

NICE in action

We have set up a [page on our website](#) to keep you informed about the NICE guideline. You will find links there to comments about what has already taken place and also what is to come. We have included links to the NICE page itself which holds all the official documents.

LDA attended the scoping workshop in February alongside a number of other patients from different groups. The draft scope has now been issued for consultation and LDA will be submitting a written comment. See our [news item](#) for details of the different ways that you can comment on this.

Running in parallel with the draft scope is recruitment to the guideline committee. This is expected to comprise approximately 10-12 professional members, from various disciplines, and 2-3 lay members. The exact composition will be up to the committee chair and the NICE staff who are supporting the process and who will help with interviews.

NICE recruitment links

[Lay member](#)

[Specialist member](#)

Application deadline April 14th

If you feel your experience of Lyme disease, as either a health professional or a member of the public, would enable you to contribute to this committee, please look at the recruitment links above and consider applying.

If you have any queries about this process, or want to contribute a comment on the scope, then contact us via email to NICE@LymeDiseaseAction.org.uk.

Epidemiology - it's all in the mind

In recent quarterly figures for the number of reported cases of Lyme borreliosis, numbers have been split into "Past" and "Acute". We discussed this with PHE as we strongly felt that the word "past" was misleading and might imply that the infection was past and over. Their rationale was that they can tell early infections from a combination of the test result detail, and clinical information such as onset of illness, EM etc. Anything else was therefore possibly an infection from the past which might not be active infection.

Our argument is that in neither case can you know whether the infection is active. We are glad to see that PHE have responded to our request and are now just reporting **Acute** cases and **All** cases. The figures for positive blood tests for 2015 are available on the [GOV.UK website](#).

This separation is potentially useful as it will enable us all to see how awareness programmes are working. Are patients noticing the rash and linking illness with a tick bite? Are doctors getting better at identifying the early symptoms?

We would hope to edge towards most cases being reported as acute which will be an indication that more cases are getting early treatment.

Chronic LB

What is it about “Chronic Lyme borreliosis” that makes it so hard to discuss and so difficult for some people to acknowledge? In untreated cases, where the diagnosis is confirmed at a later stage, why do people refer to “late complications” rather than chronic infection?

Chronic: persisting for a long time or constantly recurring. Often contrasted with acute.

[Oxford Dictionaries](#).

So let’s be motivated and see what evidence there is that *Borrelia* infection persists for a long time.

“There is nothing complicated about science, and people can understand anything if they’re sufficiently motivated.”

Ben Goldacre 2015

Well, for a start, of the 814 England and Wales cases diagnosed by positive serology in 2015, 254 were considered *not* to be acute. Were they chronic cases? Or, as some may think, just people with other illnesses who happened to have positive Lyme serology as a result of past infection or a cross-reaction to something else? We don’t have the data.

However, even just looking at UK case reports, we have -

- A man with recurrent meningitis, of which the paper¹ states “Our patient had two symptom free periods of 16 and seven months, respectively, between three episodes of acute meningitis. Serological tests were done only during the last admission. Although we cannot exclude the possibility of reinfection, which is known to occur in Lyme disease, we believe that these episodes were recurrences. ”
- A case of heart block. ² “The negative IgM direct immunofluorescence would suggest that the infection was beyond the initial acute phase.”
- A child with a 4-6 month *Borrelia* lymphocytoma - verified by biopsy and serology.³
- 3 people with Lyme carditis of more than 3 years duration.⁴
- A naval surgeon whose Lyme disease was undiagnosed for 10 years.⁵
- A retired accountant finally diagnosed 5 months after the tick bite. ⁶
- A lady with a 15 month history of illness. ⁷

Looking elsewhere in Europe, the European Federation of Neurological Societies defines late Lyme neuroborreliosis as signs and symptoms lasting more than 6 months and states “Late neurological manifestations are also entitled “chronic neuroborreliosis”.

In the study by Strle et al of patients with *Borrelia* cultivated from spinal fluid, 76% had a duration of symptoms more than 6 months (range up to 6 years).⁸

Evidence shows that Lyme borreliosis can fulfil the definition and become chronic.

