ANSWERS FROM PHE TO OUR GROUP QUESTIONS ARE IN RED ITALLICS UNDER THE QUESTIONS

MESSAGE FROM TIM BROOKS:

ATTACHED ARE THE ANSWERS TO YOUR QUESTIONS. APOLOGIES FOR THE DELAY BUT IT HAS TAKEN A CONSIDERABLE AMOUNT OF TIME TO DO THIS.

TIM BROOKS
HEAD OF CLINICAL SERVICES, RIPL

****

WE HAVE PERMISSION FROM DR TIM BROOKS TO SHARE THE ANSWERS ON THE LYME DISEASE UK WEBSITE.

PATIENT QUESTIONS FOR PHE LYME CONFERENCE 9th OCTOBER

COLLECTED FROM A UK LYME DISEASE SUPPORT GROUP

THESE ARE NOT IN ORDER OF IMPORTANCE

(If these cannot all be answered on the day of the conference, written answers at a later date would be much appreciated)

MOTHER/BABY TRANSMISSION OF LYME BORRELIOSIS

1. Dr Wilske, who has been frequently quoted as an authority by HPA, confirmed the findings of Dr Alan Macdonald that Lyme borreliosis can be transmitted from mother to the unborn child, with fatal consequences. What information, advice and treatment will the new clinic give specifically to women with tick-borne infections who are or might become pregnant?

2. What information is given by PHE to obstetricians, paediatricians, and to coroners who may be involved in cases of unexplained sudden foetal death regarding maternal-foetal transmission and congenital Lyme? Is this information publicly available?

3. Given the fact that paediatricians in the US and other countries on BOTH sides of the controversy accept that children are one of the most at-risk categories for acquiring Lyme, how does PHE account for the fact that this is not reflected in the published British statistics on age breakdown for Lyme?

4. Given the fact that the Department of Health has admitted Lyme can be a trigger of M.E./CFS, and that this condition is the biggest single cause of school absence in children, what special efforts are being made to make parents and teachers aware of Lyme and to detect it in children?

The clinic aims to see individual patients who have been referred for investigation and management of symptoms associated with Lyme disease or other causes at the request of their general practitioner or other specialist physicians. Individuals will be advised according to their needs and condition. The clinic does not provide generic advice for a

population or section of the population, and this is not the responsibility of an individual clinic. Women with acute Lyme disease in pregnancy should be treated, and follow up arranged according to their needs. General advice on preventing tick bites is freely available from many sources. Advice for medical practitioners is available from RIPL physicians.

PHE does not provide specific advice on post mortem examinations for unexplained foetal death. NHS pathologists and others involved in these enquiries all have extensive training and professional accreditation with revalidation in their subject areas, covering a wide range of causes of neonatal problems, and are expected to investigate cases according to the presentation and needs of each individual occurrence.

The British statistics are based on laboratory reported cases of Lyme disease. Cases which are diagnosed clinically are not recorded if no laboratory tests are performed. Inevitably this leads to a selection bias based on the type of presenting symptom and the willingness of physicians and patients to subject a child to a blood test.

There are no special efforts to make teachers as a separate group aware of Lyme disease, or the vast majority of other infectious diseases. Teachers are trained to note children with potential health problems, and would normally suggest that the child was referred for medical advice.

SAFETY OF THE BLOOD SUPPLY

5. Does PHE consider it perfectly safe for a person who has had Lyme disease in the past, or has it in the present, to donate blood, if he/she has no other contraindications?

The Blood Transfusion service advises all patients with active infectious diseases not to give blood, including whilst they are being treated and for a period afterwards. Resolved infectious diseases in healthy people are not a barrier to donation.

COINFECTIONS

6. Why is no further consideration given to the possibility of tick-borne co-infections in patients who test negative for these at regional labs, given that the multiplicity of strains and the fact current tests are only able to detect a fraction of these pathogens?

