Public Health England

Protecting and improving the nation's health

Public Accountability Unit
Wellington House
133-155 Waterloo Road
London SE1 8UG

Tel: 020 8327 6920

www.gov.uk/phe

By email

Veronica Hughes
request-313568-e1ecf364@whatdotheyknow.com

Our ref: 01/02/jb/551

26 February 2016

Dear Ms Hughes

Re: Lyme Disease testing

I refer to your freedom of information request, dated 1 February 2016, and made via whatdotheyknow.com in which you asked a number of questions about Lyme Disease testing. Your email has been handled as a request for information under the Freedom of Information (FOI) Act. In accordance with Section 1(1)(a) of the FOI Act, I can confirm that Public Health England (PHE) holds some of the information requested. I have set out your questions below and addressed each in turn.

1. *Is RIPL at Porton Down the only lab in the UK which tests blood for Lyme disease by western blot as part of NHS services? If there are any others, please list them all.*

This is not a valid request for information in accordance with the FOI Act as it does not ask for information held by PHE.

You may find it helpful to know that the Rare and Imported Pathogens Laboratory (RIPL) is not part of NHS England, but of PHE. The laboratory provides specialist diagnostic testing services to the NHS. As part of its Lyme disease testing service, RIPL will test referred serum samples using borrelia IgM and IgG line blots where appropriate. PHE has no definitive information about whether NHS laboratories in England and Wales use Western blots; you would need to check with either NHS England, or with each individual NHS Trust.

PHE is not responsible for Lyme Disease testing in Scotland.

2. *Does any central body in the UK gather data on the number of ELISA tests performed in Britain and the percentage of these which are positive? If so, how many people were tested for Lyme disease in Britain by ELISA or EIA and how many of them tested positive?*

The first part of this question is not a valid FOI request. There is no central body collecting this data for the UK. This information would have to be requested from each laboratory carrying out the tests.

3. *Which of the following 16 strains (took out one which was a repeat) of Borrelia, which are known to cause Lyme Disease, are used as sources of antigens for the Lyme disease test kits used by RIPL at Porton Down, or any other UK Lyme disease testing laboratory used by the NHS?*
   a. Borrelia burgdorferi sensu stricto
   b. Borrelia afzelii
   c. Borrelia garinii
   d. Borrelia valaisiana
   e. Borrelia lusitaniae
   f. Borrelia andersonii
   g. 25015
   h. DN127
   i. CA55
   j. 25015
   k. HK501
   l. Borrelia miyamotoi
   m. Borrelia japonica
   n. Borrelia valaisiana
   o. Borrelia bissettii
   p. Borrelia spielmanii

   Are any other bacterial sources of antigens used?

RIPL uses the following commercial serology assays:

Screening enzyme immunoassay: C6 Lyme ELISA from (Immunetics; prod no. DK-E352-096)

Confirmatory immunoblot: Borrelia ViraStripe IgM testkit (ViraMed; product number V-BSSMOK)

Borrelia ViraStripe IgG testkit (ViraMed; product number V-BSSGOK
The C6 ELISA uses a synthetic peptide (C6 peptide) derived from the VlsE protein sequence. No native antigens are used in this assay.

Information about the source of antigens used in the ViraStripe immunoblots is available in the manufacturer's product insert which is available online.

PHE cannot provide information about the tests used by NHS laboratories in England, Scotland and Wales.

Please note that not all Borrelia species / strains cause Lyme disease in man. From the list provided, the following are the most common causes of clinical Lyme disease in man in Europe:

- Borrelia burgdorferi sensu stricto
- Borrelia afzelii
- Borrelia garinii
- Borrelia bavariensis (related to B. garinii)

The following may cause disease in man:
- B. spielmanii
- B. bissettii
- B. valaisiana

B. lusitaniae has been implicated in human LD but its role as a causative agent remains to be proved.

B. miyamotoi does not cause Lyme disease; it belongs to the relapsing fever group of borrelia spp.

4. *The Health Protection Report on zoonoses from PHE, Infection report Volume 9 Number 41 Published on 20 November 2015, (online at this address: https://www.gov.uk/government/ uploads/system/uploads/attachment_data/file/478807/hpr4115_zoos.pdf) states the following: During the third quarter of 2015, a total of 421 cases of laboratory confirmed Lyme disease were reported, compared with 300 during the third quarter of 2014. Of these cases, 340 were acute (including 30 neuroborreliosis) and 81 were past infections.' Please specify the exact criteria by which the Rare and Imported Pathogens Laboratory (RIPL) distinguishes between acute and past infections of Lyme disease.*

This is not a valid FOI request because it does not ask for information held.

