinii* are capable of growing as biofilms in lab culture, similar to *Borrelia burgdorferi* (13). Drug combinations against *Borrelia burgdorferi* persisters were investigated (14).
- In 2016, it was found that biofilm-like microcolony structures of *Borrelia burgdorferi* could be eradicated by daunomycin and daptomycin but not mitomycin C in combination with doxycycline and cefuroxime (15). A drug combination screen identified drugs active against amoxicillin-induced round bodies of in vitro *Borrelia burgdorferi* persisters (16). Ceftriaxone pulse dosing failed to eradicate biofilm-like microcolony *Borrelia burgdorferi* persisters, which were sterilized by a combination of daptomycin/doxycycline/cefuroxime (17).

- In 2017, it was found that *Borrelia burgdorferi* manipulates innate and adaptive immunity to establish persistence in rodent reservoir hosts (18). In a study (19) in primates to comprehensively examine pathology associated with persistence of *B. burgdorferi* in the late stage of LD following antibiotic therapy, the findings "support the notion that chronic Lyme disease symptoms can be attributable to residual inflammation in and around tissues that harbor a low burden of persistent host-adapted spirochetes and/or residual antigen". No monkeys were cured with antibiotic treatment which matched or exceeded recommendations for the treatment of Lyme disease made by such authorities as the British Infection Association (BIA), and the National Institute of Clinical and Care Excellence (NICE).
- In 2018, it was shown that doxycycline, a standard of care for uncomplicated acute infection, did not clear the pathogen in immunodeficient mice. In contrast, both ceftriaxone and vancomycin cleared the infection, with vancomycin being more effective (20). A pilot study in humans (21) concluded that "Using multiple corroborative detection methods, we showed that patients with persistent Lyme disease symptoms may have ongoing spirochetal infection despite antibiotic treatment, similar to findings in non-human primates".
- In 2019, it was shown that stationary phase persister/biofilm microcolonies of *Borrelia burgdorferi* causes more severe disease in a mouse model and that a three-antibiotic cocktail clears 'persister' Lyme bacteria (22).

These are only a sample of hundreds of papers demonstrating that *Borrelia* persists via biofilm-like microcolonies and round-body forms. Scientists state that 'we are now past the denial stage' (5 at 4 mins 45 secs in). It is time for clinical medicine to catch up, to stand up to listen to patients and believe them, to address their issues, and not to deny their illnesses.

NICE and other treatment guidelines only focus on those who were lucky enough to see a tick or get a rash and get rapid administration of antibiotics. 10-20% of those who are treated with 'standard' antibiotic treatment will have treatment failure. At present, they are told they cannot get more antibiotics as it is 'post-infectious'. How clinicians can 'speculate' it is post-infectious when there is no currently available test to prove 'test of cure', i.e., resolved infection, is a mystery. Studies have shown longer treatment and combination treatments work (23,24). However, the NICE guidelines excluded review of non-European papers and so did not take account of these studies. The NICE guidelines stand by USA IDSA guidelines of the Infectious Disease Society of America (IDSA), and fail to acknowledge the currently internationally used guidelines (24) of the International Lyme and Associated Disease Society (ILADS). The debate between infection and post-infection will continue until we have antigen specific tests, both to make a diagnosis, and to measure at the end of treatment, to provide a test of cure. In the meantime we recommend clinicians should be using 'clinical judgement', which we are able to use for all other infections except for Lyme Disease.

Tick-borne Co-infections

Background

Ticks carry a large number of co-infections, which do not seem to be recognised or addressed fully in Scotland despite Scotland being considered a high-risk area. It is now considered the rule rather than the exception that ticks carry multiple co-infections (25). Prevalent ones are Anaplasma, Babesia, and Bartonella but the full range is not yet known. Even if Lyme Disease is diagnosed in Scotland, and there is a suspicion for a second or more than two infections, there are no facilities to allow identification of all tick-borne co-infections. Polymicrobial infections are common in animals in Scotland, and they are being increasingly recognised in humans.

Patients therefore suffer from unacknowledged polymicrobial illnesses that doctors are not equipped to deal with. The response received from doctors when testing cannot identify infections is that it is "all in your head". Patients are then left with the ignominy of not being believed and without treatment for some of those infections because they are not identified. We suggest that simply because you cannot test someone and diagnose them appropriately does not give a clinician the right to use terms such as 'Medically unexplained illness' or 'functional neurological disorder' or deduce the patient has a psychological condition (a label which is then very difficult to overcome), because the doctor cannot make sense of their symptoms. To put it another way, absence of proof is not proof of absence!

