

Caroline Flint MP  
Minister of State  
Department of Health  
Richmond House  
79 Whitehall  
London  
SW1A 2NS

10<sup>th</sup> May 2007

Dear Ms Flint

Thank you for your reply of 29<sup>th</sup> March 2007.

Lyme Disease Action has many concerns with the answers as supplied in that letter and we should like to comment upon many of the points you raise.

This charity would find it helpful if, before we respond further to your letter of 29<sup>th</sup> March, we clarify the patients whom we aim to represent. Our charitable objects <sup>(1)</sup> require us to address the relief of persons suffering from Lyme disease, other borrelioses and associated diseases and our area of operation is the UK and Europe. It is patients of these diseases that in all instances we refer to.

Therefore, this charity aims to represent the interests of those patients who fulfil a diagnosis of Lyme disease or Lyme borreliosis by having an active infection caused by any of the pathogenic spirochaetes within the *Borrelia burgdorferi sensu stricto/lato* group of bacteria, occurring in the UK and Europe, whether known to science or not. We take this precautionary view because, as you will be aware, several new *Borrelia* genospecies have been assigned to this group of bacteria in relatively recent times, some of which have been associated with pathogenicity.<sup>(2)(3)(4)</sup> Given that this is now a periodic occurrence, and given that the disease manifestations that may follow infection with these pathogens are broadly very similar and require similar treatment, we aim to represent all patients with this type of spirochaetal tick-borne disease. That these infections can take a major form in some patients, whilst others are not so badly affected, is widely recognised.<sup>(5)</sup>

We also seek to represent patients with any other associated co-infection since ticks are known to carry other pathogens. We advocate that these too should be looked for in patients showing a corresponding spectrum of symptoms. The scientific community cannot be certain that the full extent of the presence of tick-borne infection in the UK and Europe is known. In these circumstances we feel a patient should receive the benefit of the doubt.

If the Department views this patient group by any other definition than that in the above two paragraphs, we need to be informed of this to minimise any misunderstanding. We aim to represent the interests of patients who fulfil the clinical picture as outlined above. In the current circumstances a fully-informed patient should be allowed to opt for a trial of treatment even if seronegative to known pathological UK *Borrelia burgdorferi sensu stricto/sensu lato* (*Bb s.s./Bb s.l.*) species. We would also like to see all other possible causes ruled out, including any condition that might have given rise to false positive serology, in order that a patient can receive the best possible diagnostic analysis.

At the end of our response, we have added an empirical viewpoint formed by patients from their actual experiences for your consideration and comment. We feel that direct clinical observation needs to be taken into account whilst we still have many gaps in our knowledge about tick-borne disease.

I shall continue to answer your response of 29<sup>th</sup> March by following each of the issues raised by our *'Ten Steps to better control of Lyme disease'* in the order that they occur.

*Lyme Disease Action is calling upon the Government to take urgent steps to ensure that people who have Lyme disease are recognised and accorded their full human rights:*

*1. By ensuring that people with Lyme disease receive prompt, adequate and appropriate treatment that, in some cases, may be long-term.*

"People can be correctly diagnosed and given rapid treatment by being tested through the Health Protection Agency's (HPA's) Lyme Reference Laboratory. The use of these facilities is readily and freely available to GPs and the NHS. I understand that long-term treatment is rarely needed and long-term complications are rare."

Patients can be diagnosed, however, we have reason to believe that many are falling through the net. Possibly this is compounded by the current lack of GP knowledge about this disease. Existing tests are not reliable enough to rule out the presence of Lyme infection.<sup>(6)(32)</sup> The cornerstone of diagnosis is clinical diagnosis by a knowledgeable doctor. In the experiences reported to us by many people with symptoms and history that would fit a Lyme diagnosis, often their GPs were not aware of this diagnostic possibility. At present, only those patients who see a knowledgeable doctor will be in a position to be "correctly diagnosed and given rapid treatment." Thus, there is evidence that your answer may only refer to a minority of patients at present and the level of knowledge of Lyme amongst GPs requires attention.

It is recognised that relatively short-term treatment is usually successful if the illness is recognised and adequately treated in its early stages. Many physicians, who actively treat patients, consider that long-term treatment is often the only option for those who remain ill and undiagnosed for any length of time. There is a great deal of sound, peer-reviewed scientific data that shows that this type of *Borrelia* can survive short courses of antibiotics.<sup>(7)(8)(33)</sup> The statement that long-term treatment is not necessary is frequently based upon one paper.<sup>(9)</sup> However, the research in this paper has been widely criticised as being poorly designed.<sup>(10)</sup> Evidence-based medicine requires rigorous consideration of all the available research material and opinion. Where there is a mixed picture, we believe that the patient should be informed of the breadth of opinion/evidence and supported in making their decision regarding any treatment they wish to undertake.

