

Lyme Disease: Evidence for Change

A Seminar in the Grand Committee Room, House of Commons, 10th November 2008 at 2 pm.

Chaired by Hugo Swire MP

Miss Mel Clarke

Mel Clarke, of Taverham, Norfolk, already suffering from Reflex Sympathetic Dystrophy, was diagnosed with Lyme disease after collapsing in 2003 whilst competing at the World Archery Championships in America. The disease has left Mel paralysed from the waist down and blind in one eye. She currently holds 20 county records, 10 national able-bodied records and eight world records. Mel recently won the Bronze medal at the 2008 Beijing Paralympics.

Summary of the points made by Mel Clarke: In 2003, I went to New York, I was fine. I was in New York for the World Archery Championships. I was having a good time, then I became suddenly ill. During the next 4 weeks I was in intensive care on life support. My Dad had been phoned and told that I had 24 hours to live. He came over to New York. Whilst I was in hospital various infections were tested for and antibiotics were given to me. I was finally diagnosed with Lyme disease. I was given the antibiotic treatment and I came out of the coma. In my case I had had a massive encephalitis which has affected the nervous system. I am now disabled. Because of my high profile in the press, I was in the news. As I was in New York with Lyme disease, they knew what to look out for. I was referred back to the UK for rehabilitation and treatment at home. I do it all at home (now). I went to a top neurology consultant and he said "Lyme disease – what's that?" I carried on with the antibiotic therapy – as an outpatient. People said I would 'never walk' and never do archery again, however, I carried on and I did all right from then on.

Mel's father went on to say: - Mel didn't know much (at the time), I was told she only had 24 hours to live. When we got to New York, we couldn't believe what we saw – and I'd never heard of Lyme disease. However, encephalitis had set in, Mel's brain had swollen and that caused the disabilities. It was 2 and a half weeks and then Mel came out of the coma and started coming round. She had no speech and she could not move, or, if she did move she passed out – this was all down to the encephalitis. Here, in the UK, nothing was known by the GP, nor by Norwich Hospital. If it weren't for the fact that she was in New York, now I think that if she had been in this country she might have died. Our medical bill was enormous, thank goodness it was covered by insurance. Treatment in the US was good. They knew what they were doing there, there is a lack of knowledge here and lack of follow-on treatment.

Mr Swire thanked the Clarke family.

Mrs Stella Huyshe-Shires

Stella, a constituent of Mr Swire, worked in IT for the NHS for many years until she had to take early retirement on the grounds of ill health because of her Lyme disease. She is now an active participant in Lyme Disease Action, aiming for an improvement in the diagnosis and treatment of Lyme disease in the UK.

Summary of the points made by Mrs Stella Huyshe-Shires: I want to use my history to illustrate why so many people have contacted their MPs about Lyme disease. Some of what I am going to say, may seem a little hard and one sided, but I would be doing a disservice to patients if I did not talk today from the patient's point of view. My patient pathway started in 1999 with a 15cm expanding circular rash. I did not know about Lyme disease and neither did my doctor. I only considered the diagnosis 3 years later when I read something in an agricultural magazine, the symptoms fitted and I insisted on a blood test which was positive. Six months after treatment I still had new and continuing symptoms and over the years have been told by a neurologist, rheumatologist and infectious diseases consultant that I have had adequate treatment. Thus my symptoms "cannot be due to Lyme disease." An immunologist refused to see me because she was 'unable to help with post-infectious disease syndromes.' Recently the neurologist has declined to address dermatomal itching (due to spinal nerves) and has passed the buck to a dermatologist. My patient pathway is represented by a maze that has had many entrances but every one leads to a dead end.

The situation in 2008 is no better (Talk illustrated with quotations from other patients of experiences in both primary and secondary care illustrating the lack of awareness amongst doctors). Many people are refused

treatment because of negative blood tests. The test for Lyme is complex. It is not a straightforward yes/no/colour change on a chart. GPs don't always understand that, but the Manufacturer of the blood test kit states "Negative test result should not be used to exclude Lyme disease".

