# Notes from Public Health England Lyme conference/meeting. 9th October 2013, London.By Nicola Seal. nseal@yahoo.com

Disclaimer- these notes may contain inaccuracies. They are as accurate as I can make them but since recording of the meeting was not allowed, I may have misunderstood some things, or attributed questions or answers to the wrong people on occasion. I would urge Public Health England to allow recording of their 'open' meetings in future to increase transparency and allow patients who are too sick to attend to view the meeting in full. This would also remove transcription errors which may be present in these notes.

## Countess of Mar (Lady Mar)- Welcome and Introduction

The countess suffered ill health after exposure to Organophosphates. She knows what it's like. She gives a voice to the powerless, the chronically sick who are consigned to the 'dustbin' of M.E. C.F.S.- Lyme patients may be put in these categories despite disparities in their symptoms.

She had two letters last week. One from the mother of a 9 year old boy with tick borne disease. The doctors denying it, giving him painkillers and nothing else. Describes another case of a young woman. There is a background of medical conflict. There are huge questions over the incidence of Lyme Disease. CDC estimates are out, Germany has 800,000 cases in 2009. 20-30% cases have no rash. The incidence in the UK appears low.

Diagnostic testing is controversial with poor sensitivity for very early stage Lyme disease. We need an independent analysis for those. She asked Tim Brooks to publish the answers to our questions on their website (written questions were put by facebook group called Lyme disease UK discussion). He said he would (I think). She talked about the 'expert patient' in the BMJ- we should welcome them. There needs to be more recognition of patient expertise. Patients get well on long term antibiotics. Antibiotic resistance is a concern. There are few papers to confirm or refute. Longer courses of antibiotics frequently result in elimination of symptoms. What is the cost to the taxpayer- benefits, lost earnings. We should look beyond the NHS budget to the national budget. There are lots of questions and too few definitive answers. She asks those in a position to make decisions to listen carefully and if they don't know the answers to say so.

## Tim Brooks, Head of Clinical services, Rare and Imported Pathogens laboratory, Public Health England. Overview of Lyme disease pathology and Immunology

We need to find areas we can work together. "The world of the Germ" and challenges to detection.
There are stages to a disease progression -1) ingestion, 2) it attaches to a surface or in cells, 3) it reproduces and 4) you get systemic infection and it spreads.

The "pathological race"- whether you win or the Germ. Local infections- lots of organisms are defeated at that point. T and B cells attack. Organism tries to evade this. If it is not defeated at this point you get systemic symptoms. If it's not self-limiting, you get long term symptoms. They are trying to help us win this race.

Spirochete- can swim with flagella. Has various surface proteins. Some of the proteins and are common to other Borrelia species. There are 3370 different genes and at least 27 plasmids (linear and circular). These code for different surface proteins which give virulence. Plasmids are mobile, they can be shared between different organisms- they are

also a mechanism for moving between hosts. This presents a challenge. A tick bites and Osp (Outer surface protein) A is replaced by Osp C. Spirochetes can take as little as 12 hours to get in the human- he recognises that it's a lot less than the textbooks say (not 24 hours). *My thoughts - publicise this fact to doctors!*

Osp C antibodies are transitory. The rash isn't there in 30% of cases. *(again- publicise this to doctors!)*. Antibody responses vary between people. Organism not in blood for very long, in CSF (cerebrospinal fluid) in a few cases. Can find it in ACA (acrodermatitis chronicum atrophans) skin biopsies but not in joints. ViSE protein – the C6 peptide is the antibody to this. Epitope switching- he recognises that the ViSE protein is constantly changing. Talks about Major Histocompatability Complex (MHC) and T-cell trigger complexes.
Persistence of symptoms – this could be due to tissue damage, ongoing immune reaction or untreated disease due to insufficient or no treatment and also there is possibility of re-infection. We need research to find out which of these is involved. *(my thoughts- acknowledgement of possibility of undertreatment and active infection- good!)*. If the organism is there, we need to treat it. *(yes!)* Infection with Borrelia burgdorferi may be asymptomatic, can cause EM rash, can cause infection with no rash, can cause disseminated disease, can abort at any stage. The immune response may be abrogated by treatment, may not appear if disease self-limits early, does not protect against re-infection, is present in established infection but may be variable.