In any case, we note the advice you have received indicates that long-term treatment is rarely needed. This means that, on occasion, it is needed and an exception is made. It would be helpful to this charity, if you would explain upon what criteria long-term treatment is, on occasion, judged to be necessary.

The Health Protection Agency is recommending the use of the recent guidelines published by the Infectious Diseases Society of America (IDSA).<sup>(11)</sup> These guidelines do not recognise the existence of chronic Lyme disease, despite much evidence to the contrary.<sup>(7)(8)(11)(33)</sup> The HPA seem to imply that the vast majority of patients who have ongoing symptoms after short-term antibiotic treatment must have developed a separate, aseptic disorder and therefore long-term treatment is not necessary. This position relies on an assumption that relatively short courses of antibiotics are completely successful. However, this assumption is contradicted by much published research.<sup>(7)(8)(33)</sup> Compared to the evidence in favour of the persistence of borrelial infection, there is little evidence to support a non-infection-based hypothesis that continuing symptoms are a result of tissue damage, a triggered autoimmune process or reflects a psychiatric model of symptom persistence. The HPA's confidence in the adequacy of short-

term treatments appears to lead their recommendations to an extent that is not justified by the breadth of information available.

We ourselves know of quite a number of patients who only recovered after very long-term antibiotic treatment. Recovery has meant that they have regained their lives, stopped claiming benefit and some have returned to work. We accept that, at present, this evidence is only anecdotal, but surely any therapy that has extremely successful outcomes like this must be worth consideration by the Department of Health?

*2. By ensuring that more specialist clinicians trained in the clinical diagnosis, treatment and care of Lyme disease patients become available within the National Health Service.*

“Clinical diagnosis of Lyme disease is often done without the need for laboratory tests where people have an obvious tick bite resulting in the usual mild effects of a red raised rash in the vicinity of the bite.”

It is widely accepted that the standard serology tests are not useful in the first few weeks of infection.<sup>(13)</sup> The red rash, termed an erythema migrans or EM rash, is considered sufficiently distinctive that a diagnosis of Lyme disease can be made without the need for confirmatory testing. However, LDA has heard many accounts from patients regarding their own doctor not recognising an EM rash. The non-appearance of an EM rash cannot be used to rule out a diagnosis as studies variously show that only 35% to 59% of Lyme patients exhibit the rash.<sup>(14)</sup> Even these figures cannot be based in certainty because it is difficult to quantify a negative, i.e. the non-appearance of a rash. Current knowledge indicates that, in the UK, the tick stage most likely to bite a human is the nymph form of *Ixodes ricinus*. These ticks are very small, (1 – 2 mm) and the bites are painless, so often a tick bite will go unnoticed. Thus, “obvious tick bite” instances may be the exception not the rule. Considering all these factors leads us to conclude that substantial numbers of patients are at risk of not being recognised or treated.

“Most effects of infection are mild and if the GP is confident of a positive diagnosis on the basis of obvious clinical signs then there is no obligation to submit for a laboratory confirmation.”

Lyme Disease Action profoundly disagrees with the confidence of the statement “most effects of infection are mild” – as total numbers of cases are not known, the proportion of mild to severe cases cannot be determined. The illness can manifest in a major and very severe form. It may be that many victims of infected tick bites exhibit mild effects that appear to resolve naturally, but attention is needed for those who have not been recognised early and have progressed to develop the disease in a major form. These victims, if not adequately treated, endure constant suffering and debility. Unluckily some, it appears, become non-responsive to treatment at this stage. They may be forced to rely on others for their care.

“There is clinical specialism within the NHS. As you will be aware, the HPA is working to increase awareness of Lyme disease and provides clinical advice to physicians who care for patients who may have Lyme disease. The Agency has nationwide links to experts in infectious diseases, neurology, rheumatology and other specialties who have a particular interest in Lyme disease, to whom patients can be referred. It takes part in national and international collaborations to improve diagnostic tests and to promote evidence based treatments.”

LDA would be grateful if you could clarify the phrase “provides clinical advice to physicians.” Most of the information provided by the HPA relates to laboratory testing, and, is identical to the stance of the HPA’s Lyme Reference Unit. We were given to understand by a representative of this Unit that their function in these circumstances was purely to provide scientific information relating to testing services and not clinical advice about individual patients. Clinical assessment considers the patient’s whole history, symptomatology and response to treatment, and subsequent clinical advice is the function of a physician who

actually sees patients. Since the LRU do not give clinical advice in individual cases, we need clarification upon where physicians can turn for advice of a purely clinical nature about individual patients?