Stella illustrated patients' experiences with a diagram of a brick wall with a sign representing the IDSA Guidelines. It is the UK adherence to these Guidelines that prevents further consideration of the patient's predicament. The official position seems to indicate that there is nothing wrong with this situation. This was illustrated by a quotation from the Department of Health:- "There is adequate diagnostic capability in the NHS." Stella asked where this capability was because from the quotations everyone could see that it does not rest with doctors. Maybe it lies with the Lyme Reference Unit; but they only see the test, never the patient. This amounts to second hand diagnosis without responsibility.

The Department thinks evidence of tick bites is necessary, yet, in a recent study in the South West, amongst confirmed Lyme disease cases, 46% did not report a tick bite. Yet, we are told, one can't diagnose Lyme disease from non-specific symptoms. Frequently though that is what you have in this disease – a set of non-specific symptoms. The Department claims there is no new scientific evidence on the diagnosis and treatment of Lyme disease which makes one wonder whether they read any scientific literature.

There is evidence of a widespread lack of awareness of Lyme disease. GPs don't recognise the rash and think Lyme doesn't occur in their area; Consultants don't recognise the symptoms and the Lyme Reference Unit (at Southampton) relies on the tests but doesn't seem to apply them correctly and never sees the patient. Although awareness amongst patients is increasing, this is no good unless clinicians are also aware because if you open the floodgates then primary and secondary care will become swamped and will be seen to be failing.

What are the consequences of this lack of knowledge? Patient distress, cost to the State and patients buying antibiotics on the internet.

All this damages the reputation of the NHS.

Stella quoted a recent discussion with a vet who knows how difficult Lyme disease can be. Because vets know it works, they are treating donkeys at the local donkey sanctuary with long term high dose antibiotics. Donkeys!

Hugo thanked Mrs Huyshe-Shires. If you would like to see a Powerpoint presentation that accompanied Stella's talk please visit: <http://www.lymediseaseaction.org.co.uk/>

Mr Swire introduced Dr. David Owen.

Summary of points made by Dr David Owen: Many of my medical colleagues have never heard of Lyme disease or chronic Lyme disease (persistent Lyme disease).

When I was preparing for this talk, I was a little alarmed when some people referred to the "UK Guidelines", because I wasn't aware there were any, but in all cases, they were actually referring to what are called the IDSA Guidelines (Infectious Diseases Society of America Guidelines). There are also some published Guidelines by the ILADS group (International Lyme and Associated Diseases Society). These two sets are the only ones that people are referring to. I will compare and contrast the 2 sets of Guidelines. (Dr Owen holds them up – IDSA Guidelines (turquoise cover) compiled in 2006 by IDSA, they are peer-reviewed and have 393 references; and the ILADS Guidelines (Purple cover), also peer-reviewed with 65 references.

In the IDSA Guidelines, 5 authors declare conflicts of interest.

In the ILADS Guidelines, no conflicts of interest declared.

Both Guidelines agree that early treatment is important.

ILADS say that prompt use (of treatment) is needed to prevent the development of chronic Lyme disease.

Opposing examples can be given:

David showed an (anonymised) picture of the leg of a patient:

-This picture shows multiple Erythema migrans (EM) rash, but, this patient tested negative for Lyme disease. However, this patient did well by being given prompt treatment having shown clear clinical signs.

David contrasted this with the case of another patient with no history of tick bite, no rash, no EM or ? possible EM recorded, yet, this patient tested positive for Lyme disease. But most doctors would not know about this. Best to start treatment straight away and this patient also did well on treatment.

Both sets of Guidelines accept that Co-infection (with other tick-borne pathogens) may be important.

Who treats Lyme disease?

According to IDSA, all specialities may treat it, but in reality this does not happen.

According to the BNF (British National Formulary) "Lyme disease should be treated by those experienced in its management."