**Stella Huyshe-Shires, Chair, Lyme Disease Action. Short and Long term wins in Lyme Disease.**

She was given the title for this talk. This conference is about participation. One win is under our belt- we are here in this room talking but there is still a long way to go. James Lind Alliance (JLA)- thre were 957 questions submitted about the uncertainties, 47% of those were out of scope- they were about policy, epidemiology, other tick borne disease, clinician awareness. That is the sort of question we are dealing with this afternoon. Results of JLA- 81 unique questions of which 7 had a known answer. There were 69 true uncertainties published. They thought they'd made progress. Clinicians seemed not interested and some patients didn't see the point. There is a gulf between clinicians who 'know that 21 days of antibiotics will cure lyme disease' and patients on the other side who know months of antibiotics are needed. Inbetween are GP's. We have to close the gulf. Can we ALL acknowledge the uncertainties, not them and us. Stop the suspicion. Makes a plea to the rest of us to change the culture. Patients and doctors have to stop making assumptions about each other.

The uncertainties are logged on the DUETS database. They struggled to get doctors involved in the JLA process. Some clinicians think there are no problems and that the guidelines are fine.

EFNS (European Federation of Neurological Sciences) guidelines – if you read it, 3/5 recommendations are opinion and not based on evidence, because the evidence is not there. The UK has NICE (National institute for Clinical Excellence) guidelines (CKS- clinical knowledge summaries), but for anything other than EM rash, they say 'refer to an expert' but don't say who those experts are. Who are these people? Patients are spread thinly between infectious diseases doctors.

BIA position statement (British Infection Association)- this recommends doxycycline 100mg once a day for Lyme arthritis. This doesn't even reach MIC (minimum Inhibitory concentration) in tissues. They are a risk to patient health. Misleading and inaccurate. BIA

apparently peer reviewed it, maybe that the peers reviewing it didn't know it was wrong. Use expert patients!! Harness them. Remove the BIA position statement from the RIPL website- it reinforces distrust from patients. Stop using it as if it is guidelines. If it were on the Lyme Disease Action website, they would lose their accreditation.

EFNS guidelines – look at the response rate- 25% of patients didn't respond to Doxycycline- so not great. The response criteria was complete recovery at 12 months or persisting remission in 24 months - is this acknowledgement of persistence? Absence of OBJECTIVE symptoms – so headache, numbness etc doesn't count. What about patient based outcomes – your reflexes are ok, you are cured. No. We need to look at what is important to the patient.

She is asking the policy makers to put patients at the heart of it all. Lyme Disease Action knows more about Lyme disease than most Infectious Disease consultants. They now have a medics support line. Healthcare is done with us not to us. Can someone please promote LDA support services? Looks to panel. No link to LDA on the Health Protection Agency Website – ramblers yes- not LDA.

Are we having some regional centres of expertise? Please involve LDA in training and designing of these services. Remember the patient voice! A lot has been achieved in the last 12 months. The elephant in the room- the Ad hoc international Lyme group. Which was formed to denigrate patients. They had to mount a socio-political offensive. This is not just an academic journey for patients - there has been the death of at least one patient. Attitudes. Troubled waters need calming. There could be one quick win - if not an apology, she wants acknowledgement that they could have done better and acted sooner. Today is a good start but it's not over yet. Let's keep this boat afloat together.

**Wendy Fox, Chair of Borrelia and Associated Diseases- UK (BADA-UK) The patients need for scientific integrity**

What BADA does- awareness- educational exhibits, advice service mostly prevention but also diagnosis and treatment and patient support. She thinks she is cured but is permanently paralysed. Call for scientific integrity. There is a lack of awareness about ticks and Lyme disease and treatment in general public, doctors and vets. Showed pictures of deer keds, thrips, leech all sent into Bada mistaken for ticks. HPA website- most GP's are not aware that Lyme disease is everywhere- patients get told "there is no Lyme here". Lack of awareness that ticks can be very small. People don't realise ticks bite people as well as animals. Symptoms- on web- patients self diagnose. GP's not always aware of EM rash. Classic target and more homogenous lesions. Google is a quagmire. Difficult to navigate. Good and bad info. Patients are turning to private testing routes. Potential for misleading routes. Talks about unvalidated tests. Talks about snake oil and inaccurate info on various website. Talks about a hair test and other inaccurate info. What is post Lyme disease syndrome? Patients can end up in alternative therapies. Can suffer adverse effects from these treatments, salt/vit C protocol. Miracle mineral supplement (MMS).

(*My thoughts- I feel she labours this point too much, and it makes patients sound like they are all pursuing weird treatment and diagnostic options-I think that is only a minority of patients)*

Out of 100 patient support cases last year... present statistics... Further research is necessary, we need evidence based medicine. Without it, patients may pursue unvalidated treatments and tests, and doctors may continue to prescribe inappropriately.