A wide range of tests for tick-borne infections is available to the NHS through local laboratories and the service offered by RIPL, other PHE laboratories and associated laboratories in NHS centres. These cover everything from Crimean Congo Haemorrhagic Fever to Q Fever. Tests are selected according to the presentation of the patient, and the likely exposure history by the referring physician. If clinical details are provided that suggest another infection is involved, RIPL automatically includes relevant tests when indicated.

7. Given that the CDC has admitted it has no test capable of ensuring the blood supply is safe as far as Babesiosis is concerned, why are UK patients reporting tick bite and

babesiosis-like symptoms told this disease has been ruled out?

Who is giving whom this response, and in what context?

8. Does PHE accept that antibodies will be particularly difficult to detect in the case of intracellular co-infections and in those that actually target cells of the immune system?

NO!!!! Every viral infection raises antibody responses, and HIV, which actively invades the CD4 T cells, is diagnosed by antibody tests. Obligate intracellular bacterial pathogens such as Rickettsia and Coxiella are diagnosed by serology (antibody tests), as are facultative intracellular infections ranging from Brucellosis to melioidosis. As shown in the presentations at our open day, intracellular processing of bacteria is a key part of the adaptive immune response whatever the agent involved. Details of the immune system are reviewed in most basic microbiology and immunology textbooks.

9. What type of information does PHE provide to doctors regarding the fact that co-infections can seriously worsen Lyme disease and significantly complicate the picture in terms of diagnosis and treatment? Is this information available publicly, and if so, where?

See answers above. RIPL staff will discuss individual cases with physicians, and infectious disease consultants are trained in the diagnosis and management of a vast range of infectious diseases.

REGARDING TESTING FOR BORRELIOSIS AT THE REFERENCE LABORATORY AT RIPL

10. What percentage of Western Blots are positive at the RIPL Porton Down?

37% satisfy all criteria for positivity

11. What percentage of positive or equivocal first-tier tests have been followed by a positive Western Blot?

We have not collected the data in this way as it would require a dedicated code to be created to obtain the information. We review every case on the balance and weight of evidence and recommend treatment or follow up on this basis so we do not necessarily insist on very strict criteria for a positive blot to be met in every case. This was covered in the presentations at the conference (q.v.)

12. How many difficult to diagnose cases of Lyme disease have been confirmed by culture? How many by PCR? What are the figures for the past year, the past 5 years and the past 10 years?

We do not have this information. Relatively few cases in England have been referred for either culture or PCR, and RIPL started a PCR service formally in July 2013 when Southampton ceased offering that service. There have been 2 PCR positives in the last fortnight on skin biopsies, suggesting that this can be a useful procedure in appropriate cases if clinicians wish to use it.

13. Which species/strains of borrelia have been found to be the most prevalent in England and Wales according to PHE's findings over the last year, 5 years, and 10 years?

No systematic studies of species distribution have been made on a regular basis. The available information is that B. garinii is the most common infection, followed by B. afzelii

with B. burgdorferi ss making up only 10% or so of cases. The available information is reviewed in the presentations.

14. Given that Borrelia are notorious for the genetic variability of their antigens between strains, and the fact that patients negative on antibody tests have subsequently been found positive by PCR or culture methods, why is PHE continuing HPA's policy of informing doctors that Lyme Disease is ruled out in any antibody seronegative patient who does not recall an EM rash and is not in the immediate post-tick bite period?

RIPL clinicians review each case on the evidence available as discussed above and as shown in the Open Day presentations.

15. The new blood culture test developed by Sapi et al has shown 94% sensitivity in CDC-positive patients, and has also been successful at culturing Borrelia from the blood of many chronic Lyme patients who tested negative by all other methods. Given that the CDC's allegations of invalid results due to lab contamination have now been shown to be false, as the alleged contaminants were 200 miles away from the lab in question, will PHE now consider adopting this gold standard method for UK patients, and if not, why not?

Sapi's test takes up to 16 weeks to give a positive, which is of marginal value in acute diagnostics. The review of his method (not done by CDC) demonstrated that his isolates were nearly all genetically identical with the control strains, which would be a remarkable finding in clinical isolates. Consequently the authors suggested more validation was needed as the probability of contamination was very high. This does not equate to a "Gold Standard". RIPL is planning to evaluate a number of methods of detecting the organism as detailed in the presentations.