LDA is aware of the international collaboration and we fully support work towards improving the diagnostic tests and the concept of evidence-based treatment. Your answer does, however, indicate that there is ongoing international work proceeding to improve the diagnostic tests. There is published work that some test improvements affecting test interpretation involved re-assessments of the criteria for positivity,<sup>(15)</sup> and not solely to improvements in practical methodology. Therefore, we question how this relates to the statement assuring us that the diagnostic tests are reliable which occurs elsewhere in your answer (see section 4). There is inherent contradiction in these stated positions and this is causing great clinical confusion for patients and doctors. LDA is asking that the matter be given urgent priority since this is directly affecting patients and their future health. We also note that little research has been carried out on the effectiveness of different treatment protocols, and existing research has produced conflicting results. Under these circumstances evidence-based treatment must be extended to include the experience of Lyme clinicians in administering empirical treatment.

"The HPA has also raised awareness of Lyme disease through its website and through presentations to, and discussions with, professional and recreational and special interest groups. In addition, NHS Direct has published comprehensive information on the disease, including preventive measures, on its website."

In March 2007 the HPA website increased its advice on tick awareness, as we requested that government agencies should do in February 2007. We note that there is now more prevention advice for people walking in the countryside. We welcome these additions. However, we question whether members of the general public are especially aware of the HPA or HPA-recommended websites and leaflets. All the information needs to be made much more prominent to the public. A fully funded national awareness campaign spearheaded by central government would get the message across more effectively and this is what we are asking for. The HPA and NHS Direct websites do provide essentially the same information, although the HPA website is more detailed. We support the information on the prevention of Lyme disease, however, questions remain over the information on diagnosis and treatment and we have placed a detailed critique of this on our website. For your convenience I have enclosed a printed copy of our critique.<sup>(16)</sup> Patients have given us feedback that the verbal advice they received on NHS Direct was of variable quality and in some cases plain wrong. If these reports can be substantiated, this obviously needs to be put right.

*3. By ensuring that clinical guidelines for diagnosis and treatment of patients are developed for all medical staff and ending over-reliance on current laboratory tests in diagnosis.*

"As I have explained above, the HPA is working to improve awareness of Lyme disease. Clinicians in the UK have ready access to the best diagnostic tests available for the disease and NHS diagnostic tests conform to internationally agreed criteria and the tests are freely available."

"The best" is only a relative judgement. There is a large body of peer-reviewed evidence that shows that the tests are not reliable enough to categorically rule out this diagnosis.<sup>(6)(32)</sup> In the absence of reliable tests, diagnosis must be made on a clinical basis. This is as recommended by the US Centers for Disease Control and Prevention (CDC), "*Lyme disease is diagnosed based on symptoms, physical findings (e.g., rash), and the possibility of exposure to infected ticks; laboratory testing is helpful in the later stages of disease.*"

"Laboratory confirmatory testing is essential to diagnose Lyme disease if the typical 'erythema migrans' (red rash) is either missed, or absent, or the person is not aware

that they have been bitten by an infected tick. Ticks are usually encountered in areas where deer/sheep are present and if the person has been exposed to their environments.”

We agree that testing should be performed for every potential case of this disease, however, given the questionable reliability of the tests, a negative result must not be used to rule out a diagnosis. There is a correlation between tick numbers and deer/sheep populations, but low numbers of these animals in a given area should not be used to deny the possibility of Lyme disease. In fact, deer are non-competent hosts for *B. burgdorferi*. The real reservoir of *Borrelia* bacteria is small mammals and birds, and these are ubiquitous.<sup>(17)</sup> People follow outdoor pursuits, garden, camp, travel and handle animals/animal products. It is unsound therefore to discount anyone from diagnosis purely on the basis that they do not live in an area that has high deer or sheep populations.

4. *By ensuring that every effort be made to gain a reliable laboratory test or set of tests for Lyme borreliosis (Lyme disease) and closely associated tick-borne diseases.*

“Reliable laboratory tests have already been developed and there is an accepted international testing protocol which is followed in the UK. However, some private laboratories do not follow this protocol and their tests should not be relied upon for diagnosis of Lyme disease.”

The first statement makes an assumption that a test of the person’s immune response, as currently tested for by the two-test procedure,<sup>(18)</sup> accurately reflects their infection status. However, there are many peer-reviewed papers that contradict this assumption.<sup>(6)(32)</sup> The standard Lyme testing protocol is controversial and is not universally accepted. There is no sensitive gold standard test for the presence of *B. burgdorferi s.l.* against which different testing methods can be compared, therefore assessment of the reliability of any test is open to question.

“The internationally agreed criteria are based upon stringent interpretation of serological tests for specific antibodies to *Borrelia burgdorferi sensu lato* and are accepted and applied by the NHS laboratories in the UK.”

