

	Questions and comments raised during LRC Lyme disease educational event for Primary Care March 2021
Questions and comments	Answers and comments from Event Presenters
<b>TICKS AND BORRELIA TRANSMISSION</b>	
Which animals carry and transmit borrelia?	<p>Wild deer in Scotland are a major host for ticks. This is due to the relative abundance of deer and their large size, with deer carrying heavy tick loads in some circumstances. However, while deer can increase the size of local tick populations, <b>deer themselves do not carry or transmit</b> the <i>Borrelia</i> bacteria that cause Lyme disease. Thus, a tick feeding on a deer cannot become infected and subsequently transmit that infection to a human or other host. As deer are not a transmission host, they are referred to as a non-competent host for <i>Borrelia</i>.</p> <p><a href="https://www.gov.scot/publications/management-wild-deer-scotland/pages/14/">https://www.gov.scot/publications/management-wild-deer-scotland/pages/14/</a></p> <p>Many many animals carry ticks. The geese that fly in and out of the UK and Ireland carry ticks. Small mammals carry ticks. Domesticated animals carry ticks. In Lanzarote it is the rabbits who are carrying ticks, as there are no deer. Deer are pointed out as they are BIG and they carry many more ticks than a bird would. Ticks hop off the host, sit in the grass, and wait for the human to approach.</p>
Can insects other than ticks transmit lyme disease and other co-infections?	<p>Ticks carry lots of bacteria and viruses. But other insects can also transmit infections- such as fleas, sandflies, and mosquitoes. So some of the co infections can be carried by vectors other than ticks. However, we think that borrelia is mostly spread by ticks, but there is literature on flies carrying borrelia from veterinary studies. Whether fly bites actually transmit borrelia to humans has not been well studied but it is a possibility.</p>
<b>DIAGNOSIS</b>	
What is the best way to approach testing/diagnosing lyme disease (LD) in a child? Particularly in those with additional needs like Autism?	<p>There are no special diagnostics, different from the standard antibody tests that are imperfect, both for adults and for children. The issue is that there are many cases of pregnant women getting lyme disease (LD), and the baby getting LD, diagnosed after delivery, but the antibody test result is negative. For example, they were able to biopsy the skin, show LD, but the antibody test was negative. So, you have to use your 'clinical suspicion' and not exclusively depend on an insensitive test.</p>

	<p>We need better diagnostics, a higher degree of suspicion. And sometimes only a trial of antibiotics and assessment of response to therapy (or not) is the only way to evaluate.</p>
<p>(a) Please describe other manifestations of EM rash as they are not always a typical bullseye</p>	<p><a href="https://www.nice.org.uk/guidance/ng95/resources/lyme-disease-rash-images-pdf-4792273597">https://www.nice.org.uk/guidance/ng95/resources/lyme-disease-rash-images-pdf-4792273597</a></p> <p>EM rash can have an identical appearance to cellulitis or an allergic reaction. The history and examination are key to diagnosis. Also, the EM rash may look like ringworm - but not respond to anti-fungal creams. Sometimes a diagnosis of exclusion is required. The EM rash is the visible result of an immune reaction to the spirochaete within the skin and there is therefore significant individual to individual variation. Some people do not get an EM rash at all. It is not usually itchy (in the way that ringworm can be!) but some people seem to complain of mild itch sensation.</p>
<p>(b) Can that EM be years later or just early disseminated stages?</p>	<p>The EM rash can emerge as just one, or show up as many on the body; it can come and go or it can persist, sometimes over many months. It can be elliptical; it can be small or big. It can be hemorrhagic, it can blister. It can be prominent or very faint. So this illustrates that it is not always the classic 'bullseye'.</p>
<p>Does EM give systemic symptoms?</p>	<p>The EM rash can occur on its own without symptoms or in the context of more extensive dissemination. Sometimes the fever is noted before the EM rash. The pathogenesis of lyme is as follows. The bacteria is inoculated into the skin. After a period of replication, it spreads into the blood stream and disseminates to all parts of the body. Dissemination generally takes days/weeks but can also occur more rapidly. So, you can have a visible EM rash at the time you get dissemination, with fever, rash, Bell's palsy, joint pain, neurological problems. Sometimes the EM rash disappears spontaneously, sometimes it returns. So initially following the bite, there may be no systemic symptoms and you can certainly have a rash without systemic symptoms before wider dissemination has occurred. However, you can have an EM rash occurring at the same time as systemic symptoms.</p>
<p>Can I clarify - a negative lumbar puncture result doesn't exclude neurological lyme disease?</p>	<p>Lumbar puncture cannot be used to rule out Borrelia.</p> <p>The LP for syphilis in patients who have neurosyphilis has a positive VDRL test only in one third of cases. So you have to use your clinical suspicion for all infectious diseases, syphilis and lyme. If you have lyme neuroborreliosis you can have a clear CSF, some cells, some with elevated protein, but it does not separate from syphilis, Covid, lyme, viral meningitis etc. Remember.....clinical clinical clinical!</p>
<p>Does Bell's palsy as a symptom, indicate a tick bite behind the ear or on the neck eg in children?</p>	<p>People can get a Bell's palsy despite never being bitten behind the ear. The bacteria spreads from the EM rash site through the blood stream to the cranial nerve, not from local spread. Of course, if you get a bite contiguous to the nerve (for example around the ear) it is another way borrelia can spread.</p>