**Tim Brooks. Rare and Imported Pathogens Laboratory (RIPL) RIPL assays and services.**

We work with a wide range of diseases- about 100 diseases most are vector borne/zoonotic. 24 hour helpline for physicians. Treat Lyme differently- mass production started 1st June 2012. All automated. They use C6 elisa combined IGG, IGM virastripe. Blots are printed. Simple to interpret and can be run by machine. Unprinted blots are harder to interpret and there is more varation between technicians. Subjective. Tests for various coinfections- Bartonella, Ricketsia, Anaplasma/Ehrlichia, Babesia, other tick borne diseases, PCR- skin is best, blood CSF and synovium, biological limitations. Culture was at one time the gold standard- new techniques available now which are maybe better *(My thoughts- really?? ALL antibody tests rely on sufficient antibody production - sometimes doesn't happen - what about ALS/Sapi culture testing?).*They report the results in a detailed format *(my thoughts - much better than simply positive or negative and probably an improvement on what was reported in the past but how many are negative at ELISA stage and are the actual levels of antibody in ELISA reported?- i.e. it might be near cut-off point, doctors should be told the levels if poss.)*

The duck test. About 12,000 tests done in one year (12-13). 4187 virastripe blots done in same year. *(My thoughts- so that looks like about one third of ELISAs were positive or equivocal)*. RIPL service helpline for clinicians and the clinic starting with Dryden. They do need to update website. They don't take direct enquiries from patients but will take calls from doctors and it's ok if patients are in the same room as the doctor. Their aim is to find out what we are ill with. What is causing the symptoms. They will treat credible cases even if not every dot is crossed.

**Roger Evans. Consultant clinical scientist, NHS Highland (based at Raigmore, Inverness). Lyme disease in Scotland.**

His colleague couldn't be here today because she has Lyme disease. (*I think?*). 2003 Lyme Borreliosis testing lab was established in Inverness. 1995- 2 step testing protocol was established. They cross charge different NHS boards for testing, There is no central funding. They processed about 5000 samples in 2011. Now, in 2013, they test all of Scotland, previous to that two health boards sent their bloods elsewhere *(my thoughts- this included Grampian- my area- this was because the consultant in charge has 'links' with SOC, despite raigmore having developed tests tailored to Scottish strains)*.

2011 and 2012 saw a drop off in numbers, why? GP's are treating EM rash without testing now. GP's are aware in NHS highland and perhaps there was a drop in the tick population in 2011- European data suggests this.

Scotland, Lyme borreliosis is not a notifiable disease but Borrelia burgdorferi is a notifiable organism- odd!!!
All first time western blot positive vases are reported. Current practice is to send questionnaires to GP's. Does a positive western blot = active Lyme borreliosis?. Figures need revising- likely to be higher. There is under-reporting. GP's don't always report or send samples in. GP's are diagnosing clinically. GP's are estimating the figres are ten times higher. There is a PhD running to look for active infection with western blot. Need to revise reporting- need to include EM/cases that are not tested/seronegative.

Project on tick collections. 25 isolates and 7 identifiable species so far. Collections from Urchany had 19%, Culloden had 5.4% and Inverness had 16.7 % Bb prevalence. & wer culture positive and PCR negative. We don't know what some of these species are *(my thoughts- evidence for novel species in UK?? And quite high infection rates of Borrelia in*

*ticks)*. They are not myamoti- as PCR is based on a flagellin gene that can detect this species. Is the Borrelia geneome changing over time?

Addressing the need for active infection marker. Need to revise the epidemiology- tip of iceberg- they need to consider other tick borne infections in Scotland. *(my thoughts- great! Forward thinking, Seems keen to develop and expand the labs capabilities- proactive in development of science)*.

Question from floor- c6 ELISA? Yes, then WB. They report indeterminates.

Q. Do they they do interlab validation between themselves and RIPL? He says they should do this and have had meeting with RIPL to discuss. It is now a commercial assay, not an in house western blot as previously as they have now got lower staff numbers and it's less labour intensive. It's also CE marked on commercial assay. *(my thoughts-I wonder if this had meant a reduction in sensitivity as the old in house assay was tailored to Scottish strains)*.

**<u>Iain Farmer- G.P based in Fort Augustus, Perth and Kinross. Lyme as a GP sees it.</u>**

His practice covers the great glen, skye, invermoriston etc, a large area, 300 sq miles.

He sees patients who consistently get bitten and then some just don't. Most Lyme they see is in locals- tourists go home before they develop symptoms.

1984- no Lyme seen in his patients. Something happened about that time, new strain, increase in virulence? 1986, started seeing EM rashes. Before that, no issues with Lyme disease, old shepherds don't recall a problem. Last few weeks he's seen few cases EM rashes. They never see a bullseye rash, always a pink blush rash- uniform- not very raised, not hot, can be very faint. Usually just a pinkyness that spread. They don't do testing on these people- no point. " test is rubbish anyway" (got applause!).