LDA knows of many people who meet the clinical definition of Lyme disease, with known tick bites, EM rashes and other matching symptoms, who are effectively treated with antibiotics, and yet who have a history of negative serology. This state of affairs is also acknowledged in the peer-reviewed literature.<sup>(6)(32)</sup> Therefore, we have to question whether the serological criteria for positivity have been assessed at the correct level? Many seronegative people with this type of clinical picture respond to antibiotics. We would be failing in our duty to patients if we did not ask ‘Have the scientists who decide how to interpret these very complex tests, set the criteria of positivity within too narrow a range?’ If so, genuine cases are not being recognised.

“Internationally agreed” presents a false sense of consensus on a controversial subject. There are at least three genospecies of *Borrelia* known to cause disease in the UK, with hundreds of known strains<sup>(19)</sup>, and potentially many more yet to be discovered. The tests look for antibodies to a small number of laboratory-cultured strains, so may be insensitive to the majority of wild strains.<sup>(20)</sup> *Borrelia* genospecies in this particular branch of the genus are by far the most genetically complex bacteria known<sup>(21)(22)</sup> and have evolved to avoid detection by the immune system.<sup>(23)(24)</sup>

We would like to be informed of the advice the HPA gives to physicians regarding the possible causes and levels of false seronegativity and false seropositivity that they should consider when interpreting a serology result in the case of an individual patient.

“These serological criteria are used by the HPA Lyme Borreliosis Specialist Diagnostic

Service at the HPA's south east regional laboratory, Southampton. Details of the testing criteria are given in the attached annex.

Regrettably, there are a number of unorthodox tests that have been privately developed over the past few years and it is wrongly claimed that these tests can diagnose Lyme disease more accurately than conventional, internationally accepted laboratory criteria available on the NHS. The use of such tests for the diagnosis of Lyme disease can have serious implications for patients, both for those who genuinely have Lyme disease and require appropriate treatment, and for those who are led to believe that they have Lyme disease and go on to receive treatment that is inappropriate and may be potentially harmful.

The Chief Medical Officer remains concerned about the impact of unorthodox and unvalidated tests that can incorrectly give a diagnosis of Lyme disease and commissioned the Department's Inspector of Microbiology to investigate the use of such unorthodox diagnostic methods in the UK. Examples of tests investigated by the Inspector of Microbiology are the fluorescent antibody test (Q-RIBb) test developed by the Bowen Institute in Florida and a fluorescent test and culture method developed by a Dr Mattman.

The Inspector of Microbiology concluded that the validation of the Q-RIBb test was not scientifically sound and had been shown to be invalid in peer-reviewed literature and the Mattman culture medium is discredited as it has been shown that this medium fails to grow *B. burgdorferi*, the causative organism of Lyme disease. Such tests should not be used for the diagnosis of Lyme disease.

The Bowen Institute was inspected by a team of Inspectors from the Florida Agency for Health Care Administration and the Centers for Disease Control and Prevention (CDC), Atlanta (Bacterial Zoonoses Branch, Division of Vector-Borne Infectious Diseases). The laboratory was denied licensure and is also not certified under the Clinical Laboratory Improvement Amendments. Such certification is required for all laboratories performing clinical laboratory testing. A warning was issued in CDC's Morbidity and Mortality Weekly Report, 11 February 2005, advising caution regarding many commercially promoted tests for Lyme Borreliosis and restating the internationally accepted criteria for diagnosis. The CDC advises clinicians in the USA to use laboratory tests that are approved by the USA's Food and Drug Administration or ones that have satisfactory performance characteristics. The Q-RIBb test does not meet these criteria."

LDA has never recommended any laboratory diagnostic test given current uncertainty over the reliability of testing for this disease. The cornerstone of diagnosis is the clinical picture. In addition, LDA is aware of the MMWR warning of 11/2/05, but, as stated, we have never recommended the test(s) mentioned.

*5. By ending over-reliance on a tick bite risk assessment in the diagnostic procedures for Lyme disease.*

"Tick bite assessment is important in risk assessment as the disease can only be acquired through the bite of an infected tick."

This statement is not entirely true. It has been known since 1985 that *B. burgdorferi* can be transmitted from mother to unborn child.<sup>(25)(26)</sup> Viable *B. burgdorferi* have also been cultured from urine and breast milk.<sup>(27)</sup> There is at least a theoretical risk that *B. burgdorferi* could be transmitted sexually. It is also possible that other biting insects could act as vectors, with at least one confirmed case.<sup>(28)</sup>

An assessment of risk is potentially misleading if the information used in forming it is

incomplete. In this case, the risk assessment attempts to ascertain the probability of a person having been bitten by a tick. However, in completely ruling out the diagnosis, certainty is needed. Where only a probability can be estimated, then, we would argue, the benefit of the doubt needs to be given. Not to do so, leaves the patient vulnerable to ongoing infection which gets harder and harder to treat as time passes and this is unacceptable.