TESTING	
<p>(a) You did not cover tests from non UK sources. Please comment on the fact that tests from Armin etc are commonly dismissed by GPs.</p> <p>(b) I am a GP in Scotland and I have come across a few patients who bring German lab results and often find it difficult to know how best to approach this - is there advice about this?</p>	<p>There are private laboratories all over the world- such as Poland, Belgium, USA, Canada. And we use them to outsource all sorts of infectious diseases (including COVID-19) in Ireland. To simply say 'we don't recognise the private tests for lyme and NICE does not accept the German tests' is ignoring the science. Private laboratory tests can be helpful, but need to be a part of the analysis, with the history, symptoms and exam the critical part of the equation.</p> <p>The German blood tests were reviewed by NICE 2018 and advice given to only make a diagnosis with serology using the reference labs (RIPL and Raigmore). We consider it inappropriate to mention 'German tests' and indeed such comments are a bit prejudicial. A lot of people are using the TickPlex Plus, a test developed in Finland by a biotech company there and licensed internationally. The German labs are accredited by DACCS, similar to the UK ISO accreditation. All German labs are accredited, just like Raigmore in Scotland is accredited. So, to say the German labs are 'not accredited' and we don't accept the German tests based on NICE 2018 is a mantra without science behind it. The German laboratories, accredited to a standard the same or better than the UK, order a licensed kit from Finland - the TickPlex Plus. When these private test results are presented to many doctors in the UK and Ireland, patients are told, 'we don't accept the German tests as they are not accredited and not licensed'. Our view is that private tests can be helpful in the right clinical scenario.</p>
<p>Does NVRL in Dublin test for lyme disease ?</p>	<p>Most laboratories in Ireland do the lyme test. The NVRL does the lyme test, including ELISA and C6 peptide, and then send off to the Porton Down Lab in the UK if they need further testing done.</p>
<p>Is there any point doing serology too soon (before 3 weeks) due to antibodies not yet being present?</p>	<p>We do not know the natural history of antibody response to borrelia. So it's not as easy as saying don't do it. Medical text books say it takes 4 to 8 weeks to develop an antibody response following infection. If you have a lyme rash, you should treat. We have seen people with classic lyme symptoms whose test was negative at 3 months, and then went positive at 6 months. We have seen people positive at 4 weeks following tick exposure.</p> <p>In our experience it can take 2 weeks for a Lyme Blot result due to the fact that they run tests in batches, which may cause delay for an individual patient. The Aucott study <a href="https://bmjopen.bmj.com/content/8/6/e021367">https://bmjopen.bmj.com/content/8/6/e021367</a> showed increased rate of persistent symptoms if treatment delayed.</p>