10993 – first patient with second stage Lyme- cranial nerve involvement/palsy. They very rarely see late/second stage, mostly EM rashes. Treated this man with ceftriaxone and he got better. He joined the highland research group- wanted to look at a prevalence for positive tests- no-one wanted to do the study- no research done. He's saying there needs to be more interest in it. Financially a huge issue- tourism, lost earnings. Deer in gardens, dogs are tick collectors. We need more research. Don't know the proportion of positive patients. Need test for active Lyme disease versus past disease, need to know proportion of infected ticks.

*My thoughts- looks like this doctor and possibly highland GP's are way ahead of the game*.

**<u>Alistair Miller- Consultant physician, Tropical and Infectious Diseases Unit, Liverpool.</u>**

Sees about 20-30 patients per annum but increasing. Treat on clinical diagnosis with 14 days doxycycline. Has a CFS (Chronic fatigue syndrome) clinic. They have a dedicated 'therapy team'. Serology is often not positive. They see disseminated Lyme, mainly neurological. They also see patients who don't have any evidence of Lyme disease. Cites Huppertz et al. 1999 89% EM rash. Late Lyme disease is skin, cardiac, neurological. ACA is rare, mainly women, afzelli. Cardiac Lyme – he has never seen a case- extremely rare- *(My thoughts- well, several members of the audience including myself have cardiac Lyme, so he's just not looking properly- biased, IDSA tripe)*.

Early Lyme Neuroborreliosis. Lymphocytic meningitis. Painful radiculopathy, cranial nerve. Late Lyme Neuroborreliosis- similar to early but sometimes with encephalitic signs and peripheral neuropathy, but very rare *(my thoughts- a room full of these very rare people are sitting infront of you Dr Miller)*

Primary treatment for localised EM- doxy 100mg BD for 14 days, or Amoxycillin/cefuroxime for 14 days. Cites IDSA and BIA guidelines. Then his own study, cottle, Miller 115 patients referred to him over 5 years. 25% "didn't have Lyme" and were referred to CFS services (my thoughts- the bin). Wants to get rid of Chronic Lyme as a term, comnfusing because it can refer to late disseminated disease, PTLDS (Post treatment Lyme disease syndrome).

There is no evidence of benefit from prolonged antibiotics. 10-20% of those treated with Lyme Disease have residual symptoms that are like CFS. Post infectious syndromes happen in other diseases. Aetiology pathogenesis is uncertain. There are arguments against chronic Lyme disease. Antibodies decline over time, "no evidence that organisms can hide anywhere" and evade the immune response. *(my thoughts - good god, this man needs to do some serious reading and patients should steer well clear of him).* Patients are receiving inappropriate antibiotics in the private sector with negative effects and costly and they are relying on benefits. "serology is almost always positive in Lyme disease patients". (*my thoughts- yes, in HIS lyme patients because he clearly won't consider seronegative patients- circular reasoning-is ignoring all the evidence, contradiction of Tim brooks' words and a ton of data on seronegativity. After, in the coffee break I gave him a review paper on persistence mechanisms in Lyme (Berndtson 2013) and tried to give him the rhesus macaques Embers paper but he said he'd already read that- I said, oh really, because you said there was no evidence for persistence mechanisms in Lyme?)*

**Matthew Dryden, consultant microbiologist and specialist in infection, RIPL, PHE. A Lyme clinic in Winchester.**

We need more research. He has had a long interest in Lyme disease. He wants the clinic to be part of a national network of lyme disease Infectious Diseases expertise. There are pediatric Infectious Disease Lyme disease specialists in Southampton.

Winchester is a pilot clinic- the funding still to be established. He has until December to get it going and he may go back to his normal duties if it gets no funding.

He has seen an increase in Lyme disease over the years. 1992-2012, numbers have gone up. The incidence varies in Winchester, rate per 100,000 popln is now up to 18/100,000- v high incidence rate for UK but not as high as mainland Europe.

Variety of EM rash appearance, very varied in appearance, big, small, faint, inflamed. Most common in children and middle aged adults. Lag phase, 2-3 weeks before symptoms and often a lag before serology. 70% present with a rash, 16% neurological. They want urgent referrals and to monitor the evolution of serology over the course of the disease. They will do biopsies of the EM rash and monitor clinical progress.

What is Chronic Lyme Disease? Is it another infection? No one patient is the same. There are in his experience, two diseases. The first is Lyme disease- clear cut, positive serology, objective signs. The there are the other patients- chronic-no objective signs, negative serology, often don't get better with short term antibiotics. He wants to get to the bottom of it. Seems polarised, says two types of diseases are very different.

Chronic/persisting infections all leave clear pathological signals but persistent/chronic Lyme disease doesn't have this- they can't find the organism.