“Non-exposure to the environment where ticks are found is unlikely to give rise to Lyme disease. However, if there is any doubt, exposure to the causative organism of Lyme disease (*Borrelia burgdorferi sensu lato*) can be detected by laboratory tests long after the exposure, by detecting the specific antibody response to that causative organism.”

Ticks can be found in many environments from upland areas to domestic gardens and LDA has received reports of bites being received from ticks in other circumstances, which may amount to additional transmission pathways. Our concern is that the assessment of risk of exposure to ticks is commonly used as a weighting factor to rule out Lyme disease, when ticks are fairly ubiquitous and ruling out their involvement might not be scientifically sound.

*Lyme Disease Action is calling upon the Government to take all possible measures to form an accurate assessment of the scale of the problem and to improve disease prevention measures:*

6. *By granting notifiable status to Lyme disease throughout the United Kingdom.*  
(and)

7. *By ensuring that every effort be made to gain reliable case numbers of Lyme disease.*

“Although Lyme disease is not a notifiable disease, it is recognised as the most significant of our vector-borne diseases and is taken very seriously in the UK. Granting notifiable disease status to Lyme disease will not necessarily increase detection of the disease. Laboratory confirmed reports are already received by the HPA and this enables an estimate of the number of cases of the disease to be made. As most people suffer only mild symptoms and might miss or ignore the initial red rash and recover without recourse to their GP, making the disease notifiable would not detect these cases.”

LDA would find it helpful if the methodology of the estimate of total numbers could be made public. This estimate appears not to have changed in recent years despite the large increase in laboratory confirmed cases and increasing numbers of people contacting LDA and similar groups. We are aware there may be several factors involved.

If the HPA laboratory only provides information and advice on testing and not clinical advice on individual patients, how is the claim that “most people suffer only mild symptoms” justified? Please could evidence be supplied for this statement?

We note that Lyme disease is notifiable in Scotland and we are asking why there is considered to be a difference between England/Wales and Scotland over this issue? LDA accepts that granting notifiable status will impose an administrative burden upon GPs that may affect their willingness to make the diagnosis. However, laboratory confirmed cases might be only a small proportion of the true number of cases, and making Lyme borreliosis notifiable is likely to go some way towards better estimates of the true number of cases.

8. *By further assessment of tick surveillance procedures and their relationship to case numbers.*

“It is already known that tick populations are linked to deer populations and that areas where the public has close access to areas grazed by deer are where people are at particular risk of being bitten by ticks. The public is warned in those areas of greatest risk to take steps to protect against tick bites.”

There have been confirmed cases across the UK. Issuing warnings only in the areas deemed to be at greatest risk exposes large numbers of people to potential infection. We feel the first statement "It is already known that tick populations are linked to deer populations" is incomplete. As your letter of 29/3 states, deer and sheep populations are of relevance. In addition, we would point out that the populations of the reservoir species of small mammals and birds are also of relevance to the occurrence of infected ticks.<sup>(17)</sup>

We continue to ask for greater accuracy in the assessment of human case numbers.

*9. By taking the lead in ensuring that full information on Lyme disease and its prevention is widely disseminated to all sectors of society.*

"Information about Lyme disease is readily available to the public on the HPA's website. In areas, such as the New Forest, where the risk is greatest there is publicity about the risk to the public through posters and leaflets."

Much of the information on diagnosis and treatment on the HPA website is open to question and we have placed a critique of the Lyme borreliosis information on the HPA website on our own website.<sup>(16)</sup> Lyme disease is present across the UK, not just in the New Forest. However, we welcome the new information placed by the HPA since our last letter. As previously stated, this, in our view, does not go nearly far enough. The public need to be made fully aware on a national basis.

*10. By urgently bringing about a programme of research into all aspects of Lyme disease and associated tick-borne diseases.*

"As much is already known about the diagnosis, treatment, and the mode of transmission of Lyme disease and other tick borne diseases, further research is not currently considered as a priority."

Given the widespread dissatisfaction with the reliability of current NHS laboratory tests, there is still much research to do to get these to a position in which they can be regarded as completely reliable in detecting pathogenic borrelial infection. Research into better treatments, so that as many patients as possible can proceed into clinical recovery, clinical cure or symptom alleviation, is also much needed.

We would welcome research into the phenomenon of people who may or may not have a clear history of tick bite and/or EM rash, yet who have symptoms compatible with borrelial infection, who are seronegative by NHS testing and who improve with substantial antibiotic treatment.