16. What published peer-reviewed studies have shown the sensitivity of the C6 ELISA in use at Porton for detecting Lyme in Borrelia burgdorferi sensu lato species other than Bb sensu stricto, garinii or afzelii, given that it has now been established that species such as Borrelia valaisiana, B. bissettii, B. lusitaniae, B. spielmanii and B. bavariensis can also cause disease and have been isolated from European Lyme patients?

No-one has studied C6 across the full range of Borrelia species, not least because very, very few cases have actually been reported of other infections much less sufficient to perform a study. The structure of Borrelia spp. is remarkably similar across the species and BmpA, VlsE and OspC amongst other surface proteins are present in African Borrelia. Some patients with fever from Africa are positive in the C6 test and on some bands in Lyme blots as you might expect. C6 is a conserved section of the protein and we are conducting bioinformatics analysis to see how far this moiety is represented in other Borrelia.

17. Given that Dr Allen Steere, (in Liang et al 1999), reported that the C6 ELISA detected only 62% of "post-treatment Lyme" patients who had continuing symptoms in the US, what evidence does PHE have that it would perform any better on similar patients in Britain?

See our presentations on the clinical trials we need to undertake to study all aspects of Lyme disease and its serology. There have also been considerable advances in the ELISA technology since Steere's original publication and its sensitivity is better in later versions of the test. As above, we use all available information in reporting our results.

18. Given that the Lyme bacterium has been repeatedly detected by PCR and culture from tissues of patients who were seronegative by CDC two-tier criteria, what peer-reviewed evidence exists to indicate that the C6 ELISA would be better at detecting patients negative by such criteria who nevertheless have Lyme infection?

Since the organism as demonstrated by PCR or culture has to be present in the body for long enough to firstly express its VlsE antigen, and secondly for an immune response to appear it is clear that as in any other infection, the organism is detectable before the antibody response, and as the antibody response with the other components of the immune system controls the pathogen, the organism disappears. If the infection never progresses to the stage where VlsE is expressed, antibodies to C6 will not appear. For the whole realm of infectious disease, we believe in looking for both antigen (pathogen) and antibody, and apply this to all the diseases we deal with, depending on the clinical condition of the patient and the probable stage of the disease. However, the C6 test is positive in a number of patients who do not satisfy the full CDC criteria, and we usually assess these individually based on their symptoms and the full range of bands and responses.

19. As Dr Steere, and the Immunetics lab that makes the C6 ELISA, both agree that it has 99% specificity, and as the CDC and NIH are considering introducing it in the US as a standalone, one-tier test, why does PHE still maintain that patients who test positive must still pass the second hurdle of the Immunoblot?

See above. We do not always insist on this if other evidence of infection is available or credible.

20. Would PHE care to comment on the research findings which show that reactivity to the C6 ELISA wanes "post-treatment". And yet treated Lyme patients who continue to have symptoms react much more strongly against a different part of the VisE molecule, not assayed by the C6 ELISA, than treated patients who are well?

See our presentations which expand on this question. C6 can be used as a marker of resolving infection as the level falls in many treated patients. However, around 50% of C6 positive people have no VlsE band in their blot tests, reflecting the various forms of VlsE that are expressed by Borrelia at different times. We are very interested in the work done by Wormser's group on the different VlsE responses between individuals and are actively exploring how to increase the range of antigenic variants we seek, as well as to correlate the response to different epitopes to strain type, clinical outcome and the possible implications or on-going symptoms. This argues for continuing to run multiple assays.

21. Given that it is now known that Borrelia miyamotoi, which is not part of the Bb sensu lato group at all, can nevertheless cause serious Lyme-like illness, what published peer-reviewed evidence exists to show that the C6 ELISA is capable of detecting Borreliae that are not part of the sensu lato group?