Shows slide with numbers of Lyme patients seen in Winchester clinic in Sept 12. 11 with Lyme, 12 with CAN (Chronic Arthropod-borne Neuropathy). They want to look for unknown pathogens and give aclinical assessment. He wants to see strong association with LDA and wants the funding to continue after December. *(My thoughts- quite low numbers, about half his referrals were chronic and interesting terminology, implies they all had Neuropathy in common)*

Stella asked a question- how does he want to collaborate with LDA? I didn't record the answer. Pediatric doctor in audience- emphasising the need to develop pathways and care for children.

*My thoughts – if you have nothing to lose (i.e. aren't currently receiving treatment from your GP or other NHS source and can't afford private treatment), then try to get a referral to his clinic. You might get several months of antibiotics, he might find co-infections and treat them to a limited extent, he can see you and learn- if he never sees complex patients he is not going to learn about them. Don't expect the kind of treatment you would get from an LLMD though - he has a lot to learn.*

**Jackie Duggan – Principal Scientist, Special Initiatives, RIPL, PHE.- (she develops new technologies).Next Generation Assays.**

Microscopy – not recommended. Culture- poor success rate- low numbers of organisms in blood. *(my thoughts- do they know about the Sapi/ALS culture test?)*. PCR- low sensitivity. IFA (Immunoflourescence assay) lacks specificity and is subjective. ELISAS are automated and easy. C6 ELISA does not elicit a very high IgM response. They sample share with other labs to cross quality control and validate tests.

Assay development- culture. They don't currently do this but they want to do this using the same method that Inverness do *(my thoughts- I wasn't aware Inverness did culture- that's progressive)*. They want to do this so they can grow different strains for validation. However it might be possible to use a few for diagnostic purposes.

They have the Abbott-Plex machine which is a PCR/Mass Spec. It can assay 8000 organisms. Can detect all Borrelia strains as well as other pathogens. Uses DNA hybridisation to concentrate DNA from blood. RIPL is one of 8 labs worldwide with this machine. It is currently taken off the market due to problems with the software. They lists the coinfections it can detect- Anaplasma/Babesia/Bartonella?Coxiella?Ehrlichia etc. Agreement with Abbott for 2 year evaluation- tesing it against clinical assays and other assays and to look for other tick borne infections in Lyme negative samples.

Limitation- will only detect pathogen is it is there in sufficient numbers but Abbott are doing a concentration method.

They are planning clinical studies- recruit volunteers to follow their immune response at different stages of the disease. Recruitment will be through GP's and primary care centres from early to late disease. Blood samples, skin biopsies etc. *(My thoughts- this is a study worth conducting, I hope they are aware that the immune response in early disease can be undulatory and that they won't automatically prevent seronegative patients from being in the study and the selection criteria will include clinically suspected cases)*

They want to look at different proteins within Borrelia and use Microarrays. They have not got enough funding.

I asked if they will include seronegative patients in their study following the immune response over time and they said yes, they would.

**Amanda Semper- Scientific programmes manager, RIPL, PHE. Beyond the next generation- data mining and T-cells.**

Current analysis of virastripe blots- for IgM they say it's a positive result if 1 of 5 bands is greater than the cut off threshold.

For IgG it's if 3 of 12 bands is positive.

Variation in band intensity holds more information. Patterns of bands and relative intensity gives more information for disease progression over time (serial samples). Different stages of the disease- they might data mine their data to look for patterns and see how the test results might compare with the clinical picture.

Early diagnostic tests are challenging as you are relying on antibody responses- B cells and T cells are slow to develop. The innate immune response is more rapid but relatively non specific. It just recognises 'foreign proteins'. There are some cells called invariant natural killer T cells which have moderate specificity- they recognise glycolipids and could be useful. T cells are a focus for new tests. A memory T cell proliferates when it encounters a *Borrelia* antigen. LTT and T cell proliferation assays also LTTM ELISA (a bit like LTT).

These assays work in a research setting and are valuable for that. They have been investigated as diagnostic tools but there is no scientific consensus as to it's value as a diagnostic test, there is conflicting data. It has poor specificity. Can be a false negative with poor sensitivity. May be useful for monitoring the treatment course *(my thoughts- this is what BCA mainly use them for)*. They may have a role in early disease. She thinks LTT should only be run in parallel with other tests- serology etc.

The interferon gamma Elispot (elispot/immunospot/ispot lyme) these are newer, there is less data on them. Rapid but haven't been thoroughly investigated as diagnostic tools and there is no consensus in the data. Spirofind from Boulder diagnostics an innate response-pattern within Borrelia being recognised- cytokines- non specific? They are testing it. It is cumbersome to use not likely to be a useful diagnostic test.