There is a differing vocabulary between the two sets of Guidelines.

Persistent infection – IDSA say this is implausible in the absence of clinically objective signs.

Comparison between the IDSA and ILADS Guidelines – (see accompanying powerpoint slides).

David Owen continues:-

There are difficulties in designing studies – case definition is difficult; case matching is difficult.

The two sets of Guidelines differ in this situation vis a vis the patient. IDSA don't recognise

ILADS say that informed choice should occur for the patient.

There is a concept of Two Standards of Care, one embodied by the IDSA approach and the other by the ILADS approach.

Conclusions

*The two sets of Guidelines cannot be reconciled.

*Unknown numbers are involved.

*Length of treatment based on clinical response (ILADS) as opposed to a rigid statement of length of treatment (IDSA).

*Informed patient choice should be key.

Mr Swire thanked Dr Owen. If you would like to see a Powerpoint presentation accompanying Dr. Owen's talk please visit <http://www.lymediseaseaction.org.uk/>

Mr Swire introduces Professor Sarah Randolph, University of Oxford.

Professor Randolph is Professor of Parasite Ecology in the Department of Zoology, University of Oxford.

Professor Randolph has studied tick ecology as a fundamental basis for understanding the epidemiology of tick-borne diseases since 1970. She is now exploring the causes for the massive upsurge in incidence of Lyme borreliosis over the past two decades – artefact, environment or a complex nexus of biological and non-biological (human socio-economic) factors?

Summary of the points made by Professor Sarah Randolph: Is the increase in cases of Lyme an artefact? Is it environmental? Or Can it be due to Human socio-economic factors?

I am a biologist not a clinician. There is Lyme disease in the UK.

The tick species involved is *Ixodes ricinus* and it can be found at the top of the vegetation, waving forelegs and looking for a host. They can carry the organisms causing Lyme borreliosis, these organisms are spirochaetes.

Where do they occur? Sarah showed a map with dots indicating the field stations where figures are recorded.

Like any recording, it is incomplete – one has to look for correlations – extrapolate and make a risk assessment.

These things are called Predictive Risk Maps and they do match observations pretty well.

Ticks are to be found throughout the UK, but they are not everywhere. They favour certain environmental conditions, especially woodland. Due to the robust nature of the transmission of *Borrelia burgdorferi*, wherever there are ticks, there are *Borrelia* bacteria, to a greater or lesser extent.

Graph of cases of Lyme borreliosis, laboratory confirmed. (This shows a graph with a step-wise increase over recent years).

Some of the steps can be easily associated with changes in public health surveillance.

i.e. (1) There is a step increase in recorded cases between the time before surveillance and the point of surveillance commencing.

(2) then another step when enhanced surveillance commenced.

These moves improved reporting, and the increase in incidence shown on the graph can be ascribed to known causes.

However, the graph shows two further step-wise increases and we don't really know what these are associated with.

There are estimated to be 1000 to 2000 clinical cases diagnosed without a laboratory test, and this is fine, there is no problem with this.

What is the evidence? Has there been an actual increase in ticks? (i.e. a real increase in tick numbers, not just in reporting).

It is not possible to do retrospective studies, but a survey approach has been possible.

We put around a questionnaire (to the field observatories) in the UK as to the presence and abundance of ticks. We had 173 replies of which all agreed that ticks were present both now and in the past. 122 of the reports did give relative tick abundance and indicated that it may have increased over the last 50 years.

Only 8 reports indicated a decrease in ticks over the last 10 years.

It is clear there is a strong association between ticks and deer. Why is there an association between ticks and deer? The tick relies on deer. Each tick life stage feeds only once on anything that passes.

