

29th May 2007

Your MP may be interested to view the full response made by Lyme Disease Action to a letter from the Minister for Public Health, Caroline Flint MP, also dated 29th March 2007, which is on LDA's website at the following link: <http://www.lymediseaseaction.org.uk/releases/flint.htm>

Lyme Disease Action's abridged response to a letter from Caroline Flint MP, Minister of State for Public Health, in response to MPs enquiring about Lyme disease on behalf of constituents.

Each paragraph of the Department of Health standard reply to MP's enquiries on Lyme disease is presented below, with the LDA response following *in italics*.

"Thank you for your letter of (date) to (Minister) enclosing correspondence from your constituent (the letter writer) of (location) about Lyme disease. I am replying as the Minister responsible for this policy area.

I would like to reassure (the letter writer) that clinicians in the UK have ready access to the best diagnostic tests available for Lyme disease. NHS diagnostic tests for Lyme disease conform to internationally agreed criteria and the tests are freely available. Though 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."

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 and did not investigate it.

People who have symptoms suggestive of Lyme disease frequently contact LDA. They often report that they are not taken seriously by their GPs. We have heard many accounts of visits to GPs and specialists who admitted they knew little about Lyme disease, yet had dismissed the possibility with minimal investigation.

With regard to the diagnostic tests, "the best" is only a relative judgement. There is a large body of peer-reviewed evidence which shows that the current serology tests are not reliable enough to rule out this diagnosis.⁽¹⁾ In the absence of reliable tests diagnosis must be made on a clinical basis.

LDA knows of many people who meet the clinical definition of Lyme disease, with known tick bites, and EM rashes and other matching symptoms, who are effectively treated with antibiotics, and yet who have negative serology tests. Patients are finding that often reality does not reflect the statement that "Lyme disease is taken very seriously." Patients need an answer as to why this is happening.

"The internationally agreed criteria for diagnostic tests for Lyme disease ensure that correct diagnostic methods are used in each laboratory. These 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. These serological criteria are used by the Health Protection Agency's (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."

*As we note above there is much peer-reviewed work which calls into question all serological testing for Lyme disease.⁽¹⁾ Therefore "internationally agreed" presents a false sense of consensus on a controversial subject. The standard serological test procedure does not detect the bacterium itself, rather antibodies produced by the human immune system. *Borrelia burgdorferi* s.l. are, by far, the most genetically complex bacteria known⁽²⁾⁽³⁾ and have evolved to avoid detection by the immune system of many hosts, including humans. People vary in the immune response their bodies are able to mount.*

Making the current testing procedure the ultimate arbiter of what is correct is unsound in the above circumstances. Indeed, Ms Flint's response itself indicates in her following paragraph that the tests are still being improved. (q.v.)

Ticks can harbour many pathogenic micro-organisms, and more are discovered periodically, yet testing is rarely offered for any other tick-borne pathogens.

Stringency in testing is necessary to some extent to minimise the possibility of false positive results, but there is worldwide concern that current criteria for a positive test are set within too narrow a range, thus potentially excluding many genuine sufferers from diagnosis and treatment.

“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 specialities 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 welcomes the increased work on disease awareness, although we feel that this does not yet go far enough to fully inform the public about Lyme disease.

The advice currently given by the HPA relates to laboratory testing. This is, by definition, scientific advice not clinical advice relating to individual patients. A representative of the HPA’s Lyme Reference Unit has told LDA that they do not give clinical advice. LDA has asked for clarification as to where physicians can gain access to clinical advice about individual patients.

LDA notes that little research has been carried out on the effectiveness of different treatment protocols, and existing research has produced conflicting results.⁽⁴⁾⁽⁵⁾ Under these circumstances evidence-based treatment must be extended to include the experience of Lyme clinicians in administering empirical treatment. We believe that the patient should be fully informed of the breadth of opinion/evidence and supported in making their decision regarding what treatment, if any, they wish to undertake.

“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.”

The HPA and NHS Direct websites provide essentially the same information, although the HPA is more detailed. We support the information on prevention of Lyme disease on the HPA and NHS Direct websites. However, much of the information on diagnosis and treatment is open to question.⁽⁶⁾ Patients also tell us that the verbal information given by NHS Direct is of variable quality and instances of wrong information being given have been reported to LDA. As stated above, we welcome the additional awareness measures, although we feel that this does not yet go far enough.

“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.”