No-one has studied C6 across the full range of Borrelia species, not least because very, very few cases have actually been reported of other infections much less sufficient to perform a study. The structure of Borrelia spp. is remarkably similar across the species and BmpA, VlsE and OspC amongst other surface proteins are present in African Borrelia. Some patients with fever from Africa are positive in the C6 test and on some bands in Lyme blots as you might expect. C6 is a conserved section of the protein and we are conducting bioinformatics analysis to see how far this moiety is represented in other Borrelia.

22. Re: the Virastripe Immunoblot:

a) According to the manufacturers, Virastripe Immunoblot, used as the second tier of the testing protocol at Porton, contains several natural antigens, none of which are derived from Borrelia garinii. As garinii is the species most known to be associated with Neuroborreliosis, which is the main manifestation of Lyme in Europe, what is the justification for this?

Firstly, the test was extensively validated in European samples and detects a wide range of infections from all 3 common species. Secondly, if you follow through the detailed references, DbpA proteins are derived from B. garinii, and other proteins are found in very similar forms in all species.

b) Leaving aside the synthetic VlsE antigen (whose sensitivity is known to be poor in "post-treatment Lyme"), what peer-reviewed studies indicate that the antigens on the Virastripe blot are sufficient for detecting Bb sensu lato species other than Bb sensu stricto and B afzelii, from which they are derived?

As above

c) As Borrelia miyamotoi, which is not in the Bb sensu lato group altogether, is now proven to cause serious Lyme-like illness, what peer-reviewed evidence exists to show that Virastripe blot can detect Borrelia which are not part of the sensu lato group?

The structure of Borrelia spp. is remarkably similar across the species and BmpA, VlsE and OspC amongst other surface proteins are present in African Borrelia. Some patients with fever from Africa are positive in some bands in Lyme blots as you might expect.

DR DRYDEN, THE NEW LYME CLINIC & PHE

We understand that Dr Dryden has treated hundreds of patients with borreliosis with no treatment failures.

23. How do you define treatment success in borreliosis and what measures are used to validate that the infection has been eradicated and the patient cured? (e.g.: blood tests, SF-36, CFQ scores, return to work, study, sports etc.)

I believe there are two categories of disease - Lyme disease defined as objective clinical symptoms with positive serology and CAN (chronic arthropod borne neuropathy). The former get better with short course antibiotics and generally have no further symptoms. The latter have an illness whose aetiology is poorly understood and who respond poorly to any current treatments. It is the CAN group that require, with patient support and involvement, a clear case definition and agreement about what a clinic can offer.

24. For how long has Dr Dryden followed up his borreliosis patients in the past? How long will he follow the course of recovery or relapse in cases that will now present at the new Lyme clinic, and what form will the follow-up take?

I am happy to follow up CAN patients for as long as necessary. The Lyme patients I have seen (>500) get better with short course antibiotics and generally have no further symptoms. They only require follow up for a month or two, although I have seen many of our local patients for years afterwards and they remain entirely well. We need to agree how we offer patients diagnostic testing (I think we should look for unknown pathogens and

other strains of known pathogens using RIPL technology), how we monitor patients, how we measure improvement or not, and how we investigate potential treatments

25. Given that borreliosis can result in tertiary illness occurring many years after an initial infection with borrelia, how many of Dr Dryden's previous patients have subsequently relapsed or developed health problems that could be related to their infection?

No patients that I have seen who have had clear cut seropositivity and have been treated according to current guidelines with short course antibiotics have subsequently relapsed.

26. We know from published data in the US that many Lyme patients had a previous d diagnosis of ME/CFS, fibromyalgia or indeed psychosomatic disorders. Who is culpable, in medico-legal terms, for the enormous damage inflicted on a patient given one of these labels, when in fact they have an ongoing Borrelia infection?

I don't know the answer to this question and I would be grateful for support in identifying the clinical criteria that that make up these chronic illnesses. We need a case definition. The cases CAN seen in the clinic so far have a number of infective insults which could have precipitated their condition. A few of them may be due to ongoing Borrelia infection, and we need to find a way to prove that this is the case. Blood culture using the Sapi method may be a way forward and PCR as well as the novel RIPL techniques. Some patients with CAN are likely to be found to have other infections or unusual strains.