The larvae (i.e. Newly hatched ticks) quest low down in the undergrowth – Will take a host of any size but they do tend to be things that are low down e.g. Small mammals. Nymphs quest at a mid-level in the vegetation, and tend to latch onto mid to larger hosts, and this can include humans. The adults quest a bit higher still and tend to latch onto the larger passing hosts such as deer (and humans again are incidental hosts). Abundant deer will therefore maintain an abundant breeding population of ticks. The *Borrelia* bacteria has a wide host range - i.e. They can use lots of animals as transmission hosts. The only exception we know of is deer. Deer are not active in transmission, but lots of deer does equate to lots of ticks.

Roe deer have increased in the UK over the last 10 years. There is quite a compelling correlation with Lyme borreliosis cases. Is it co-incidental or causal?

Fallow Deer too have increased. There is a spatial correlation which makes us ask whether this is underpinned by causality.

This might give a picture of an increase in deer, meaning an increase in ticks and hence, an increase in Lyme disease cases.

However, changing methods in sheep husbandry may be relevant.

Sheep are no longer dipped to kill parasites such as ticks in the fleece. When sheep were dipped they acted as 'lethal mops' i.e. Attracted a lot of ticks which were then killed by the pesticide.

Also there has been a decrease in the farming density of sheep, so ticks must look further afield for a meal. An increase in tick numbers might be an unexpected consequence of laudable changes in agricultural practices.

Other factors may include the greater emphasis on outdoor recreational activities.

In addition, of course, there is the question of 'Is changing climate involved?' Our work indicates minimal impact on tick abundance but maybe the advanced onset of Spring, if it co-incides with a human holiday such as Easter, may provide an additional boost in case numbers, which might be a further (partial) explanation for the rise.

Two problems needs addressing:

*Problem of Missed diagnosis – Increase of serious symptoms. Awareness of the disease amongst GPs improved but still low, but Sarah felt, don't brand all of them as unknowing.

*Problem of Misdiagnosis – cases of tick-borne disease are non-specific and resemble other illnesses of unknown cause, for example ME, CFS, MS. There are unorthodox doctors and patients following antibiotics regimes which could be harmful. Best opinion says – there is no chronic infection. Whether or not this is treatable with antibiotics is a great controversy.

Mr Swire thanked Professor Randolph and **introduced Dr. Sue O'Connell** who is the head of the Health Protection Agency (HPA) Lyme Reference Unit at Southampton. HPA was made a special health authority in 2003 when it received a new mandate.

Summary of points made by Dr. Sue O'Connell: First of all I'd like to say how sorry I am to hear Mel's story. I am surprised that Norwich did not know about Lyme disease. There has been research in the area, Thetford Forest is a Lyme research area. This has happened over 15 years and done by a group from Charing Cross Hospital. So it is disappointing that this has occurred and I am very sorry about that.

We provide reference testing for the UK in England and Wales. (Scotland has its own centre).

We at HPA promote prevention rather than pick up the pieces. We are trying to increase awareness and we do joint collaborations on this. A EUCALB collaboration is currently reviewing the European guidelines collected from France, Switzerland, Germany and the Netherlands. All have their own guidelines – and they are all very similar to the IDSA guidelines. However, they are not in English, so, we recommend the IDSA guidelines because they echo all the things in the European countries own guidelines. It may be that we will make a stronger recommendation for oral antibiotics in neuroborreliosis.

Lyme borreliosis

- *Not new, there was a report of a recognisable case recorded in 1883.
- *It has been extensively researched – a lot of money has been spent on it and there is a lot of knowledge.
- *It exists in many temperate areas of the world.
- *There is some variability between European and US *Borrelia* types but there are similarities too.
- *Sue felt the differences are over-stated.

It is caused by spirochaetes. These, for instance, are the same type of organism that cause syphilis. There are three Lyme disease types in Europe, they are *B. afzelii*, *B. garinii* and *B. burgdorferi sensu stricto* (found more in USA).

All three can cause Erythema migrans (EM) and nervous system complications.

They can cause arthritis symptoms too.

Interesting to note that of the organisms found in Europe, the further west one goes, the more one tends to find *B. valaisiana* in the ticks. *B. valaisiana* is non-pathogenic and so dilutes the rate of Lyme borreliosis.

