For Lyme Disease Awareness & Action

Committee Secretary
Standing Committee on Health
PO Box 6021
Parliament House
Canberra ACT 2600

31st July 2015

Inquiry into Chronic Disease Prevention and Management in Primary Health Care
Lyme Disease Association of Australia Submission

Dear Secretary,

Lyme disease is a complex and poorly understood infectious disease caused most often by a bite from a tick carrying the bacteria, Borrelia. Ticks also carry other diseases referred to as co infections. It must be treated within weeks of the bite or the disease can degenerate to a chronic state and can be fatal if left untreated. However, if treated early the chronic disease can be prevented.

According to the United States Centres for Disease Control and Prevention[1] Lyme disease mimics many other diseases or conditions such as influenza, arthritis, fatigue, Bell's palsy, insomnia, cognitive difficulties, psychiatric, neurological and heart issues. Patients suffering from these chronic conditions in Australia are not currently being assessed for Lyme-like disease so could be misdiagnosed, leaving some of them with a chronic but treatable disease.

Federal and state governments and the Australian medical fraternity have denied the existence of Lyme disease in Australia while thousands of Australians have developed chronic disease and sadly some have died. Many Australians with Lyme-like disease spend years in the Australian medical system misdiagnosed or denied treatment while the pathogens that are infecting their bodies have a chance to propagate, resulting in further debilitation.

While the debate about Lyme disease in Australia continues, the term Lyme-like is often used to avoid the debate being distracted by which species of the bacteria causes Lyme disease. Some antagonists assert that the only species that causes Lyme disease is Borrelia burgdorferi - the common North American strain originally identified in Lyme Connecticut USA. LDAA asserts that the more substantive issue is that the genus Borrelia has hundreds of species and many of them make people sick. Additionally, it is highly likely there may be a uniquely Australian species so research and pathology tests that look exclusively for a few foreign species may not isolate the cause of the illness in Australia.

The Department of Health is waiting to find the "causative agent" before policy is developed to care for Lyme-like patients. This is based on the premise that evidence based policy is most appropriate, in spite of a lack of evidence. We have reports that even though a causative agent has been found by the Murdoch University research this is still seen by the government and associated agencies as not enough evidence that

[1] http://www.cdc.gov/lyme/signs_symptoms/index.html

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Lyme-like disease exists in Australia. Lyme Disease Association of Australia (LDAA) does not believe that taxonomical arguments about which microscopic species of the bacteria are causing illness in Australia is sufficient cause to justify waiting for policy that ameliorates their suffering and could prevent new cases from degenerating to a chronic and potentially fatal state.

An interim policy is required that utilises world's best practice pathology, the Australian doctors who are successfully treating Lyme-like illness and the highly acclaimed international treatment guidelines.

After years of struggle to get the disease recognised Australian patients with Lyme-like symptoms and positive test results from overseas labs are left bearing the burden of proof while the Australian medical system conveniently dismisses the disease, cherry picking research outcomes to prove their point that Lyme does not exist in Australia. Australians with Lyme-like illness get better with internationally recognised Lyme treatment. Lyme disease should be classified as an emerging infectious disease, with patients being treated with best practice medical knowledge while research scientist progresses towards finding clear proof of the causative agent.

This situation is untenable. Thousands of Australians are getting sick; thousands of Australians are remaining misdiagnosed in the Australian medical system. A majority of these Australians were fully functioning members of society who were actively contributing to the Australian economy before they got sick. If the federal and state governments fail to see Lyme-like illness as a priority the stress on the health system will only increase.

LDAA is pleased to have the opportunity to present the issues and implications to the Australian primary health care system of this chronic disease and I commend the LDAA submission to the committee.

Warm Regards,

Sharon Whiteman
President

PO Box 137, Stockton NSW 2295
info@lymedisease.org.au | www.lymedisease.org.au

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Examples of best practice in chronic disease prevention and management both in Australia and internationally

Prevention through early diagnosis and treatment

As an example of best practice, German doctors are educated to treat the early flu like symptoms that occur as the result of the tick bite with antibiotics. This is expected to have a 90% success rate if treated early i.e. in the first 4 weeks after the start of infection.[1] Early intervention has great success in stopping the disease from progressing to a debilitating and potentially fatal illness. Australian doctors have not been educated to consider this course of action nor are they supported with effective pathology testing.