27. What precautions are being taken now, or planned for the future, to prevent delayed diagnosis or misdiagnosis? Will there be a proactive medical education programme to inform doctors about vector-borne diseases in the UK? Will there be a definite statement advising all doctors that the serology tests are far from perfect, and that the GPs and consultants in the UK must become better informed about vector-borne diseases, so that they are able to make clinical diagnoses without relying totally on serology?

We will be developing updated Lyme guidance with PHE and patient involvement. As we do more work around CAN we will all be in a better position to publish our findings in peer reviewed journals, present at conferences and educate the public and the medical profession.

28. Many UK borreliosis patients are aware that the previous Lyme expert in the UK, Dr Sue O'Connell, informed patients' GPs that they did not have borreliosis because their laboratory tests were negative. Will Dr Dryden disassociate himself from the practice of HPA and RIPL staff and others misinforming doctors about the reliability of tests and diagnosis?

I am working closely with PHE and RIPL, as well as patient advocacy groups to improve case definition and develop diagnostic methods.

29. Are there any plans to open clinics in other regions?

I have run an ad hoc clinic for many years within the NHS. I have asked my Trust to negotiate with the DH and PHE to fund the Lyme clinic in Winchester. At present this is far from secure financially and if the funding is not available, my Trust will insist that I do my regular microbiology and infection specialist role. If and when this clinic is up and running securely, we can consider clinics elsewhere.

30. How many patients are there now on the waiting list for the Winchester NHS Lyme clinic?

There has been huge demand since publicity from LDA. We are currently booking patients for Jan 2014.

31. How many Lyme patients are on the waiting list for the private clinic of Dr Dryden at Winchester?

I do not routinely run a private clinic for Lyme.

32. How will Dr Dryden and his colleagues at the Winchester clinic manage to consult with patients who are too ill to travel, or who cannot afford to travel to the clinic?

We plan to develop a diagnostic range of tests. Samples could be collected locally and sent by the local lab to RIPL. We will also be developing a patient symptom questionnaire and advice.

33. What advice will Dr Dryden give to Lyme patients about future blood and organ donation?

There is currently no concern from the BTS and organ donation teams about Lyme disease. Dr Drydens advice is that blood and organ donation can proceed in patients who have had Lyme disease.

EPIDEMIOLOGY

34. PHE reports an annual Lyme incidence of 1.73 per 100,000 in England and Wales, and has stated its belief that the maximum possible cases, including those diagnosed on EM rashes in GP clinics, could not exceed 3,000, yet our neighbour Holland, with equivalent flora, fauna and ticks to us, reported an incidence of over 100 per 100,000 based on EM rashes alone. How do you account for this discrepancy, given that birds migrating from the Continent are well known to be reservoirs of Borrelia and/or carry Lyme-infected ticks?

I do not know who made this statement on PHE's behalf, if any such statement was made in this form, but all infectious diseases we deal with have a significant number of unreported cases and an even larger number of subclinical cases so there may be significantly more Lyme disease than the raw numbers from laboratory diagnoses suggest. Birds, ticks, Borrelia and many other organisms migrate across countries and spread diseases. The outcome of this process depends on local ecology of vectors, reservoirs and human activities and is not consistent from region to region, let alone country to country.

35. In the light of the CDC suddenly revising the official US incidence from 30,000 to 300,000 cases per year, a tenfold increase, will PHE now investigate to see if it has been making errors of a similar scale?

See above. All infectious diseases we deal with have a significant number of unreported cases and an even larger number of subclinical cases so there may be significantly more

Lyme disease than the raw numbers from laboratory diagnoses suggest. Birds, ticks, Borrelia and many other organisms migrate across countries and spread diseases. The outcome of this process depends on local ecology of vectors, reservoirs and human activities and is not consistent from region to region, let alone country to country. Our presentations and those from Scotland and Wales, make it clear that the problem is greater than the cases reported solely from laboratories.