Thus we see a lower rate of infection on the west of Europe than in central Europe.

There are 200,000 cases per year in Europe with the highest numbers being in Eastern and Central Europe. Scandinavia has high rates too. Over 90% of cases result in EM only.

Complications affect the nervous system, the joints and the heart.

The illness is treatable at all stages but one does want to treat it early, because that ameliorates so much tissue damage occurring. Late neuroborreliosis occurs at rate of less than 1 in a 1000 of untreated infections. These figures come from Germany. Neuroborreliosis is shown by palsy and meningitis. We do see a more indolent neuro-expression in Europe and not so much of this presentation in the US. This can result in an MS-like state, but, Sue stated, Lyme does not cause MS or MND.

Response to treatment:

You can always treat a case of Lyme disease.

There is no evidence of resistance developing and penicillins, tetracyclines and cephalosporins can be used. Some patients will take time to recover. The disease is serious and it will take time to recover. Some patients do have symptoms following on.

I am not going to go into the Tests today.

None of the symptoms are diagnostic. Laboratory tests are there to help.

Antibody tests are used, and these are to look at the Immune system response to infection.

In late stage – tests are good to 99.9%. But antibodies are often not there in early disease. This is similar to HIV where you get a window of apparent negativity before a positive result develops.

You can get false positives.

There is concern about unorthodox tests and unvalidated tests used in some laboratories. It has been shown that false positives are as high as 50%.

Work on this field will all be published soon.

Chronic Lyme disease

What does this mean?

*Late disease can occur in a previously untreated patient, and we do see late disease, and those people require treatment.

*In some studies, there are up to 40% with no clinical Lyme disease, i.e. This is misdiagnosis.

*There are patients who have had Lyme disease in the past, but now they have another condition and this is a missed opportunity to treat them for a current condition.

*Persistent Lyme disease: - Patients require careful assessment for possible treatment failure, and re-treatment if there is any doubt.....

*How much of a patient's symptoms is underlying tissue damage?

*How much (of the apparent symptoms) are another disease?

Disease Severity

Prevention and early recognition is the best strategy against this.

Why do some patients follow the Post Lyme disease syndrome type? .A pattern that also happens in other diseases. (For example there are parallels in the situation and a similar picture is recorded in: Epstein Barr virus, Q fever and Ross River virus infection).

What is the evidence of Persistent Infection?

*Need to keep an open mind, studies are continuing.

*It does occur in immuno-compromised animals, yes. There are immune-altered mice, and mice are reservoirs for *Borrelia* bacteria (very tolerant of them). The mice studies have flaws and mice clear

antibiotics rapidly, the dose in the studies would be cleared in 16 hours and no antibiotic left. Whereas in a human it would be 24 hours, so this study does not reflect the human condition.

*A lot of studies into Post-Lyme syndrome – show there is no good evidence of continuing infection. Sue recommended a review by Dr. Adriana Marques.

Commenting on the ILADS guidelines:

Case definition and symptom list – both non specific.

Put ILADS non-specificity to consultant colleagues and they were horrified (that it is being used for diagnosis). References in the ILADS guidelines – Sue has some issues with them, some are non-Medline references, others are only conference reports, so they are not peer-reviewed. Sue offers to go through it with anyone.

IDSA guidelines use selected quotations from good papers and the citations are accurate.

In ILADS guidelines, there is an over-reliance on early studies – when patients got inadequate treatment by modern standards and the tests were less accurate.

Not everything is hunky-dory, but we have to work from the best available evidence.

Mr Swire thanked Dr. O'Connell.

QUESTIONS

Questioner 1: - asked what the HPA is doing about raising awareness and amongst GPs? And about disease prevention in general? The questioner lives near Richmond Park and the doctors she saw there knew nothing.

Dr. O'Connell replied that she was surprised at this, since there have been efforts to inform GPs in that area. Kingston Hospital have run Seminars. As regards how the HPA works is this – it operates in areas throughout the UK. The HPA Unit has liaised with local doctors and with the Royal Parks.