<p>(a) Are we doing patients in particular and the wider cause of Lyme recognition, in general, a disservice by treating EM rashes without doing blood tests?</p> <p>(b) Wouldn't it be difficult to remember so many co-infections to select individual tests for each?</p> <p>(c) Would it not be easier for labs to automatically look for Lyme disease AND co-infections when blood is sent away after a tick bite?</p>	<p>Studies by Aucott in the USA have shown that it can take many months before a person will test positive. Hence one cannot depend on a negative test, as it can be a false negative. Again, if you have a lyme rash, you should treat. The NICE guideline specifically says initiate treatment without waiting for results if there is clinical suspicion of Lyme disease.</p> <p>RIPL request form advises to contact RIPL directly to discuss testing for co-infections - foreign travel may be relevant.  <a href="https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/720437/P2_RIPL_Lyme_request_form.pdf">https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/720437/P2_RIPL_Lyme_request_form.pdf</a></p> <p>You do not need foreign travel to get a co-infection. The ticks in Ireland are carrying borrelia, anaplasma, babesia.</p> <p>Testing for some co-infections is not always available. As before, RIPL request form advises to contact RIPL directly to discuss testing for co-infections.  <a href="https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/720437/P2_RIPL_Lyme_request_form.pdf">https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/720437/P2_RIPL_Lyme_request_form.pdf</a></p> <p>Raigmore also has guidance online on what tests are carried out, and a SLDTRL test request form.  <a href="https://www.nhshighland.scot.nhs.uk/Services/Documents/MicroRefLabs/SLDTRL%20request%20form.pdf">https://www.nhshighland.scot.nhs.uk/Services/Documents/MicroRefLabs/SLDTRL%20request%20form.pdf</a></p>
<p>A delegate commented that " tests should not exclude a diagnosis of Lyme Disease" was true for Erythema Migrans but was not true for early disseminated or late Lyme disease. Does the NICE Guideline and other guidance agree?</p>	<p>Part 1.2.12 of the NICE GUIDELINE says to use a combination of clinical presentation and laboratory testing to guide diagnosis and treatment in people without Erythema Migrans. In essence, do not rule out diagnosis if tests are negative but there is high clinical suspicion of Lyme disease.</p> <p>Since publication of the NICE guidelines, the CDC has also published a disclaimer and reinforced the message that the sensitivity of the two tier test is insufficiently sensitive to be relied upon for exclusion of Lyme disease at any stage.</p> <p><a href="https://globallymealliance.org/news/cdc-agrees-to-add-disclaimer-to-lyme-disease-case-definition/">https://globallymealliance.org/news/cdc-agrees-to-add-disclaimer-to-lyme-disease-case-definition/</a></p>

	Our clinical and personal experience is that some patients do have persistently negative serology over many weeks, in spite of the presence of a definite EM rash (and/or a significant illness directly following a known tick bite that is clinically, highly consistent with Lyme disease).
In cases of strong positive Babesia and mycoplasma pneumonia and weak positive borrelia, where the main symptoms are heart palpitation, air hunger, fatigue and panic and anxiety, should we start by treating Babesia and mycoplasma, or should we add in treatment for lyme as well?	The challenge with all of the testing is that a positive test means either active disease or past infection. You have to make that determination. And also, symptoms overlap, so all of these infections can cause 'CNS' symptoms. You cannot say which one is causing the symptoms., and you can't treat everyone for every positive antibody test they have in their body. We need better diagnostics! And a better understanding of these conditions.
<b>TREATMENT</b>	
In the early phase of Lyme disease, where doxycycline or amoxicillin can't be used, is Azithromycin or Cefuroxime a better option? ( CDC and IDSA recommends Cefuroxime and NICE recommends Azithromycin)  A delegate commented that amoxicillin may not work for an EM rash in children. What antibiotics can you give then?	No studies have been done comparing one to the other. In early infection, all of these agents have activity. The issue is with longer standing infection, some antibiotics penetrate better into the cells and deep tissues than others ie azithromycin has better deep tissue penetration.  All antibiotics work for lyme, independent of age, which includes amoxicillin, doxycycline, azithromycin, cefuroxime. The issue is what is safe to give to children. Doxycycline should not be given to young children; but the other agents are fine.
In terms of Chlamydia Pneumonia if a lot of research suggests 30 doxycycline and rifampicin is effective. If doxycycline can't be tolerated is Cefuroxime a good alternative?	You have to match the right bacteria to the right antibiotic. Cefuroxime works for LD, but is not active against Chlamydia. Azithromycin is a better choice. Chlamydia pneumonia and trachomatis (the STI one) have the same antibiotic sensitivities.
What was the triple therapy regime mentioned?	<a href="https://clinicaltrials.gov/ct2/show/NCT03891667">https://clinicaltrials.gov/ct2/show/NCT03891667</a>  <a href="https://bmresnotes.biomedcentral.com/articles/10.1186/s13104-020-05298-6">https://bmresnotes.biomedcentral.com/articles/10.1186/s13104-020-05298-6</a> There is an ongoing trial looking at disulfiram for Lyme disease and there is some early suggestion, with further studies needed, on the potential beneficial use of dapsone in combination with antibiotic treatment (as well as other potential treatment combinations). In the absence of further RCT evidence, this is not available within mainstream clinical practice currently.