36. As most British Lyme is acquired in this country, not abroad, and as Lyme is not a notifiable disease in most of the UK, so the prevalence is unknown, what is the justification for consigning it to a lab for "Rare and Imported Pathogens"?

RIPL covers a wide range of disease, especially zoonoses and vector-borne diseases, which fits neatly with Lyme disease, as well as giving access to a much wider panel of diagnostic tests for related illnesses. The laboratory has a dedicated assay development group, and the clinicians are experienced in dealing with complex infections, which gives us the capability to actually improve Lyme diagnostics, and to re-evaluate the dogma that has surrounded this disease for a decade.

MEDICAL ETHICS AND PUBLIC ACCOUNTABILITY

37. Recent disclosures in answers to Freedom of Information requests have shocked many UK Lyme patients and the public in general. We learned that Dr Sue O'Connell, former head of the borreliosis Reference Laboratory in Southampton, collaborated with others in an apparent attempt to force the views of the Infectious Disease Society of America (IDSA) onto UK patients and doctors and to suppress alternative views.
http://www.poughkeepsiejournal.com/Interactive/lyme_ties/mcsweegan.pdf

Were Dr Dryden, Dr Brooks, Dr Miller or any other NHS/PHE/HPA/RIPL staff, members of the group that Dr O'Connell refers to and have they been or are they in contact with any members of that group?

Neither Dr Dryden nor Dr Brooks had heard of this group until informed of its existence by LDA. Dr O'Connell had no influence in the laboratory service offered by RIPL, and the assays we use are not based on her practice.

THE LYME VACCINE

38. Do the HPA/PHE or Dr Dryden believe a vaccine is necessary and if so, why?

Vaccines have been available in the past, and demonstrated good efficacy which would justify their use. The vaccine was withdrawn for commercial reasons by its manufacturer some years ago.

39. Have the HPA/PHE or staff in those organizations or Dr Dryden or Dr Brooks been contacted or communicated with others about the vaccine and if so, with whom and what was the nature of the communication?

We have had no contact or communication regarding Lyme Disease vaccines, although

someone once sent a news article review on the withdrawal of the vaccine.

ADVANCES IN BIOMEDICAL RESEARCH

40. As recent papers by Berndtson (2013), Sapi's discovery of Borrelia biofilms (2012) and Embers' study of persisting Lyme in rhesus macaques (2012) provide robust evidence of chronic Lyme infection despite antibiotic treatment, how does PHE justify its continued denial of chronic Lyme, and its policy of telling doctors and insurance companies that chronic Lyme does not exist?

The immune evasion mechanics of Borrelia were discussed in detail in the presentations given in our conference. We also discussed the persistence of symptoms, and the possible mechanism for this including untreated or inadequately treated disease as well as the relatively frequent cases of re-infection. Sapi's paper refers to in vitro *studies of biofilms which does not reflect the conditions* in vivo*, whilst Embers study demonstrates low level of persistence of spirochaetes in a an arboreal macaque. Even if humans responded in the same way (and closely related macaques have very different susceptibilities to diseases such as melioidosis and plague depending on their natural habitat), the finding of isolated organisms does not necessarily indicate that they are causing a problem. This is an area which needs more detailed research in man and one which we may obtain some data on through clinical studies in the future.*

41. Given that fact that Borrelia has been recovered from the autopsied brains of Alzheimer's victims, what efforts are being made by PHE to investigate this serious connection, especially as there are hundreds of thousands of people with Alzheimer's in Britain, and the numbers growing exponentially?

Alzheimer's disease and its causes are being actively studied by a number of groups in the UK and elsewhere.

42. Given that neuroborreliosis can present with symptoms and even an MRI picture identical to MS, what efforts will be made to alert doctors to this, so that patients with Borreliosis do not end up treated with ineffective and potentially harmful drugs intended for MS, and suffer a likely death from the progression of their untreated neurological infection?