Questioner 2: We should be unhappy about the general lack of awareness. The lack of knowledge in Norwich (Mel Clarke's area) and Richmond, despite heavy HPA involvement in both areas, demonstrates that nothing is working so far.

Dr. Owen agrees. It is important that there is an increase in awareness, because testing is problematic.

Mrs Huyshe-Shires: Regarding the complaint that ILADS case definition is non-specific, one has to ask, apart from EM if present, what are the specific symptoms of Lyme disease?

Dr. O'Connell: Using non-specific symptoms does not give a diagnosis. By all means put Lyme disease into the fray but one must also consider the alternatives.

Dr. Sarah Chissell, consultant obstetrician: - As regards non-specific symptoms, we (clinicians) look at the patterns that are occurring, we must develop a sense of the pattern of an illness. Do you see patients?

Dr. O'Connell: I do see patients, I have no in-patient beds but I do go on the wards, I am not just in the laboratory.

ID consultant 1: Many infectious diseases have non-specific symptoms that are attributable to infection. Differential diagnosis for Lyme disease – non-specific symptoms. If you are a 'lumper', these can be considered to be in the chronic fatigue group. Need to know which of these are specific for disease and which haven't the ability to distinguish a disease. But this (Lyme) is not common. Common things are common. How do you make a diagnosis of Lyme? Maybe a challenge with intravenous Ceftriaxone might be helpful. Often tests are not positive. But if the patient has a tick bite, then you have a therapeutic dilemma.

There is a danger that patients think they have Lyme disease and they haven't.

Dr Owen answers him: From the point of view of those of us who diagnose – it is difficult to know who will respond to treatment and who will not. For instance, in chronic fatigue – one can be disappointed. But one cannot distinguish who will respond to treatment in advance. If there is a history of a tick bite then we must use clinical judgement. Patients who've had one or two courses of antibiotics by the GP and not got better – Is it still Lyme? - I look for other things, not just antibiotic failures. I'm not seeing a way round this, but the IDSA guidelines are too mechanical and likely to result in doing nothing.

ID consultant 1: There may be other ways they could be treated if antibiotics fail. I think it unlikely that spirochaetes are in the body. So then, antibiotics not important (in therapy). If we've not got therapies, then patients have to use self-help strategies – for instance, in chronic fatigue, there is a major trial (of self-help type measures) going on at the moment in chronic fatigue research.

Dr Owen: If antibiotics are not helping, may need to continue rather than have an insufficient trial. Perhaps keep going longer. There is nothing to guide us.

Dr. O'Connell: What is not appreciated is the Anti-inflammatory effects of some antibiotics (esp tetracyclines and beta-lactams). Doxycycline has anti-inflammatory properties and has been trialled as an anti-inflammatory and more recently Ceftriaxone shown to have powerful neuro effects. National Institutes of Health looking into it. Modified Ceftriaxone looked at as a possible treatment for MND and this has nothing to do with the antibacterial effect. People need to consider this.

Anne Milton MP, Shadow Health Minister: Today has raised many issues. Thank you for the organisation of today. Very useful. I have constituents with this diagnosis. Onto mundane fact: Patients need diagnosis and early intervention. True of Lyme and true of other common conditions. Need to raise the breadth of GP knowledge. There is an opportunity for government to influence this – maybe CPD payments for incentives to GPs. Lots of conditions e.g. Diabetes, epilepsy, mental health - all benefit if identified and treated early. And the consequences with Lyme disease are serious.

Mrs Stephanie Woodcock, LDA: A few comments about own case. I found that when I had this illness (25 years ago), I had to keep on treatment for 9 months before I was even sure I was recovering. I had to at that stage, consider this as therapeutic diagnosis, nothing else to base it on in those days, would infectious disease specialists like to comment on such a case?

ID consultant 1: You may well have got better anyway.