Epidemiologists within PHE compile the Infection and Zoonoses reports based on information provided by RIPL. Epidemiologically, it is important to report acute cases for public health reasons; it is NOT to measure the burden of disease – especially for something as complex as Lyme Disease.

Acute cases are identified by RIPL based on reported clinical information. For example, reported tick bite/ symptoms and timing together with an interpretation of the lab tests, particularly a positive IgM blot in the absence of a positive IgG blot. Where insufficient clinical information is submitted to RIPL with a sample, results cannot always be interpreted.

'Past infections' is a term used in the Infection report Volume 9 Number 41 Published on 20 November 2015. It is not intended to imply that an infection has necessarily resolved, merely that it was acquired in the past i.e. not acute. For clarity, in the most recent PHE Infection Report (volume 10, number 6; published 12 February 2016) the use of this term has been removed; Lyme disease numbers are now reported as 'All cases' (i.e. all lab-confirmed LD diagnoses) and the number of these that were acute.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/500321/hpr0616_zoos.pdf

5. *In Western blot tests performed by RIPL at Porton Down, which bands are taken into consideration when evaluating infection with Lyme disease, and which bands are excluded from consideration? There has been considerable discussion in recent years over the justification for the inclusion and exclusion of various bands. Please explain the reason for the exclusion of each of the bands which are excluded from the test performed by the RIPL, and the evidence upon which this reasoning is based.*

Immunoblots used by RIPL are interpreted according to the criteria defined by the manufacturer. All bands are taken into consideration. This information is provided in the manufacturer's product information sheet which is publically available.
In exceptional cases, where the symptomatology and clinical history support a probable Lyme diagnosis, recommendations may be made to treat the patient even if an equivocal or negative immunoblot result has been obtained.

6. How many people are tested at RIPL for Lyme disease each year by western blot? How many of them, or what percentage of them, have a negative result and how many of them, or what percentage of them, have an equivocal result?

PHE does not hold data precisely in the format you have requested and public authorities are not obliged to create new information in order to respond to a request for information. RIPL data is held as the number of samples tested rather than the number of patients tested.

Each sample that is tested for Lyme disease by Western blot receives both an IgM and an IgG line blot. The information on the number of negative and equivocal Western blot test results as held by RIPL is given below. Only IgG blots give indeterminate (equivocal) results based on the manufacturer's criteria for interpreting the tests.
There will inevitably be a slight variance between these sample numbers and the actual number of individual patients tested, caused by some patients having sequential samples tested by Western blot in the same year.

	2014	**2015**
No. of samples receiving Borrelia Western blots	4749	5776
Of those samples:		
No. of samples with negative IgM	3539	4213
% of samples with negative IgM	*74.5%*	*72.9%*
No. of samples with negative IgG	3513	3936
% of samples with negative IgG	*74.0%*	*68.1%*
No. of samples with indeterminate (equivocal) IgG	542	620
% of samples with indeterminate (equivocal) IgG	*15.3%*	*14.7%*

7. *Please state the manufacturers of all test kits used by the NHS in the UK labs (RIPL and elsewhere) to test for Lyme disease and please specify which kit is made by each manufacturer.*

Public authorities are required to provide any information it holds in order to respond to a FOI request, they are not obliged to respond on behalf of other public authorities.

For serology tests used by RIPL, see answer to Q3 above.

RIPL may also use PCR tests to look for the borrelial pathogen. For this an in-house assay is used, based on the following publication:
"Routine diagnosis of Borrelia burgdorferi (sensu lato) infections using a real-time PCR assay. Schwaiger M, Peter O, Cassinotti P:Clin Microbiol Infect 2001, 7:461-469."

An alternative pan-borrelia PCR is also under development.

8. *For how long has each of these test kits been used by NHS labs (RIPL and elsewhere) in the UK?*

RIPL have used the C6 Lyme ELISA and the ViraMed lineblots since June 2012 when it took over responsibility for the PHE-led Lyme diagnostic service. Since PHE is not part of the NHS we cannot answer on their behalf.

9. *What research or objective testing has been carried out upon these kits to evaluate their level of reliability? Who carried out the evaluation, who paid their research costs, and what were their findings?*

As part of PHE's internal validation process, an in-house evaluation was carried out comparing the performance of the ViraMed line blots and the previously used Western blot test system from Trinity Biotech. The findings of this evaluation have been released in response to a previous FOI:

https://www.whatdotheyknow.com/request/porton_down_lyme_disease

This work was funded as part of RIPL's service development budget, using funding from DH.