NHS neurologists are already aware of the differential diagnosis of MS and investigate cases accordingly, including for borreliosis when appropriate. The diagnosis of all these conditions is based upon a combination of clinical information, laboratory investigations, imaging and other physical tests. The investigation of neuroborreliosis is a topic within the guidelines planned for the management of Lyme Disease.

43. In view of the unreliability of current testing, will SPECT scans be used as part of the diagnostic work-up for assessing neuroborreliosis in Lyme patients?

Imaging systems of all types are used in diagnosing any medical condition when appropriate.

44. ILADS has addressed the failings of studies such as the Klempner trial (2001), which purported to show that long-term antibiotics are of no benefit in Lyme, or that chronic Lyme does not exist. Will PHE be prepared to respond specifically to the many criticisms they

raised of these studies, rather than issue blanket condemnations of anyone with an alternative view, as exemplified by the Duerden document on the HPA/PHE website?

PHE will be rewriting the website pages over the coming months and intend to produce a UK set of guidelines on the management of Lyme disease and related conditions based on the presently available evidence.

45. Will any research aims of the Winchester clinic and of PHE be published? If so, where?

The research aspirations of RIPL are described in several of the presentations published from the Open Day. All of these are dependent on obtaining funding in competition, and that in turn depends on calls for proposals being issued by funding bodies in the area of Lyme or related diseases.

MISSED CASES OF LYME DISEASE

46. Given that it is extremely frequent for Lyme patients to have a previous misdiagnosis of fibromyalgia, what efforts will be made to alert doctors to this risk, leading to neglect and worsening of their Lyme infection?

47. Given that many Lyme patients had previous misdiagnoses of psychosomatic illness, what efforts will be made to alert doctors to this risk, leading to a serious infection going untreated, potential use of inappropriate drugs, and a massive social stigma which may engender relationship breakdown/divorce, abandonment by friends and family, ostracism by neighbours/employers/colleagues/classmates, and ultimate suicide?

48. Given that children with Lyme disease have been misdiagnosed with psychosomatic illness, or falsely cast as victims of parental abuse (see Sherr et al http://www.ncbi.nlm.nih.gov/pubmed/15925450), what efforts will be made to ensure that children with Lyme receive correct diagnosis and do not end up with untreated, worsening illness, or be forcibly taken into care and their parents imprisoned?

49. Given that there are documented cases of Lyme patients being wrongly diagnosed with the horrific disease MND/ALS , for which there is no cure and which is generally rapidly fatal, what efforts are being made to ensure that a treatable Borrelia infection is considered in the differential diagnosis of this condition?

50. Given that the Department of Health has acknowledged that Lyme is a potential trigger for ME/CFS, what efforts are being made to ensure that doctors consider Lyme in the differential before issuing this diagnosis, as an error could result in worsening of the infection, as well as the patient being forced to suffer the major social stigma that has been attached to the label ME/CFS, widely promoted by Prof Wessely as a psychosomatic disease or "illness behaviour"?

51. Lyme support groups around the world have identified suicide as a major risk affecting

ill patients who are told they do not have Lyme, or no longer have Lyme after a short antibiotic course, when they (and perhaps one or more of their doctors) believe they do. What consideration has HPA/PHE given to this problem in the past, and what strategies has it put in place to ensure this terrible outcome is averted?

46-51. PHE has committed to working with LDA and others to update the information on our website and to distribute evidence based information on the diagnosis and management of Lyme disease. For any given patient, their management depends on obtaining an accurate diagnosis of the cause of their symptoms. Since many different specialities are potentially involved, each of which has its own continuing medical education programme, and each patient has their own set of possible causes and needs, it is impossible to issue a document to cover every eventuality.