Research into all clinical areas is vitally important from a patient-centred point of view. Not to recognise that these measures are necessary appears extremely short sighted.

Ticks themselves have a complex lifecycle and harbour many pathogenic micro-organisms. The interactions between the microbes, the ticks and the hosts are only partially understood. For example, it was discovered relatively recently that immunosuppressive substances found in tick saliva can subdue a human immune response and facilitate infection by *Bb s.l.* genospecies.<sup>(29)</sup>

LDA also notes the great genetic complexity of *B.burgdorferi* genospecies<sup>(21)(22)(23)(24)</sup> and we question whether all relevant information regarding pathogenicity and pathogenic genospecies within this group of bacteria has been discovered. We note the research undertaken by Anda et al. in their investigation of a novel borrelial species.<sup>(30)</sup> In this study the investigators searched for ticks in the whole environment of the people who became ill with what appeared to be a new illness. The all-inclusive methodology resulted in a new *Borrelia* species being discovered. We feel that more research along these lines would be desirable.

Testing is not routinely carried out for the many pathogens known to be carried by ticks, therefore the extent of co-infection by multiple organisms, possibly including new spirochaetes, is unknown. Patients need to be asked in a meaningful way about their observations of tick-bite, or any other bite or possible skin invasion in the period prior to becoming ill. We are aware many will not remember, but that does not mean that useful information cannot be gained from patients.

Short sightedness regarding further studies, both clinical, epidemiological and biological that are needed could be having a dire effect on the health of patients.

“As I have stated, Lyme disease is already acknowledged as the most important vector borne disease in the UK, though its incidence is not high.”

The phrase “incidence is not high” is open to interpretation. The true incidence in the UK is unknown. Reported incidence rates across Europe vary from 16/100,000 in France to 120/100,000 in Slovenia.<sup>(31)</sup> Applying the French figure to the UK would give an incidence close to 10,000 cases each year. Whilst the incidence in the UK may be lower than that in France, we note quoted figures were published in 1998, and, from the HPA's own figures, laboratory-confirmed cases have trebled between 1998 and 2005. What is the HPA's explanation for the lack of increase in their overall estimated figure?

LDA feels that the number of patients who fulfil the clinical picture is certainly high enough to be causing justified public concern. Many cases report very slow, incomplete recovery and severe cases may report non-recovery. This will mean that prevalence is higher than incidence, representing ongoing human suffering and a significant burden of ill health and social care that must be supported from the public purse.

“Finally, your letter does not make clear whether those people contacting your trustees have been tested by the NHS and received negative results for Lyme disease. The most appropriate course of action for anyone who is concerned that they may have the disease is to consult his or her GP about being tested for Lyme disease by the HPA's Lyme Borreliosis Specialist Diagnostic Service.”

LDA is contacted by people with a range of symptoms and histories, and always recommends that people should first consult their GPs. Not everyone who contacts us will have Lyme borreliosis or an associated tick-borne infection. Some have borderline symptoms that make them difficult for a physician to assess. Many have known tick bites and matching symptoms but negative serological tests. Some have known tick bites, matching symptoms, and positive tests, but are still refused diagnosis and adequate treatment. Of those we know who have taken adequate treatment that went beyond symptom resolution, many of these improve markedly or make a clinical recovery. The Department of Health needs to take note of those recoveries that were not predicted by current tests and provide a credible explanation for them.

“It is important to stress that many of the syndromes currently attributed to Lyme disease are not, in fact, due to this infection. It is vital that, where there is concern, proper laboratory testing is undertaken using the Lyme Borreliosis Reference Laboratory, which has foremost expertise in the diagnosis and treatment of this disease and can advise clinicians throughout the UK and internationally.”

The HPA has provided no evidence that Lyme disease is over diagnosed. As stated previously, testing is not reliable enough to rule out a diagnosis. Our experience would indicate that cases of active disease are slipping through the net and not being recognised.

LDA would find it helpful to understand upon what information or advice the Department's confidence that “many of the syndromes currently attributed to Lyme disease are not, in fact, due to this infection” is based?

Lyme disease symptoms can be similar to a number of other conditions. These conditions may be misdiagnosed as Lyme disease, but that also means that Lyme disease may be misdiagnosed as a number of other conditions. In practice, the lack of knowledge about this disease amongst doctors, and the current accepted belief that Lyme is very rare, make it more likely that genuine cases will be missed.