**Jolylon Medlock- Head of medical entomology and zoonoses ecology, PHE.**

*Please note- I was writing questions to be submitted for the panel at this point so took few notes. The slides are relatively self-explanatory anyway.*

Black striped mouse is in continental Europe not UK- it's a very good hosts for ticks and Borrelia burgdorferi, much higher numbers of ticks and spirochetes than other mice- maybe one reason why the UK figures are lower than the rest of mainland Europe? Deer and sheep are dilution hosts but can get co- feeding and infection between ticks if they feed within 9 cm of each other.

**Robert Smith- Clinical Scientist (Zoonoses), Health protection division, Public Health Wales. Epidemiology of Lyme in England and Wales**

Passive and enhanced surveillance since 2010. England and Wales are required to notify all lab diagnoses of Lyme borreliosis to PHE but not all places/cases are reported. The enhanced surveillance was via questionnaires which were sent by sounthampton to doctors until 2003 when doctors topped being bothered to return the questionnaires. Other labs didn't always report their lab confirmed cases to HPA. 1201 serologically confirmed cases in 2011, 1163 in 2012 in UK. 2000-3000 cases per year expected overall. *(My thoughts- this 2-3000 estimate has not changed for many years despite the confirmed numbers rising and they differ from the 5 to 10 times underestimate suggested by Raigmore)*.

There has been an overall increasing trend in the past few years which is partly reporting bias, partly genuine increase in tick populations in some parts of the UK, expanding deer ranged, milder winters, damp summers, increased recreational activities outdoors, increased numbers of imported cases, UK population going abroad and migrants from highly endemic areas. Lyme Neuroborreliosis has stayed steady over the last 5 years. He says this is good- sentinel (??). Much lower numbers than most of the rest of Europe. *(My thoughts- could have been taken straight off the HPA website- outdated information/attitude and no mention of under recording, doesn't seem progressive and interested in improving like the Scottish epidemiologist. Ridiculous to stop enhanced recording just because clinicians got bored, try something else or make it easier for them)*

**Panel questions the Panel consisted of Roger, Stella, Matt, Tim, Alastair, Warren and the Scottish GP though questions were mainly for Stella, Tim and Matthew.**

Q- will there be a nationwide re-education programme for GP's in light of the new research emerging?

Stella- difficult for GP's, they need short info. The LDA are doing a GP training video through RCGP- they need CPD points and this 20 minute video is being produced for that- they hope GP's will do it. PHE have put a leaflet out LDA want PHE to continue *(My Thoughts- PHE leaflet was super-brief, not at all sufficient and not very useful)*

Q- Alastair Miller mentioned that 33% of his patients their diagnosis was undetermined but they definitely didn't have Lyme, was he happy about this?

Tim Brooks- not we are not happy, we are working to close the gaps. Alastair Miller- no, we can't make them better, not possible to achieve a diagnosis- non specific symptoms- fulfilled CFS criteria. *(My thoughts- open your mind, do some reading Dr Miller and you might find that you can diagnose more of your patients rather than consigning them to the CFS bin)*

Q- who in the UK knows how to treat active Lyme with co-infections? And if you can't, will you bring in experts from abroad?

Answer (I did not record who)- Bartonella is not uncommon but they've not found much Babesia at the Liverpool School. Knowledge resides in the UK.

Q- how long should you treat Lyme for- an arbitrary time or until all symptoms have gone?

Matt Dryden- there are lots of guidelines, we follow international guidelines. We treat with short courses of antibiotics. He talked to some people at lunch- interesting that some people need longer courses of antibiotics and wax and wane- need more research.

Q (one of my questions)– Will Dr Drydens clinic prescribe long term antibiotics (more than 3 months) for patients if they are benefiting from them? Since there is uncertainty about whether persistent Lyme is due to ongoing infection or not. If patients relapse when taken off antibiotics, will they be given a repeat course?

Matt Dryden - Should be wary of lab results- you may not believe it but we respect that everyone is different. I'm not going to deny antibiotics if the weight of evidence is enough if there is benefit but need evidence of Lyme disease with clinical diagnosis- if EM rash- don't hesitate to treat with short courses of antibiotics- there is very little evidence that prolonged antibiotics has any benefit.
*(my thoughts- he seems to be wavering here, not entirely IDSA obsessed)*

Stella- there are no good quality European trials.

Q- Reliance of US labs- if people go to the states, how reliable is that?