<p>With chronic neurological manifestations, can triple antibiotic therapy help or do they need IV ceftriaxone?</p>	<p>The only indications for IV antibiotics in Lyme neuroborreliosis is in the early stage. With IV antibiotics, you achieve higher blood levels, with better penetration to the brain. But for most situations, oral antibiotics in high enough doses will give you good levels. We do not advise GPs to be treating chronic longer standing infection with combination antibiotics unless being supported by a specialist to do so.</p>
<p>It was suggested that Bell's Palsy in children and adults suggests Lyme disease until proved otherwise; and should be treated with steroids and antibiotics according to NICE 2018 to avoid damage to the facial nerve. Is there evidence to support this combination of steroids and antibiotics in Lyme disease?</p>	<p>There are no studies in Lyme disease to use steroids in combination with antibiotics for a Bell's palsy caused by borrelia. The only study of combined anti-infectives with steroids is that of Bell's palsy caused by VZV the zoster virus. So treat Lyme, including Lyme associated Bell's palsy with antibiotics!</p>
<p>What is the best way to manage a Herxheimer reaction?</p>	<p>This is a very rare reaction. Less than one in ten people are likely to experience it. If the patient experiences problems, stop the treatment; give it a couple of days to settle. And then re-introduce the medications.</p>
<p>Is antibiotic resistance a concern with long-term treatment?</p>	<p>These are slow growing bacteria and resistance is not thought to be an issue, but you cannot grow these bacteria and do sensitivity tests as you can for a urine sample growing <i>EColi</i> for example</p>
<p><b>COMPLEMENTARY THERAPIES</b></p>	
<p>(a) What are the herbal medications that have been mentioned a couple of times now as treatment?</p> <p>(b) What role can physios, nutritionists, herbalists play in the care of patients with persistent symptoms?</p>	<p>There are a number of herbal protocols. Check out the Cowden protocol, Buhner protocol. Napier's Herbalists in Scotland have a Lyme protocol. Just Herbs has a product called "sublime" which is a combination of supplements. These protocols help support patients, but we still think antibiotics are the best way to kill off bacteria. Some of these other supplements can be supportive.</p> <p>"Chronic Lyme disease" is a highly complex multisystem illness best dealt with by a multidisciplinary team. Supporting the function of the immune system (and minimising dysfunction) with excellent nutrition, sleep, appropriate physical activity and attention to stress management is fundamental to achieving this.</p>



<p>Please suggest books on cognitive bias.</p>	<p>Professor Pat Crosskerry has written a number of articles on cognitive biases in medicine.</p> <p>Thinking Fast and Slow as an incredible book for insight into our human cognitive biases.  <a href="https://www.rcpe.ac.uk/college/journal/cognitive-bias-clinical-medicine">https://www.rcpe.ac.uk/college/journal/cognitive-bias-clinical-medicine</a> is a useful article from a clinical perspective and "Black Box thinking" by Matthew Syed for insight into cognitive bias in medicine in particular.</p>
<p>This event is voluntary to attend. How can we ensure this education reaches all Primary Care practitioners?</p>	<p>RCGP accredited educational resources are available. Patient support groups are working to raise awareness amongst health practitioners. Patients themselves can direct their GP to the RCGP Lyme disease Toolkit. The resources shared at the event are also available on the LRC website to signpost health professionals to – recorded presentations, slides or summary notes, and short bite educational videos on ticks, Lyme disease and co-infections. You can find them all here:  <a href="https://www.lymeresourcecentre.com/prof/learning">https://www.lymeresourcecentre.com/prof/learning</a></p>

\*1 RIPL Lyme request form

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\*2. Raigmore SLDTRL Lyme request form

<https://www.nhshighland.scot.nhs.uk/Services/Documents/MicroRefLabs/SLDTRL%20request%20form.pdf>