Lyme Disease Action is very concerned by your response of 29<sup>th</sup> March. Instead of putting clinical observation of the patient at the centre of diagnosis and treatment, your response appears to give priority in assessing the situation to the current interpretation of a very complex area of laboratory science that is frequently under review. We note the recoveries being made by patients who have taken adequate treatment that went beyond symptom resolution and who clinically fulfil this diagnosis even without positive serology. We ask what can be learnt from these recoveries to improve clinical outcome for all UK patients in the future? We ask that the Department of Health give these points very serious consideration.

Yours sincerely

Stephanie Woodcock  
Chair  
Lyme Disease Action

#### REFERENCES

For Lyme Disease Action  
Dated 9/5/07  
In response to Caroline Flint  
Dated 29/3/07

(1) Charitable objects of Lyme Disease Action are as follows:-

The relief of persons suffering from Lyme disease, other borrelioses and associated diseases in particular but not exclusively by:

1. Raising awareness of the public at large including conferences, information and support.
2. Scientific and medical education and research in topics related to Lyme disease, other borrelioses and associated diseases provided the useful results of such research must be published.

(2) Collares-Pereira M, Couceiro S, Franca I, Kurtenbach K, Schafer SM, Vitorino L, Goncalves L, Baptista S, Vieira ML, Cunha C.

First isolation of *Borrelia lusitaniae* from a human patient.

J Clin Microbiol. 2004 Mar;42(3):1316-8.

(3) Postic D, Ras NM, Lane RS, Hendson M, Baranton G.

Expanded diversity among Californian borrelia isolates and description of *Borrelia bissettii* sp. nov (formerly *Borellia* group DN127).

J Clin Microbiol. 1998 Dec;36(12):3497-504.

(4) Postic D, Gerniera M, Baranton G.

Multilocus sequence analysis of atypical *Borrelia burgdorferi* sensu lato isolates – Description of *Borrelia californiensis* sp. nov., and genomospecies 1 and 2.

Int J Med Microbiol. 2007 March 17 (E pub ahead of print).

(5) Benach JL, Coleman JL. Overview of spirochetal Infections. In 'Lyme Disease' ed. Coyle

PK. St Louis: Mosby-Year Book Inc., pp61-68. 1993  
and Reik L. Neurological Aspects of North American Lyme Disease. In 'Lyme Disease' ed  
Coyle PK. St Louis: Mosby-Year Book Inc., pp 101-112.

(6) Oksi J, Uksila J, Marjamaki M, Nikoskelainen J, Viljanen MK.  
Antibodies against whole sonicated *Borrelia burgdorferi* spirochetes, 41-kilodalton flagellin, and  
P39 protein in patients with PCR- or culture-proven late Lyme borreliosis.  
J Clin Microbiol. 1995 Sep;33(9):2260-4.

(7) Phillips SE, Mattman LH, Hulinska D, Moayad H.  
A proposal for the reliable culture of *Borrelia burgdorferi* from patients with chronic Lyme  
disease, even from those previously aggressively treated.  
Infection. 1998;26:364-7.

(8) Hunfeld KP, Ruzic-Sabljić E, Norris DE, Kraiczy P, Strle F.  
Risk of culture-confirmed borrelial persistence in patients treated for erythema migrans and  
possible mechanisms of resistance.  
Int J Med Microbiol. 2006 May;296 Suppl 40:233-41.

(9) Klempner MS, Hu LT, Evans J, Schmid CH, Johnson GM, Trevino RP, Norton D, Levy L, Wall  
D, McCall J, Kosinski M, Weinstein A.  
Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history  
of Lyme disease.  
N Engl J Med 2001 Jul12;345(2):85-92.  
NOTE: this is the correct reference, the HPA website reference is incorrect at time of writing.

(10) A detailed criticism of Klempner et al "Two Controlled Trials of Antibiotic Treatment in  
Patients with Persistent Symptoms and a History of Lyme Disease." (Ref 9) can be found at  
[www.ilads.org/position2.html](http://www.ilads.org/position2.html). It is widely accepted that the longer a patient has Lyme  
Borreliosis the more difficult it is to treat. In effect this study was of short term treatment of  
patients with a long duration of illness, and was therefore almost guaranteed to show poor  
results.  
(Peer-reviewed references support this document – enclosed).

(11) Wormser GP, Dattwyler RJ, Shapiro ED, et al.  
The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic  
Anaplasmosis and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of  
America.  
Clinical Infectious Diseases 2006; 43:1089-34.

(12) Johnson RC. Borrelioses. In Topley and Wilson's Principles of Bacteriology, Virology and  
Immunity, 9<sup>th</sup> edition, Volume 'Bacterial Diseases' Chapter 50, section 1 Lyme borreliosis. p  
955-62. 1998.

(13) O'Connell S. Lyme borreliosis.  
Medicine. 2005 May;33:106-8.

(14) Stricker RB, Lautin A.  
The Lyme wars: time to listen.  
Expert Opin Investig Drugs 2003 Oct;12(10):1609-14.