Anaplasma

A recent study (26) showed that 73% of sheep and 40% of deer in Scotland are infected with Anaplasma.

Human disease as a result of Anaplasma infection is not currently acknowledged and may be confused with ME/CFS. There is currently no test available for Anaplasma in Scotland though we believe the National Reference Laboratory at Raigmore Hospital is developing one (27). Anaplasma is being increasingly recognised as a cause of human disease.

Babesia

The same study (26) found that "Babesia ventatorium ... was detected in 9% of healthy sheep. Babesia divergens was found in 11% of wild red deer ... Additionally a Babesia odocoilei-like parasite was found in 15% of wild red deer". Another study (28) found Babesia in 59.6% of blood samples from Scottish badgers. In 2017, a number of co-infections were found in UK ticks, including Babesia venatorum, Babesia vulpes sp. nov., Babesia divergens/Babesia capreoli, Babesia microti, and Babesia canis (29).

However, despite veterinary understanding of the burden of Babesia in Scotland, there is no recognition of human Babesiosis in Scotland. As far as we are aware, only two cases have been diagnosed since 1979. Babesia is increasingly being recognised as a disease of immunocompetent human patients, not just those with splenectomies. Anecdotal accounts

from US physicians suggest that European patients are being infected by *Bartonella duncanii* as well as *Babesia divergens* and *Babesia microti*.

Bartonella

Bartonella is emerging as a complex infection with multiple species involved, including *Bartonella henselae*, *Bartonella quintana*, and others. There is no blood test for *Bartonella* in use in Scotland. Patients with positive tests from private laboratories are having difficulty being assessed for *Bartonella* or getting their infections acknowledged.

There are studies of *Bartonella* being identified in ticks, in association with *Borrelia*, but we know of no studies in the UK. Anecdotal accounts from US physicians suggest that European patients are being infected by a number of species. There is a large body of information in the medical literature of *Bartonella* infection, presenting with symptoms similar to Lyme Disease.

Other Co-infections

Recent European (30) and French (31) studies found many other pathogens in ticks. A study in Australia, a country previously thought to be free of Lyme Disease, found "considerable presence of *Borreliosis* in Australia (32), and a highly significant burden of co-infections accompanying *Borreliosis* transmission", including *Babesia*, *Bartonella*, *Anaplasma*, etc. We believe that if a similar study was done in Scotland it would show the same. In a US study (33), patients were found to be infected with up to 16 infections, with 64% being infected with 5-8 infections. Much more focus needs to be placed on identifying all tick-borne co-infections.

Our Message

We wish to communicate the following messages to NHS Scotland:

- Lyme Disease and co-infections are common in Scotland
- Ticks are prevalent throughout Scotland, in urban gardens as well as rural moors and forests
- Patients in both rural and urban areas are affected - urban people visit rural areas and Scots travelling widely across the world bring back non-local infections
- Training in Lyme Disease appears to be missing in medical schools
- Most doctors are not Lyme literate and do not think of Lyme as part of their differential diagnosis, even in clearly recognised Lyme endemic areas.
- The erythema migrans rash of Lyme is not always the 'classic bulls eye rash' - it is easily misdiagnosed as ringworm or cellulitis. Moreover, many infected with Lyme Disease do not exhibit such a rash.
- Prevention messages, while important, are not sufficient in themselves, i.e., avoid ticks, insect repellent, and tick removal devices. An integrated strategy is needed to cover all elements relevant to decreasing the impact of Lyme Disease on humans.

- Future working groups should include infectious disease consultants, antimicrobial pharmacists, microbiologists, patient representatives, and veterinary and agriculture specialists in addition to input/groups lead by Health Protection Scotland.
- Testing should be acknowledged as imperfect and clinicians should not depend on current testing to make a decision to treat. History, examination and clinical suspicion should be enough to take a decision to treat. This has been advocated by the French guidelines that were ratified by the French Minister of Health and their Senate in 2018.
- Decisions on continued treatment should be based on individual response to treatment, and not driven by guidelines alone. If patients are not better after three weeks antibiotic treatment then they should be prescribed an additional three weeks treatment (as defined in the NICE guidelines). If the patient gets better but then gets worse on stopping antibiotic therapy then a longer course is required. Until we have antigen specific tests that show eradication of infection, clinical judgement, as used as a basis to treat for all other infectious diseases, should also apply to Lyme Disease and other co-infections.