*Lyme Disease Action has never recommended any of the tests referred to. The cornerstone of diagnosis is clinical diagnosis by a knowledgeable doctor. The reason ‘unorthodox’ tests have been developed is the questionable reliability of conventional tests. 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. Sensitivity and specificity vary amongst all types of test, so test results should only be used by trained Lyme clinicians to support a clinical diagnosis, not to supplant it. This highlights the very great need for research into improving testing methods.*

The dangers of long-term courses of antibiotics in this context have been exaggerated. A great number of sufferers are treated with long term antibiotics, with no or minimal adverse effects. The single documented case of death associated with antibiotic treatment for Lyme disease was due not to the antibiotic, but to complications arising from a broken catheter tip.⁽⁷⁾ Large numbers of these catheters are routinely used around the world for intravenous drug delivery. The occasional very rare complication should not be used as a reason to deny treatment.

In the case of Lyme disease the risk from a false positive is giving unnecessary treatment. Serious complications associated with antibiotic treatment are rare and more common but less serious complications can be minimised if basic precautions are taken. A false negative leading to a refusal of treatment may potentially lead to lifelong disability with an extremely unpleasant, unpredictable and often progressive illness. A false negative, therefore, risks a far worse outcome than a false positive.⁽⁸⁾

“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 QRIBb 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 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 have never recommended this or any other serological test. It is strange that such a large portion of this letter should be devoted to a criticism of one particular test available in the USA. There is currently no serological test that is reliable enough to confirm or rule out a diagnosis of Lyme disease with certainty.

Experienced Lyme disease clinicians make clinical diagnoses, which may include results of any tests, but will equally consider the pattern of symptoms, any known tick bites and all other relevant information. This is as recommended by the world authority on infectious disease in the United States, The Centers for Disease Control and Prevention (CDC) who advise the following: “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.”

Validation of the two-stage serology test, (as outlined in the Appendix of the letter of 29/3/07 from Caroline Flint), is problematic as there is no sensitive gold standard test by which other tests can be measured. The HPA Southampton laboratory recommends guidelines published by the Infectious Diseases Society of America (IDSA). These guidelines define Lyme disease in part by positive serology. A test that is part of the definition of an illness cannot be properly validated. Therefore, the only certain claim that the test can make is its ability to detect antibodies matching a limited number of laboratory cultured reference strains.

“I hope this reply is helpful.”

Yours Caroline Flint.

Annex: Testing Criteria for Lyme disease (*Borrelia burgdorferi*)

Serum samples for the detection of antibodies to *B. burgdorferi* should be analysed by a two-test procedure:

- * a sensitive screening test (such as ELISA or IFA). All samples judged to be reactive or equivocal in the screening test should then be confirmed by:
- * a Western blot for antibodies to specific *B. burgdorferi* antigens.

The Western blot should be used only in succession with an ELISA or IFA test. Detailed interpretive criteria for Western blots differ between Europe and the USA, to take into account differences in the geographic distribution of the infecting genospecies.

Lyme Disease Action is very concerned by the above response from the Minister responsible for Public Health, Caroline Flint MP, as it gives priority in assessing the situation to the current interpretation of a very complex area of laboratory science that is frequently under review. We believe that clinical observation of the patient should be at the centre of diagnosis and treatment, and that the current approach leaves many patients inadequately treated or untreated. The Department of Health needs to note the recoveries being made by patients who clinically fulfil this diagnosis and yet test negative, and must ask what can be learnt to improve the clinical outcome for all patients of this type of tick-borne disease in future.

References

1. "Seronegativity in Lyme borreliosis and Other Spirochetal Infections" Abstracts of 84 peer-reviewed papers on *B. burgdorferi s.l.* testing can be found at <http://www.lymeinfo.net/medical/LDSeronegativity.pdf>
2. http://www.pasteur.fr/recherche/borrelia/Bb_strains_alphabetic.html
3. Phillips SE, Harris NS, Horowitz R, Johnson L, Stricker RB. Lyme disease: scratching the surface. *Lancet* 2005 Nov 19;366(9499):1771.
4. Klemperer et al. Two Controlled Trials of Antibiotic Treatment in Patients with Persistent Symptoms and a History of Lyme Disease. *N Engl J Med* 2001;345:85–92 *
5. Wahlberg P, Granlund H, Nyman D, Panelius J, Seppala I. Treatment of late Lyme borreliosis. *J Infect* 1994 Nov;29(3):255-61.
6. Lyme Disease Action "Position statement on HPA information on Lyme Borreliosis"
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7. Patel R, Grogg KL, Edwards WD *et al.* Death from inappropriate therapy for Lyme disease. *Clin Infect Dis* 2000;31:1107-1109.
8. Woodcock S. Lyme Disease Testing. *Lancet Infect Dis* 2006 Mar;6(3):122.

* This study has been widely criticised, see www.ilads.org/position2.html