Answer (didn't record who) People go to get overseas testing because they get a negative in the UK and they think they've got Lyme disease. The BCA has no accreditation- not specific to Lyme disease, doing the patient a disservice with unaccredited labs- better off investing in something else? *(my thoughts- BCA is awaiting accreditation certificate, it's pending. Igenex are accredited to the extent that they are accepted by many state health boards and have two insurance companies accepting their results. They are not FDA accredited because they refuse to use the flawed FDA/CDC criteria for western blots. They chose this question because it was an easy opportunity to criticise private testing).*

Q. from the floor- someone pointing out that there is a difference between accredited labs and accredited tests.

PHE- we have instances of CE marked tests being used inappropriately. Data needs to be made public from these labs so we can see the data- it needs to be published *(My thoughts- totally agree, but this also needs to be applied to NHS testing- total transparency is needed.)*Tests for Borrelia need to be specific, false negatives and false positives- both are bad. All tests need to be interpreted in the correct clinical context. (Someone from the floor points out that BCA do also use clinical picture, they diagnose with a range of tests and symptoms, you have to have two initial consultations there for a diagnosis).

Alastair Miller- testing if no symptoms or exposure to Lyme disease, don't test. Talks about a doctor (GP) who used microscopy to diagnose patients and was investigated by GMC. A test is a point in time, responses evolve. *(My thoughts-We all know who he is talking about. If they really looked at what other labs are doing re microscopy, they might find it a valuable tool- for instance the Romanian lab that uses it or Dr Alan Macdonalds work. I agree, it's time consuming and probably not going to be useful as a routine screening test but for serious/complex/persistent cases and research purposes, it's potentially useful- don't write it off so easily)*

Q. - Tony Bent- It should not be down to LDA and BADA to educate medics – it's an important role and public health should not be left to charities and it shouldn't be, negative blood test, you haven't got Lyme, PHE need to do more.

Then there was a discussion on education, I pointed out that there would be one quick, easy win if PHE would disseminate LDA's booklet on Neuroborreliosis- which I said has the information standard and might be very helpful to GP's. Stella said she'd like it to go to neurologists as they are the ones dealing with neurological symptoms. The lady from PHE said it was dependant on funding. I said that the booklet had already been produced (I think she was looking for excuses). A GP in the audience then said that GP's might be sceptical about information from a patient led organisation, so it needs to be PHE actively endorsing the LDA information.

Q . from Andrew Gold – convalescent serology of Chronic fatigue syndrome (CFS) had been mentioned – we need a formalised follow up process, at the moment it is all individually done and what are the outcomes for people?

Alastair Miller replied- Cognitive behavioural therapy for Chronic fatigue- 30% improve, 30% recover and 30% have no benefit from it. This is thoroughly recorded for CFS, unless we do it as a research project, we don't have the money to do follow-up.

Stella said that through the JLA process documenting uncertainties, they would be (or he could?) asking for funding from NHR for research like that.

Q. from Joanne Drayson – Dr Dryden has given patients aproforma to complete before they come to his clinic- a good idea- LDA could help fine tune that. This could be a way of following people up- by getting them to fill in the same pro-forma months/years down the line- cheaper than face to face consult.

Matt Dryden- possibly we can do that. It is important to define what chronic Lyme is. It's a non-specific illness-nebulous- what are we dealing with? Regular serological tests may help.

Joanne Drayson- there are GP's and a few doctors in the UK who have had personal experience of Lyme- can you work with them in your clinic?

Matt Dryden – yes (!)

Q. – what are your plans for a network of clinics?

Matt Dryden – across the country there are a network of ID doctors and paediatric ID clinics. Resource around the country already. We want to define what the clinical cases are.

Q- CDC have recently revised their stats on Lyme- are there any plans for PHE to revise their estimates?
Robert Smith – we don't have access to GP data – this might change in the future. Will it always remain a problem? Worth linking in with Liverpool to pick up additional patients.

Q- 90 cases neuroborrelisosis in 2011, what was the basis of the diagnosis?

Robert Smith- neurological symptoms such as facial palsy, have to be seropositive western blot.

Q- CDC say there are ten times the number of recorded cases- GP cases- this is important- expand it.

Robert Smith- we will explore it in the near future.

Q – Germany are using the EM ‘code’ for looking at the numbers of cases.

Roger Evans- looking at GP practices- we think it is 5-10 times more than recorded numbers- we need hard data. Need to do a database search of Scottish hospitals. Will take 18 months to set up. Want to move it to the whole of Scotland- we need this data if we are going to put forward our case for funding, we can only do it if we have good epidemiological data.

Comment from GP- what about the read codes – use these, but some patients have a Lyme-like illness and some definitely have Lyme, sometimes reluctant to put a read code to a lyme-like case.

**Tim Brookes – future plans**

In the UK there are no guidelines. It would be useful to have a set of UK guidelines. Guidance should be clear with a flow chart for GP’s, ID physicians. Each group of doctors will have a different take on it. It should be a dynamic document- needs constant updating. Unless we can take people from both sides with us, we won’t have those guidelines- a challenge.