The Australian General Practice (GP) community has little, if any knowledge of Lyme-like disease or how to diagnose and treat it. Also as Australia is outside the reported endemic areas for Lyme-like disease and the Health Departments have long denied that Lyme-like disease exists here, many doctors are lead to conclude it's an impossibility. However, it seems highly implausible that Australia would be the only continent on the globe without Lyme-like disease.

If a patient encounters a doctor educated enough to suspect Lyme disease and order the appropriate tests, testing in Australian public health laboratories will, in a majority of cases, produce a negative result. Australian physicians rely upon ineffective laboratory testing protocols which are acknowledged to be 'discordant', for example a patient might test in two different laboratories which return two completely opposite results.

Unfortunately, the prevailing wisdom is that clinical diagnosis is considered invalid and laboratory testing is purported to be the key to providing clarity about the cause of illness.

In other countries Lyme disease is diagnosed on clinical signs alone if a 'bullseye' (EM) rash is present. The bullseye rash is known as a 'pathognomonic' sign that warrants an immediate diagnosis of Lyme disease as it is unique to Lyme disease; this is a CDC-agreed diagnostic position, negating the need for any diagnostic test. In Australia we don't educate doctors about this sign. The NSW Department of Health, which provides the preeminent advice to guide physicians, is not specific on the presence of the bullseye rash. Instead, they recommend that physicians pursue costly and unnecessary laboratory testing which, for many Australian patients, is highly unreliable.

Management through long term antibiotics

In the rare event that a patient with Lyme-like disease tests positively for the key Lyme-like pathogen, *Borrelia*, a common but tragic experience of Lyme-like patient in Australia is that infectious disease specialist will follow the Infectious Disease Society of America's (IDSA) practice guidelines. This advises antibiotic treatment for a month or less which is seen as vastly inadequate by any medical professional that is educated and experienced in treating Lyme-like disease successfully and is definitely not best practice.

Long term treatment is required as:
Medical practitioners will have to treat more than one pathogen

- Ticks are able to transmit more than one pathogen, known as co-infections.
- The LDAA Australian patient report indicates that 55% of Australian patients reported they have been diagnosed with one or more co-infections.
    - The most common co-infection reported was *Babesiosis*, followed by *Bartonellonsis*, *Chlamydia Pneumoniae, Mycoplasmosis* and *Ehrlichiosis*. Compared to patient data in the US, this report indicates that Australian figures for co-infection are much higher than those reported in the US.
- Lyme disease patients who are co-infected with other tick–borne infections have a more prolonged and severe illness than those who are infected with Lyme disease only.[2]

[1] http://www.borreliose-gesellschaft.de/Texte/guidelines.pdf
[2] Krause, P. 1996, Concurrent Lyme disease and babesiosis. Evidence for increased severity and duration of illness. JAMA, 275 (20), pp. 1657-60.

- In 2013, Franke, Heldebrandt & Dorn reviewed the current scientific literature and found that "co-infections with *Borrelia* and other pathogens, such as *Babesia spp., Rickettsia spp., A. phagocytophilum*, or tick-borne-encephalitis-virus (TBEV) often lead to more severe or atypical clinical outcomes of Lyme B and problems in diagnosis and treatment occur."[3]
- Treatment pathways will be complex because Australian patients are presenting with different infections and different manifestations.

Lyme-like pathogens are hard to eradicate

- Researchers have found that *Borrelia* spirochetes cover themselves with a bio-film, a fibrous layer that protects them from antibiotics. Long-term treatment introduces drugs that breakdown biofilms so that the hidden spirochetes can be eradicated.[4]
- A recent study by Northwestern University also found that *Borrelia* forms dormant persister cells, which are highly tolerant to antibiotics. They recommend pulse dosing of antibiotics over time.[5]
- German scientists modelling *Borrelia* found that it "recovers from a strong initial immune response by the regrowth of an immune-resistant sub-population of the bacteria". As such, the chronic phase "appears as an equilibration of bacterial growth and adaptive immunity". They concluded that their findings have major implications for the development of the chronic phase of *Borrelia* infections, as well as on potential protective clinical interventions.[6]
- In his review of evidence for immune evasion and persistent infection in Lyme disease, Berndston wrote, "The question is no longer whether LD (Lyme disease) can survive an antibiotic challenge in order to become a persistent infection. High quality studies show not only that it happens, but they also show how it happens."[7]