The tests used by PHE have been the subject of some published evaluations of Lyme diagnostic tests. For example:

Diagn Microbiol Infect Dis. 2013 Jan;75(1):9-15. doi: 10.1016/j.diagmicrobio.2012.09.003. Epub 2012 Oct 11.
Single-tier testing with the C6 peptide ELISA kit compared with two-tier testing for Lyme disease.
Wormser GP1, Schriefer M, Aguero-Rosenfeld ME, Levin A, Steere AC, Nadelman RB, Nowakowski J, Marques A, Johnson BJ, Dumler JS.

J. Clin, Microbiol. 2008 46 (7): 2216-2221 Evaluation of two commercial systems for automated processing, reading and interpretation of Lyme borreliosis Western blots. Binnicker MJ, Jespersen DJ, Harring JA, Rollins LO, Bryant SC and Beito EM

Each test is evaluated by its manufacturer and the data is submitted as part of their application for CE marking. You would need to contact the manufacturers for more information about how they evaluate their products.

10. *In the 'Suggested Referral Pathway for Patients with Symptoms Related to Lyme Disease' document issued by Public Health England, the following recommendation is made: Patients with positive tests from non-NHS laboratories should have repeat serology performed through an NHS laboratory. If these are positive, management should follow the pathway above. Some private laboratories use accredited tests, so advice should be sought from RIPL.'*
    Which foreign labs use accredited tests for Lyme disease which are reliable according to the RIPL and which they would recommend to GPs in the UK as valid proof of a Lyme disease diagnosis? Or does RIPL advise UK doctors that no diagnostic test for Lyme disease in the world is reliable, other than its own?

The Referral Pathway document contains an error. The final sentence is meant to read: 'some private laboratories use unaccredited tests, so advice should be sought from RIPL.' We will ensure that this error is corrected on the gov.uk website.

RIPL advice to doctors is that a positive Lyme disease result conducted by an unaccredited lab, or using a test that has not been approved by a recognised regulatory agency e.g. EMA for Europe; FDA for the USA, should be treated with caution.

11. *The PHE infection report (Volume 9 Number 41 Published on: 20 November 2015) reports that RIPL (Rare and Imported Pathogens Laboratory) diagnosed 377 cases of Lyme disease by blood test in 2014, yet the NHS Choices website (http://www.nhs.uk/Conditions/Lyme-disease/Pages/Introduction.aspx) states:*
    It's estimated there are 2,000 to 3,000 new cases of Lyme disease in England and Wales each year.' Upon what evidence is this estimate based? And who, within which organisation, conducted the research and performed the analysis of the data?

The published numbers of acute Lyme disease cases are based on laboratory confirmed diagnoses of Lyme disease made by RIPL. This will be an underestimate of the true incidence of acute Lyme for reasons including:

- Any positive diagnoses made by an NHS laboratory that is not referred to RIPL for confirmation will not be included in the published figure.
- Many new cases of Lyme disease will be diagnosed by GPs on clinical grounds alone. There is no national system for collecting this data.

Estimates of 2000-3000 new cases of Lyme disease in England and Wales each year are just that – estimates. Improved collection of data from GPs and NHS diagnostic labs will be needed to obtain more accurate figures.

12. *RIPL made, in total, 598 diagnoses of acute Lyme disease in 2013 and just 377 cases in 2014. Does RIPL have any opinion on what has caused this dramatic 37% drop?*

This is not a valid request for information and we are not obliged to speculate in order to respond to an FOI request.

Based upon extensive knowledge gained from many years of specialising in this field, our scientists, epidemiologists and entomologists believe that numbers will fluctuate from one year to another based on factors influencing tick abundance and activity, especially the weather. In support of this, PHE's medical entomologist, with responsibility for tick surveillance, has commented that tick activity was reduced in 2014. It should be noted that numbers of laboratory-confirmed cases of acute Lyme disease rose again in 2015 to 618 cases (PHE infection report, Volume 10 Number 6 Published on: 12 February 2016).

If you have any queries regarding the information that has been supplied to you, please refer your query to me in writing in the first instance. If you remain dissatisfied and would like to request an internal review, then please contact us at the address above or by emailing foi@phe.gov.uk

Please note that you have the right to an independent review by the Information Commissioner's Office if a complaint cannot be resolved through the PHE complaints procedure. The Information Commissioner's Office can be contacted by writing to Information Commissioner's Office, Wycliffe House, Water Lane, Wilmslow, Cheshire SK9 5AF.

Yours sincerely

Jonathan Bennett
Freedom of Information Officer