(15) Evans R, Mavin S, Ho-Yen DO.  
Audit of the laboratory diagnosis of Lyme disease in Scotland.  
J Med Microbiol. 2005 Dec;54(Pt 12):1139-41.

(16) <http://www.lymediseaseaction.org.uk/releases/hpa.htm>  
(Peer-reviewed references support this document – enclosed).

(17) Gern L, Estrada-Pena A, Frandsen F, Gray JS, Jaenson TG, Jongejan F, Kahl O, Korenberg  
E, Mehl R, Nuttall PA.

European reservoir hosts of *Borrelia burgdorferi* sensu lato.  
Zentralbl Bakteriologie. 1998 Mar;287(3):196-204.

(18) As described in the Annex to your letter to us of 29<sup>th</sup> March 2007.

(19) [http://www.pasteur.fr/recherche/borrelia/Bb\\_strains\\_alphabetic.html](http://www.pasteur.fr/recherche/borrelia/Bb_strains_alphabetic.html)

(20) Schwan TG, Burgdorfer W, Garon CF.  
Changes in infectivity and plasmid profile of the Lyme disease spirochete, *Borrelia burgdorferi*, as a result of in vitro cultivation.  
Infect Immun. 1988 August; 56(8):1831-36.

(21) Phillips SE, Harris NS, Horowitz R, Johnson L, Stricker RB.  
Lyme disease: scratching the surface.  
Lancet. 2005 Nov 19;366(9499):1771.

(22) Casjens S, Palmer N, van Vugt R, Huang WM, Stevenson B, Rosa P, Lathigra R, Sutton G, Peterson J, Dodson RJ, Haft D, Hickey E, Gwinn M, White O, Fraser CM.  
A bacterial genome in flux: the twelve linear and nine circular extrachromosomal DNAs in an infectious isolate of the Lyme disease spirochete *Borrelia burgdorferi*. Mol Microbiol. 2000;35(3):490-516.

(23) Liang FT, Yan J, Mbow ML, Sviat SL, Gilmore RD, Mamula M, Fikrig E.  
*Borrelia burgdorferi* changes its surface antigenic expression in response to host immune responses. Infect Immun. 2004;72(10):5759-67

(24) Embers ME, Ramamoorthy R, Philipp MT.  
Survival strategies of *Borrelia burgdorferi*, the etiologic agent of Lyme disease. Microbes Infect. 2004;6(3):312-8.

(25) Schlesinger PA, Duray PH, Burke BA, Steere AC, Stillman MT.  
Maternal-Fetal Transmission of the Lyme Disease Spirochete, *Borrelia burgdorferi*.  
Ann Intern Med. 1985 Jul;103(1):67-8.

(26) O'Connell S.  
Lyme disease in the United Kingdom.  
BMJ. 1995 Feb 4;310(6975):303-8.

(27) Schmidt B, Aberer E, Stockenhuber C, Klade H, Breier F, Luger.  
Detection of *Borrelia burgdorferi* DNA by polymerase chain reaction in the urine and breast milk of patients with Lyme borreliosis.  
Diagn Microbiol Infect Dis. 1995;21(3):121-8.

(28) Luger S.  
Lyme disease transmitted by a biting fly.  
N Engl J Med. 1990;322(24):1752.

(29) Hannier S, Liversidge J, Sternberg JM, Bowman AS.  
*Ixodes ricinus* tick salivary gland extract inhibits IL-10 secretion and CD69 expression by mitogen-stimulated murine splenocytes and induces hyporesponsiveness in B lymphocytes  
Parasite Immunology. 2003 Jan;25(1):27-37.

(30) Anda P, Sanchez-Yebra W, del Mar Vitutia M, Perez Pastrana E, Rodriguez I, Miller NS, Backenson PB, Benach JL.  
A new *Borrelia* species isolated from patients with relapsing fever in Spain.  
Lancet. 1996 Jul 20;348(9021):162-5.

(31) Smith R, O'Connell S, Palmer S.  
Lyme Disease Surveillance in England and Wales, 1986-1998.

Emerg Infect Dis. 2000 Jul-Aug;6(4):404-07.

(32) Abstracts of 84 peer-reviewed papers on " Seronegativity in Lyme borreliosis and Other Spirochetal Infections" can be found at the following website:

<http://www.lymeinfo.net/medical/LDSeronegativity.pdf>

Many papers that support reference 6.

(33) Abstracts of 67 peer-reviewed papers on 'Relapse/Persistence of Lyme disease despite antibiotic therapy' can be found at the following website:

<http://www.lymeinfo.net/medical/LDPersist.pdf>

Many papers that support references 7 and 8.