There will need to be a wide team- GP’s, ID physicians, microbiologists, neurologists, rheumatologists, psychologists/psychiatrists, paediatricians, LDA and BADA.

Takes a long time- 2 years iterative process. Need to look at symptom association with different borrelia species. Plex machine- he wants to look at pattern of disease and using T cells, killer cells, boulder diagnostics. Tests need to be validated and cross referenced to clinical data. His dream study would be 2 parallel clinical studies following patients through their journey and the course of the disease (longitudinal) and cross sectional studies to help build up a picture.

Need help from clinicians and patients- patients have to consent.
Can only do this together, it will be demanding.

Punch biopsies of skin needed. CSF (lumbar puncture) will be an important part of teh study. 5-10 years time we will be a lot further on. As Jackie said, it costs money. Needs big research grants from major funders, NIH, MRC etc- competitive to get funding. Even with good bids- don’t necessarily get the money. Need an action plan, what is one? (this question was left hanging).

Q- from the floor- NICE guidelines, are we in danger of re-inventing the wheel- IDSA/EFNS?

Tim Brooks- EFNS guidelines are not v useful or helpful. NICE would be good but they have a long queue and backlog of work. We want to do it according to NICE principles so they are pseudo NICE, a compromise.

Q. from Joanne Drayson- were they aware of the work of Lyme research UK? Maybe Kate Bloor would be useful.

Tim Brooks- she had been invited to be on the panel, she said she could help when and if she was able.

Q from myself- I said it was a very good thing that Dr Drydens clinic was starting but I felt that knowledge in the UK still lagged behind that of some overseas Lyme doctors (said I was being treated by a doctor from America). Would they consider bringing in foreign doctors to work with them?

Tim Brooks- said they would if foreign doctors were using evidence based medicine, said it might be difficult to get them to participate as partners in studies- I said that is true, but they are not all quacks I felt the level of expertise far outstrips that of the UK and some such as my doctor were fairly conventional. Tim reiterated the need for evidence based medicine. *(my thoughts- define evidence based???, how much evidence is used currently in so called 'evidence based' medicine- sometimes very little!. I felt it best not to push this point further and the chair was pressing to move on)*

**Lady Mar- concluding remarks**

*Borrelia burgdorferi* was very clever. We are all different- she hopes that the gulf has been narrowed a bit. She was reading about cyberchondria in the telegraph. Most people don't have this- they are not cyberchondriacs. She turned to Matt Dryden- Matt please keep your scientific curiosity. Policy makers- please fund this work and get sick people well. She remarked that the presentation of Roger Evans was good. It will be a long time before we get results- Tim confirmed this. Very interesting day, intense and there is a long way to go and a lot to learn. Information exchange. Do not forget the patients who are a huge source of knowledge.

**Points of conversation that I had afterwards with Dr Dryden**

Dr Dryden came up to me to speak to me after the meeting. He asked about my doctor. I told him it was Dr X, he said he had heard of him (which I thought encouraging). He asked what the treatment regime was, told him pulsed combination oral antibiotics with antiprotozoals and biofilm/co-infection treatment. He asked if Dr X gave Steroids- I said NO!!! Never, totally contraindicated with Lyme. I said Dr X treats with conventional medicines, using the available published research but that he recognises that there is not much data on long term treatment and as such he treats patients empirically, and according to their response. He asked how do I know I wouldn't have improved anyway, with time (not on antibiotics). I said that I relapsed after a couple of weeks when stopping antibiotics.

We talked about culture of Borrelia- he doesn't know the details of the Inverness culture method but is interested in culture. I asked about the possibility of using ALS culture method, said they may be opening a lab in the Netherlands. He seemed interested- he said for research purposes (culturing different strains) and for diagnostic purposes. I suggested he contact Eva Sapi, he said he would email/phone her.

I asked would he consider re-treating patients with antibiotics if they were responding but relapsed after his 3 months were up. He said that would be interesting. I said he should bear in mind the JLA uncertainties and the fact that we don't know if chronic/persistent Lyme is active infection but it could be. He acknowledged that uncertainty.

I talked to him about the Abbott-Plex machine. Told him Dr X said he thought I had coinfections, Babesia, Bartonella, possibly Ehrlichia and Protomyxzoa rheumatica. He raised his eyebrows. I said I thought new machine was very promising. He said they hadn't found many co-infections so far but he conceded that they hadn't seen many patients to

test so low sample size. He said these people had been tested elsewhere (I think he said Liverpool) as the Abbott-Plex was not yet up and running. He said the clinic is booked up until the end of December. I thanked him for taking an interest and being open minded.