Long-term treatment can work

- The Australian Government argues that there's no evidence of any benefit for the Lyme patient who chooses to undergo long-term treatment for Lyme-like disease and that it may cause more harm than good. This ignores the growing body of evidence that long-term treatment is working for many Lyme patients and the growing body of research supporting the effectiveness of long-term protocols.
- More than 200 (65% of respondents) Australian patients reported in this survey that significant improvement occurred with treatment beyond 30 days.
- Stricker reviewed the pathophysiology of *Borrelia burgdorferi* infection and the peer-reviewed literature on diagnostic Lyme disease testing, standard treatment results, and co-infection with tick-borne agents, such as *Babesia, Anaplasma, Ehrlichia*, and *Bartonella* species. He also examined uncontrolled and controlled trials of prolonged antibiotic therapy in patients with persistent symptoms of Lyme disease and concluded that, "Prolonged antibiotic therapy may be useful and justifiable in patients with persistent symptoms of Lyme disease and co-infection with tick-borne agents."[8]
- There are a number of patient-focused studies[9] that demonstrate verified persistent infection, even after antibiotic treatment, necessitating long term treatment is required.

Research into Lyme-like disease diagnosis and treatment cannot stand alone without proper examination of the potential co-infections. Global guidelines including German Borreliosis guidelines and International Lyme and

[3] Franke J, Hildebrandt A & Dorn W. 2013, Exploring gaps in our knowledge on Lyme borreliosis spirochaetes – updates on complex heterogeneity, ecology, and pathogenicity. Tick Tick-Borne Dis.; 4: 11-25.
[4] Sapi E, Bastian SL, Mpoy CM, Scott S, Rattelle A, Pabbati N, et al. (2012) Characterization of Biofilm Formation by Borrelia burgdorferi In Vitro. PLoS ONE 7(10): e48277.
[5] http://www.northeastern.edu/news/2015/06/researchers-discovery-may-explain-difficulty-in-treating-lyme-disease/
[6] Binder SC, Telschow A & Meyer-Hermann M. 2012, Population dynamics of Borrelia burgdorferi in Lyme disease. Frontiers in Microbiology (22 March).
[7] Berndston K. 2013, Review of evidence for immune evasion and persistent infection in Lyme disease. International Journal of Medicine, 6, 291–306.
[8] Stricker, R. Counterpoint: Long-Term Antibiotic Therapy Improves Persistent Symptoms Associated with Lyme Disease, Clinical Infectious Diseases. (2007) 45 (2): 149-157.
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Associated Diseases (ILADS) guidelines provide medical practitioners with long-term treatment protocols and can be utilised as a basis for developing effective Australian treatment protocols.

In addition, researchers in the United States in particular, are discovering better ways to treat Lyme-like disease. This progress must be taken into account and funds must be allocated to Australian research to address the specific nuances of Lyme-like illness in Australia and find ways of managing the disease for a population that is already in the chronic long-term stage of illness.

Prevention through effectively testing blood donations

There is a growing body of evidence suggesting that Lyme-like disease and other vector-borne pathogens and bacterial infections can be spread through blood transfusion.

B. burgdorferi survive storage under blood banking conditions and transmission of the pathogen by blood transfusion is theoretically possible.[10] A recent case reported that a nine year-old boy was infected with a Lyme-like co-infection, *Ehrlichia* after a blood transfusion.[11]

A number of other studies in the US indicate there were 159 known cases of *Babesiosis* caused by transfusions where blood bank officials were able to trace back to 136 donors.[12] Alarmingly, 30 of the cases reported were traced to only 12 donors because blood supplies were split and used in multiple recipients.

The Australian Red Cross does not have a consistent approach to testing or screening donated blood for Lyme-like pathogens. Given the issues with the current Australian testing there would be no certainty in the efficacy of the testing anyway. There remains considerable public health risk for the many blood recipients, as there are likely many donors with Lyme-like illness who are as yet undiagnosed or potentially misdiagnosed. To date anyone in Australia receiving blood transfusions is at risk of acquiring Lyme-like illness.