Proposed Action

Lyme Resource Centre believes that the following actions are needed to measurably reduce:

- the number of people infected by tick-borne diseases
- the number of people who miss the early treatment window
- the number of people who are treated yet go on to develop chronic illness
- the number of people with chronic Lyme disease who are left untreated

A National Action Plan

We urge the Scottish Government to develop and implement a comprehensive National Action Plan to Combat Tick-borne Infections now, similar to that developed and currently being implemented in France (34). Public education will form a small part of that plan, but there is so much more which needs to be done, including better testing, better guidelines on treatment, GP and consultant education, and tick-control. It is expected that such a plan will be fluid and will evolve as more is understood about tackling this issue. It will involve multiple agencies and should include:

Testing

1. In order to help understand the extent of the problem, make all forms of Borreliosis and emerging co-infections notifiable, whether diagnosed through testing or clinically.
2. Comprehensively evaluate Borrelia diagnostic methods: DNA, antigen, LTT, Elispot, PCR, etc., for all genospecies found in Scotland, including *Borrelia miyamotoi* and *Borrelia valaisiana*.
3. Evaluate and introduce testing for all co-infections, to include multiple species of the co-infections *Bartonella*, *Babesia* (including *Babesia duncanii*), and Anaplasmosis, allowing comprehensive testing for polymicrobial illnesses.
4. Undertake epidemiological studies of all tick-borne pathogens in Scotland.

Treatment

1. Establish a specialist treatment centre involving a multi-disciplinary team of specialists in infectious diseases, cardiology, immunotherapy, functional medicine and nutrition, and collaborating with Lyme Disease specialists in other countries. Ensure patient follow-up and documentation and analysis of treatment outcomes.
2. Develop SIGN Guidelines for all tick-borne infections, covering the complexities which arise when ticks carry multiple pathogens. In the meantime, require GPs and consultants working in Scotland to follow the guidelines of the International Lyme and Associated Disease Society (35), currently the only approved Lyme treatment guidelines in the US National Guidelines Clearinghouse.
3. Provide GPs with a standardised assessment, e.g., based on the questionnaire developed by Dr. Richard Horowitz (36), describing the list of examinations allowing a complete diagnosis in anyone with symptoms suggestive of a tick-borne infection.
4. Provide resources for research and development into the treatment of chronic tick-borne infections in Scotland.

Education

1. Educate consultants working at the clinic in persistence and the complexity of multiple co-infections by using the ILADEF Physician Training Program designed by the International Lyme and Associated Disease Society (37).
2. Require GPs to undertake mandatory training in tick-borne infections.
3. Communicate to all medical professionals, including consultants, GPs, pharmacists and nurses, to ensure they are aware of the lack of reliability of tests, the lack of markers of current infection, the emerging research on persistence, the possibility that ticks can transmit multiple infections from the same bite and the added complexity this introduces, and to provide clarity about existing and new testing procedures for all tick-borne diseases. A formal partnership with NHS Education for Scotland should be established to deliver this.
4. Comprehensively cover all tick-borne infections in student medical training.
5. Run a public awareness campaign including easily digestible leaflets, web-based resources, an online Facebook and Twitter campaign, and possibly a TV campaign, directed at human health, to include information on tick bite avoidance, tick removal and initial signs of illness to look out for after a bite.
6. Require landowners to display information notices at visitor centres and car parks throughout Scotland.

Tick Control

1. Provide funds for research into effective tick control methods.
2. Establish further methods for tick surveillance.
3. Increase measures for tick control.
4. Reintroduce the requirement for tick treatment under the Pet Travel Scheme.

Lyme Resource Centre would be willing to develop a draft National Action Plan which could be used as a starting point for multi-agency discussions.

Development of SIGN Guidelines

Current NICE treatment guidelines are imperfect and cover only treatment of early infection. In the absence of evidence within the limited evidence base that was chosen, information from outdated guidelines from 2006 was given precedence, thus preserving the status quo.

Much has changed since 2006. The French have now changed their National Guidelines to reflect those changes in knowledge, understanding and treatment strategies. They have listened to patients and sought to learn from new scientific findings. Scotland should be modelling our testing and treatment strategies on those of the French, not following those of England which are lacking vision and compassion towards patients.

NHS Scotland has taken on board new discoveries for Hepatitis C virus (HCV) that were developed between 2006 and 2019, and they are now recognised as world leaders in HCV elimination. There is therefore no reason why Scotland should not be leading the way in dealing with the rising incidence of Lyme Disease.