52. PHE have repeatedly stressed the dangers of so-called antibiotic treatment

in Lyme. What are the potential adverse effects of the following treatments, which may be given in cases where Lyme is misdiagnosed as something else:

Steroids, oral or intra-articular injection

SSRIs

Drugs used in MS

Psychotropic drugs

Anti-cancer therapies for B-cell lymphoma secondary to a borrelia infection

Spinal surgery

Hip replacement

Knee synovectomy

The side effects of drugs are available in the British National Formulary at www.bnf.org and in each manufacturer's datasheet for the product. All of the drugs you mention are used in a wide range of conditions. If they are used in patients with Lyme disease this may be to alleviate other symptoms or contribute to the total care of that patient, in which case they may be beneficial. In the uncommon event that patient is misdiagnosed then the side effects remain the same as for the base drug, but the primary condition would be untreated until recognised. The surgical procedures are used to treat deformity, reduce pain and restore function to a body part or limb, whatever the root cause of the original problem (whether it be infection, trauma, degenerative diseases or other causes). If a treatable cause is identified, and further treatment is required then this is offered at the time that diagnosis is made. The side effects of any given procedure are available through NHS pages.

53. Is it medically justified to deny antibiotics to Lyme patients who report improvement when on them, yet relapse when taken off?

That depends on the circumstances, the therapy used, the duration of the treatment and the drugs given, underlying diseases, the evidence for Lyme disease and numerous other factors.

54. Dr Brooks, Head of the Rare and Imported Pathogens Laboratory at Porton, submitted a report to the HSE's Advisory Committee on Dangerous Pathogens (ACDP), which they

considered at their meeting on 16 October 2012. This report was titled "Lyme Disease and services in the HPA", (ACDP/99/P6).

http://www.hse.gov.uk/aboutus/meetings/committees/acdp/161012/acdp_99_p62.pdf

The ACDP's Annual Report states that, after considering Dr Brook's report, "The committee concluded having considered ... that there were no knowledge gaps that fatally undermine the committee's belief that the current approach to the diagnosis and treatment of Lyme disease in the UK is appropriate."

How does this reflect the James Lind Alliance findings that there are still many uncertainties when it comes to the diagnosis and treatment of Lyme disease?

Many of the uncertainties were covered in our talks at the Open day, and are highlighted in our review to ACDP.

55. Does Dr Brooks intend to submit a report to this month's ACDP meeting? Will there be any changes in the information issued about Lyme disease?

A report has been submitted and will be made public on the PHE website and supplied to LDA.

56. What is PHE's position on private laboratories such as Infectolab and IGeneX? We understand that there are some uncertainties about whether IGeneX offers the most appropriate testing for European strains of borrelia but UK patients travel to North America. IGenex is licensed to conduct tests by the States of California, Florida, Maryland and New York. Is it conceivable that IGeneX would be accredited to this extent if their tests for Lyme disease were inaccurate and unreliable? They have chosen not to use FDA approved test kits so they can report more bands on their Western Blot than CDC approved tests. If a UK patient presents with a positive IGeneX test result, on what grounds should this be dismissed out of hand if the clinical picture is also consistent with Lyme disease?

Igenix supply little information on their tests, and have published little on the criteria for the blots they use. It is therefore difficult to say what the tests mean. If tests from a NHS laboratory accord with Igenix, then there is no cause for concern. Igenix have agreed to meet with PHE and LDA to discuss their tests.

57. Infectolab in Germany uses CE approved test kits and has passed its preliminary DaKKs accreditation reviewing process. Once Infectolab achieves DaKKs accreditation, will results from this laboratory then be accepted by NHS physicians?

The issue is not the CE marked tests Infectolab uses (the C6 ELISA) but other tests which are sued with little or no scientific evidence to support their validity.

58. What investigations are PHE doing to examine these overseas laboratories that many UK patients use and what evidence is there to suggest that PHE are using superior tests?

PHE has no responsibility for overseas laboratory services and no legal way to investigate them. The serological tests that PHE use are all CE marked, used in many international state laboratories, and are based on peer reviewed literature.

59. Would PHE welcome a channel of communication, which would provide a route for questions to be put to PHE about Lyme disease, and to disseminate answers forthcoming so that a comprehensive FAQs database could be built up? It is noteworthy that the LDA have made a start in this respect and their website lists about 15 questions and answers.

PHE will add some FAQ's to the website in due course. RIPL do not have the resources to answer many individual enquiries or enter into debate and maintain a service for patients.