References

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3. Keh SM, Vestey JP, Ho-Yen D, et al. Ear presentation of Lyme borreliosis in a child. *J Laryngol Otol* 2012; 126: 1176–8.
4. Langhorne P, Balogum M, Dunn F. Unexpected cardiac abnormalities in Lyme disease. *Br Med J* 1993; 307: 736–737.
5. Wilson CJF. My years with Lyme disease. *BMJ* 1999; 319: 649–649.
6. Williams F, Ginsberg L, Brenner R, et al. An exotic cause for confusion in the garden. *Pract Neurol* 2008; 8: 256–9.
7. Huda S, Afzal M, Tyne H, et al. POC26 A protracted course of Neuroborreliosis, the debate continues. *J Neurol Neurosurg Psychiatry* 2010; 81: e41–e41.
8. Strle F, Ruzić-Sabljić E, Cimperman J, et al. Comparison of findings for patients with *Borrelia garinii* and *Borrelia afzelii* isolated from cerebrospinal fluid. *Clin Infect Dis* 2006; 43: 704–10.

Persisting LB following treatment

So chronic LB exists - can it persist following treatment? What part does it play in the broader concept of Lyme disease?

Monica Embers, a USA researcher who is working on persistence, says

“While we have shown that intact *Borrelia* spirochetes can persist following a standard duration of treatment following disseminated infection, we do not know if those spirochetes linger and cause disease or if they are eventually cleared.”

This uncertainty underpins one of the key questions raised by our James Lind Alliance PSP which documented known uncertainties in diagnosis and treatment of Lyme disease:

Are continuing symptoms following conventional recommended treatment due to continued infection, an immune response or other process?

At a scientific level there is proof of concept for each of these issues and the fact that *Borrelia* is known to cause immune problems should not negate the evidence on persistence, but it does add a further level of complexity. This is most relevant on an individual patient basis, where it may not be possible to be certain about the underlying cause of symptoms and what it is that needs treating.

In some cases the answer is clear because a patient has an obvious relapse when ceasing antibiotics and a very clear recovery when starting again followed by an eventual complete recovery. This was documented by a retrospective UK study¹ which found “three patients had evidence of persistent infection after treatment and two required intravenous therapy”.

So clearly part of the answer is “Yes, infection can persist beyond the first course of treatment” and this has been demonstrated in humans, not just monkeys. That does still leave those cases with a less clear cut response to treatment and a less clear cut relapse. In the absence of tests that can distinguish active from past infection, and assess autoimmune problems, patients have to rely on their doctors doing what they would do in any other condition where there is uncertainty: use clinical judgement.

It may not be possible to be sure about the main underlying cause of symptoms, but late-stage Lyme borreliosis is treatable with antibiotics. The consequences for the patient of possible untreated Lyme borreliosis may be further chronic illness with a profoundly negative effect on their quality of life and cost to healthcare services.

This highlights of course one of the most important of the uncertainties in treatment uncovered by the JLA project:

What is the best treatment for children and adults presenting with late Lyme disease of any manifestation? To include consideration of drug(s), dose, duration.

A simple acknowledgement of this key uncertainty would undoubtedly improve patient care.

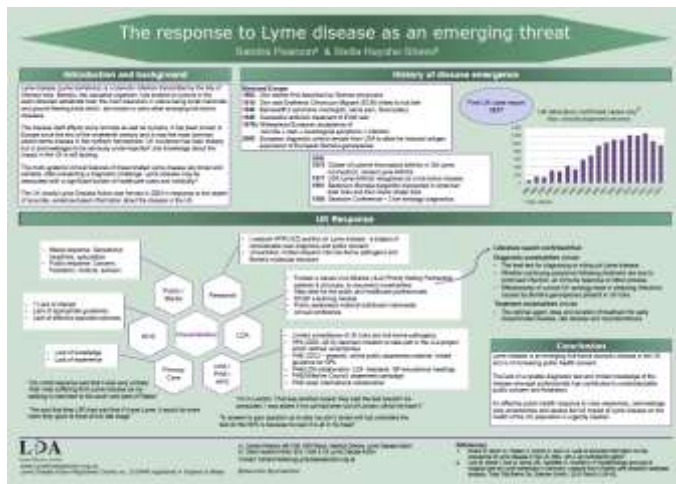
Enrolling every UK patient treated for Lyme disease into a study with long term follow up, using patient based outcomes, would go a long way towards finding answers to inform doctors’ and patients’ decisions.

1. Dillon R, O’Connell S, Wright S. Lyme disease in the U.K.: clinical and laboratory features and response to treatment. *Clin Med* 2010; 10: 454–7.

LDA presenting posters

LDA has presented 2 posters at scientific conferences in the last couple of months, to some interesting receptions. Click on the posters to read them together with discussions of the conferences.

NIHR Health Protection Research Unit in Emerging and Zoonotic Infections Annual Conference: The response to Ebola and other emerging threats



The HPRU has a substantial sum of money to perform research into emerging and zoonotic infections and this was [an interesting conference](#).

We were able to talk to PhD students working in this area, one whose Lyme disease project is underway, and one who has only just started.