The burden of disease estimate of $240 million pa in Australia

Lyme disease has been a nationally notifiable condition in the United States since 1991.[13] In 2013 the Centers for Disease Control and Prevention (CDC) revised its annual estimate of Lyme disease cases in the United States from 30,000 to 300,000[14], a sobering 10 fold increase. Unfortunately the LDAA keeps the only available national figures of Lyme-like disease in Australia, collected through the voluntary bi annual survey. If figures official were available the burden of disease could be formally calculated and the impact on the health budget would be understood.

In March 2015 Professor Norbert Mencke, Head of Global Communications Bayer Health Care said, “Even the economic impact of a vector-borne disease, such as Lyme disease in the United States, is estimated to be over $3 billion annually. The spread of these diseases, combined with their economic burden, only affirms our commitment to prevent companion vector-borne diseases.”[15]

LDAA anticipates that the incidence in Australia would be statistically similar if Lyme-like disease was a notifiable disease and if patients had access to reliable diagnostic tests and educated doctors. If so, a per capita estimate based on the USA burden of disease of $3 billion pa would be $240 million pa in Australia. The implementation of best practice reporting and awareness of such costs may assist the government to prevent and manage this chronic disease.

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[10] Nadelman RB, Sherer C, Mack L, Pavia CS & Wormser GP. 1990, Survival of Borrelia burgdorferi in human blood stored under blood banking conditions. Transfusion.

[11] Regan J, Matthias J, Green-Murphy A, Stanek D, Bertholf M, Pritt BS, Sloan LM, Kelly AJ, Singleton J, McQuiston JH, Hocevar SN & Whittle JP. 2013, A Confirmed Ehrlichia ewingii Infection Likely Acquired Through Platelet Transfusion, Clin Infect Dis. 56 (12): e105-107.

[12] Herwaldt, BL, Linden, JV, Bosserman, E, Young, C, Olkowska, D, & Wilson, M. 2011, Transfusion-associated babesiosis in the United States: a description of cases. Annals of internal medicine, 155(8), 509-519.

[13] http://www.cdc.gov/lyme/stats/survfaq.html

[14] http://www.cdc.gov/media/releases/2013/p0819-lyme-disease.html

[15] http://www.pharmiweb.com/pressreleases/pressrel.asp?ROW_ID=111400#.VRpcnkKAiE6#ixzz3Vx01bMJy

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Opportunities for the Medicare Payment system to reward and encourage best practice and quality improvement in chronic disease prevention and management

Medicare to cover Lyme-like disease blood tests that are reliable and effective.

Medicare payments requires pathology testing laboratories to be accredited by National Association of Testing Authorities (NATA). Currently NATA is the only endorsed assessing body for pathology accreditation.[16] LDAA believes the current pathology regulation is flawed and is contributing to the discrimination and neglect of Lyme-like patients.

Australian government endorsed laboratories use inconsistent and scientifically disputed test kits that are relevant to infections found in other areas of the world but not necessarily to Australia. For example, in Australia we historically tested for three strains of *Borrelia*, when we know there are many more.[17]

An additional complexity is that not all patients mount an appropriate immune response to a Borreliosis infection. In fact, Borreliosis suppresses the immune system and prevents sufferers' antibodies from reacting to these stealth pathogens. Applying a limited 'three strain' antibody test approach to people whose immune system may be significantly impacted by a stealth infection (that could be any one of multiple strains or in fact a totally different species of the Bacterial infection) is rarely going to be effective as, in most cases, there will be no immune response registering and, therefore, no antibodies.

The recent Murdoch research published on 25th June 2015 in the journal *Parasites & Vectors*[18] concluded that Lyme-like pathogens (*Borrelia)* are shielded or encased by other bacteria and without the use of specific blocking primers applied during laboratory diagnosis, the *Borrelia* pathogens are often concealed. Pathology tests that ignore the endosymbiont relationship of other organisms who block the detection of *Borrelia* will make it almost impossible to detect the pathogens. This could help explain the plethora of false negative tests received from the Australian laboratories.