Lyme Resource Centre suggests that the Scottish Government sets up a new working group with a panel of 'new thinkers' who are willing to look at the new data and are prepared to be open-minded. This should be a multi-agency group who are not entrenched in the thinking of the 2006 IDSA Guidelines, and who are bold enough to consider that Post Treatment Lyme Disease Syndrome (the term used for continuing symptoms after short course treatment) is really under-treated chronic infection. We believe Post Treatment Lyme Disease Syndrome should be renamed to Partially Treated Lyme Disease Syndrome. In our experience, if you treat for longer periods of time many patients get better and stay better on discontinuation of antibiotics. We have the same treatment model for most other infectious diseases, so why not for Lyme Disease? Patients need treatment which reflects the complexity of this illness.

Lyme Resource Centre wishes to help the Scottish Government improve the health of the Scottish people by participating in this re-evaluation process.

External Review

We propose that the Scottish Government conduct an external review of the Scottish Preparedness for Tick-borne Infections, using the membership of the Lyme Resource Centre to conduct such a review. We believe this needs a fresh approach, using new personnel who will be open to considering and reappraising all elements without prejudice and pre-judgement. We would not wish to lose this opportunity to see new science, new knowledge, new international and world class literature be considered fully and openly. Otherwise, the same process that denied recognition of chronic Lyme Disease within the NICE Guidelines will repeat itself, disenfranchising many sufferers in Scotland. A new guard must be chosen, or else the status quo will continue, new evidence and approaches will be blocked, and patients will be denied recognition of their 'mystery' illnesses.

Lyme Resource Centre wishes to help the Scottish Government by participating in such a review.

Cost

If the cost of action and treatment seems high, consider the cost of not treating. It is not just the healthcare costs that must be considered. Account must be taken of the huge wider economic burden of very sick people who can no longer work due to Lyme Disease, both in Scotland and the wider UK. A recent study (38) concluded that "If governments do not finance IV treatment with antibiotics for chronic Lyme Disease, then the estimated government cost for chronic Lyme Disease for 2018 for the USA is 10.1 billion USD and in Europe 20.1 billion EUR. If governments in the USA and Europe want to minimize future costs and maximize future revenues, then they should pay for IV antibiotic treatment up to a year even if the estimated cure rate is as low as 25%. The cost for governments of having chronic Lyme patients sick in perpetuity is very large".

Who We Are

Lyme Resource Centre is a newly formed charity registered as Scottish Charitable Incorporated Organisation (SCIO) SC049151 with website <http://www.lymeresourcecentre.com/>

We have a mission to educate the public and medical profession about Lyme Disease and related tick-borne co-infections and work with others to research ways to combat all tick-borne illnesses and to better understand the complexities of treatment for infected patients.

Our lead trustee, Prof. John Lambert, is a Professor in Medicine and Infectious Diseases at Mater Misericordia University Hospital and UCD School of Medicine, Dublin. He was director of the National Isolation Unit for Highly Infectious Diseases at the Mater Misericordiae University Hospital 2008 to 2017, and a member of the National Viral Hemorrhagic Fever Committee of the Irish Health Executive. He has also been involved in the Sexual Health Strategy group in Ireland and teaching GPs in Ireland on the subject of STDs. He leads in projects on HIV PEP and PrEP in Ireland, and in roll out of the Irish Hepatitis C strategy through his Leadership as Principal Investigator of the EU funded HepCare Europe, 2016-2019, with €1.8 million funding.

He has presented widely in the field of Lyme and co-infections since 2016 through EU and USA conferences supported by the International Lyme and Associated Diseases Society (ILADS). He has undertaken specialist training through ILADS and has significant experience of treating Lyme Disease and co-infections. He is on the scientific committee of the EU ILADS committee. He organised and ran the 1st European Crypto-Infections Conference, looking at the science behind Lyme Disease and co-infections, held in Dublin in May 2019.

Over the next few months, the Lyme Resource Centre will be accumulating a body of important PubMed and peer-reviewed articles that have been ignored during development of the NICE Guidelines. These articles cover:

- imperfect diagnosis
- evidence of co-infections

- evidence of chronic persistent infection
- benefits of individualised treatment and not guideline triggered treatment
- information on the burden of disease of Lyme and co-infections within Scotland and Europe.

Lyme Resource Centre will be fundraising to reach out and provide education at multiple levels, from community to hospital:

- distribute prevention information
- facilitate outdoor signage
- advocate early intervention, and avoid late complications.

And for those with already missed diagnoses and late stage complications, we will:

- provide better information through well designed studies
- through distribution of quality research findings, improve their situation and reverse the damage that has occurred from long standing infection during this period of misdiagnosis and lack of care from NHS Scotland.
- provide support and guidance

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