The first part of all these projects is a review of the current literature and getting up to speed on who has published what and where the unknowns are.

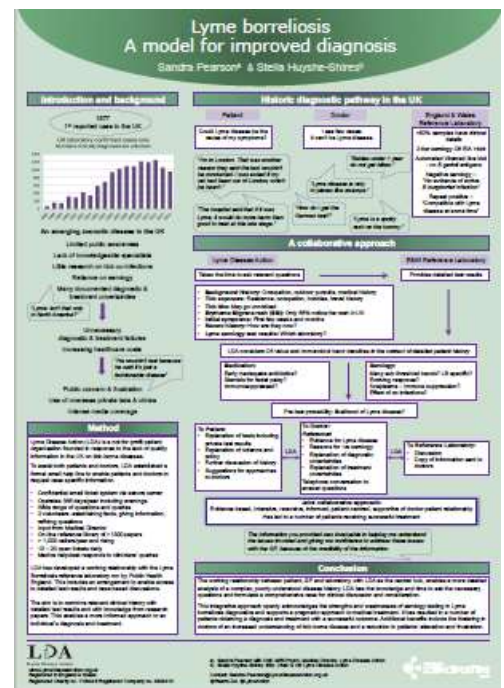
The second conference was NordTick 2016: Ticks and tick-borne diseases

The Scandinavian countries have more experience with tick-borne diseases as their tick populations have a much higher rate of infection than ours in the UK. Sweden, for example, has an incidence of Lyme disease in ticks of about 20%, whereas the UK incidence sits around 6%. The Nordic countries all have similar problems to those we have in the UK.

Our poster for this conference describes the LDA helpdesk and the interaction we have as a hub between the Lyme borreliosis reference laboratory at PHE Porton, and patients and doctors.

This help desk, staffed by three unpaid volunteers, has now been in operation in its current form for two and a half years with cases steadily rising. It has been instrumental in facilitating successful treatment for an increasing number of patients through a careful and thorough examination of patient history and detailed test results. We ask the questions that doctors unfamiliar with tick-borne diseases do not know to ask; we join detailed clinical history with detailed test results.

The Scottish Reference laboratory at Raigmore is also keen to interact with LDA. We will need more resources, and some NHS commitment, to roll this service out more widely.



The PLEASE trial reports

The clue is in the title - **Persistent Lyme Empiric Antibiotic Study Europe**. The trial participants had symptoms of proven or possible persistent Lyme disease **despite previous treatment**.

The participants were all, judging by baseline characteristics, significantly unwell and some had had symptoms for more than 5 years. In the trial they were given 2 weeks IV ceftriaxone - note that this is on top of treatment they had already had and 17% had already had IV. After this new course of IV they then had 12 weeks of either

- doxycycline
- clarithromycin plus hydroxychloroquine
- placebo

Result? All three groups improved, but no group did statistically better than any other. So in other words, **a repeat course of antibiotics appears to make a difference**. Most people appear not to have read the paper, and are only reporting "Long term treatment doesn't work"; [even the journal itself!](#) It is surprising how blind people can be when they don't want to see.

The patients were still not completely recovered at the 50 week follow up, but they were better than they had been. So perhaps it is the repeating of a course of antibiotics that makes a difference, rather than the length of a single course.

There are some interesting points about this study, and the questions it raises, and we shall provide a further commentary on our website. Meanwhile, take the media reports with a pinch of salt, as the analysis and comment is not all over yet!

Meanwhile, UK research....

Huddersfield University, as you will know if you have attended [our conferences](#), are conducting research into the outer surface proteins of Borrelia. Here are two undergraduates, Sophie and Abi, presenting a poster of their work at The British Conference of Undergraduate Research: Characterisation of an OmpA-like protein of Borrelia afzelii.



Bristol University - [The Big Tick Project](#), screening ticks collected from pets for pathogens, some of them being [screened for Babesia](#) by **Exeter University**. **The Thomas Hardy School**, Dorset is screening Dorset ticks for Borrelia, with Exeter University help.

Bath University - Research on ticks; **Salford University** - More research on ticks, see our [2014 conference](#); **Public Health England** - Lots of work on ticks and, with Liverpool, the [Tick Activity Project](#) (lots of volunteers contributing ticks) which has just received some funding to screen collected ticks for Borrelia.

Liverpool University, the Health Protection Research Unit - Two PHD projects: one looking at the diagnostic potential of biomarkers in early LB, the other at epidemiology of LB, and finally, **Leicester University** - possible [phage therapy](#) for LB.

Here's a question: How many of these can you match to the [top 10 priorities for research](#) that we identified in 2012?