Red Tape

Some Australian laboratories use an alternative method to the limited commercial test kits. Instead, these laboratories isolate organisms via Polymerase Chain Reaction (PCR). This means that they locate the actual DNA of the organism and do not rely upon the potentially compromised immune system's antibody response to an organism. When they are able to isolate the organism, they pass it to the Australian Genome Research Facility, a NATA-accredited lab, which consistently finds organisms related to known *Borrelia burgdorferi* strains. This indicates that there is potentially an indigenous strain of *Borrelia* in Australia. However, because the original isolating laboratory is not yet NATA-accredited due to red tape issues, the entire chain of results is disregarded.

It is unclear to LDAA what the exact nature of the relationship is between NATA and the Royal College of Pathology Australasia (RCPA). What is clear is that the RCPA's influence is extensive. The LDAA has previously highlighted the inconsistency and extreme bias in the RCPA's stance on Lyme disease.[19] When the RCPA has been the agency most actively and widely promoting the position 'there is no Lyme here', this stance places them in a significant conflict of interest when called upon to exercise the impartiality and scientific objectivity required of their role in accrediting laboratories, particularly in relation to a laboratory which consistently isolates organisms that are able to be successfully sequenced as a 'species' of Borrelia. One lab consistently identifying Borrelia - Australian Biologics has had NATA accreditation 'pending' for more than a year and the imposition of continual delays for NATA accreditation are professionally inexplicable.

[16] http://www.health.gov.au/npaac accessed 20 July 2015
[17] See full outline in http://www.lymedisease.org.au/wp-content/uploads/2010/11/20140129LDAAScopingStudyResponse.pdf
[18] http://www.parasitesandvectors.com/content/8/1/345/abstract
[19] http://www.lymedisease.org.au/wp-content/uploads/2010/11/20140408ResponsetoRCPAPositionStatementFinal.pdf

Furthermore, RCPA continually publically denigrates the use of overseas testing laboratories and maintains the position that these tests are not to be relied upon. Australian patients want to know why, for example, Infectolab's results aren't accepted here if they are an accredited lab, which has reciprocal rights. Infectolab is accredited by the German accreditations office DAkkS in accordance with DIN EN ISO 15189:2007, an accepted standard.

Numerous Lyme-like patients have received positive test results from overseas laboratories and have been successfully treated overseas or by one of the scarce Australian doctors trained in Lyme-like disease. However, it is normally a long road to a diagnosis as Lyme-like patients are routinely referred to Australian laboratories that are ineffective in isolating the Lyme-like pathogens. This often results in false negative test results and the consequential denial of a diagnosis, treatment and the abhorrent degeneration to a state of chronic disease.

Discordant results in Lyme-like pathology testing

Australia's Chief Medical Officer (CMO), Chris Baggoley, acknowledges the discordant results in Lyme-like pathology testing. The Department of Health has recently sourced funding for its study comparing different serology assays currently used to diagnose Lyme disease in Australia. However, LDAA is not confident that the methodology nor the selection of laboratories will be effective. The process lacks transparency and fails to take into account that the disease compromises the immune response and hence the antibodies they will be testing for. If overseas labs are effectively isolating the pathogens it would seem essential that there be international harmonisation of Lyme-like testing as soon as possible and further exploration of genetic testing technologies.

An objective and credible identification of laboratories that are effective in isolating both locally and internationally acquired Lyme-like pathogens is required as a matter of urgency. Ideally tests undertaken in these laboratories would be covered by Medicare.

The role of State and Territory Governments in chronic disease prevention and management

The LDAA participated in the now concluded Clinical Advisory Committee on Lyme Disease (CACLD), which was established and run by the Chief Medical Officer (CMO), on behalf of the Australian Government.

A diagnostic case definition

One of the outcomes of CACLD was the identification of the need for a case definition of Lyme-like disease. The federal Department of Health has stated in their response in late May 2015 they will be working with state and territory health agencies on a diagnostic case definition which will assist Australian medical practitioners to better recognise Lyme-like disease. In its first iteration the document is focussed on infection acquired in endemic areas overseas. Unfortunately this will not of itself help in cases acquired locally. The first draft of the case definition was completed more than 7 months ago, we are still awaiting its publication.

Disseminate Lyme-like disease information

The CMO also advised that Chief Health Officers in the State and Territories should disseminate Lyme-like disease information to health professionals and the general public.[20] To date this advice has not been effectively implemented.

[20] http://www.health.gov.au/lyme-disease#progress