Professor T. Daymond: Thank you (to the consultant) for making it clear that you do look after the patient. Even the indeterminate patients need to be looked after as patients. Peer-reviewed papers say – it is not the test that is crucial in this, it is a clinical diagnosis. Some may be Lyme disease, some Chronic Fatigue syndrome and Lyme disease may be a cause of ME. But we need to think of the patient, and doctors often don't look after the patient – they tell them to go away, time and time again.

ID Consultant 2: An initial diagnosis is like looking down a telescope – one is fairly certain what one should be doing. Some patients will have a different diagnosis (to the one proposed) – those patients are very unlucky. Patients benefit very much from early treatment. This is what should all be aiming for. HPA can tell us about things, but it is not their job to train doctors. Doctors must listen to patients and consider the possibility that the patient may be right. Not necessarily think that if the patient suggests it, it must be wrong. Patients do know things. And baby ticks are so small. May have to listen to exposure. Late untreated Lyme disease – very often – subtle features – recognised especially skin, nerves and brain, but heart features rare. You can treat and should treat them until they have stopped getting better. Rarely several months empirically – quite risky.

There is a problem of people who feel ill and have lots of symptoms, it's very frightening and it is not a specific disease – a lot of time and tests – and there is no sign of inflammatory disease in the tests then they are unlikely to have Lyme disease. There are diminishing returns in antibiotic treatment. Patient says 'I feel ill', so I must have treatment. Trying things empirically, often they don't help. Lyme disease is a spiral bacteria – comparing with syphilis, treating in late syphilis usually futile to treat and the footprint of the disease remains.

Dr Owen replies.: You say Inflammatory markers would be raised in Lyme disease – I'm not sure all would agree with that. Indeed, there is an absence of any certain biomarker for chronic LD. If there were a simple inflammatory marker we could look out for, that would be great, but there isn't.

ID consultant: always raised inflammatory markers in Lyme disease.

ID consultant 3: Looking at our cases of Lyme disease, if they have Erythema migrans, we give them medication there and then, we've only had three treatment failures and one of these responded to re-treatment. Looking at patients with chronic ill health and the label Lyme disease And fatigue – very difficult to assess. We look for Q-fever and Brucella, no hints for Lyme disease especially in not-treated individuals. Serology ought to be positive if it is chronic Lyme disease. I have an example of a patient result slip (from an unrecognised lab) and at the base was the proviso (from the lab) saying the results were only for research purposes not for treatment or diagnostic use. Some of these retested blind through Fort Collins (CDC laboratory) and positive results never materialise. So, we have to interpret tests in the light of circumstances.

Dr. O'Connell: Makes the point that there is a loophole in US licensing law, if laboratories use in-house tests, they don't have to be FDA approved and these are 'home brew' tests, they are not required to go through the regulatory hoops that standardised tests do to meet the stringent requirements for licensing etc. Unorthodox interpretations of Western blots – only 50% specificity – these are expensively unreliable.

Mrs Huyshe-Shires: UK tests are very good for the 3 (named) bacteria, yes, but even so, some patients will fall outside of this, and negative tests should not be used to exclude Lyme. Patients are driven to unorthodox tests and if the NHS is failing them, patients look elsewhere.

Dr. O'Connell: One should not rely just on tests to confirm or exclude Lyme. Have to bring clinical skills into play. If there is a low prior probability of Lyme exposure followed by a positive test – one has to ask, is it a true positive? However, in these circumstances, the chances of it being a true positive are not high. This could lead to misdiagnosis and mistreatment. The clinical presentation should be properly evaluated. What is the possibility of Lyme being present? Doctors need to order tests wisely. If they truly think it is Lyme disease, and if the test is negative – it is possible to discuss and have additional tests, does not prevent one from managing the patient appropriately.

Professor T. Daymond responds: Why don't we have something to record this in the UK, a register for Lyme disease patients? Why isn't Lyme disease notifiable?

Dr. O'Connell : One of the reasons for notifiability is because immediate action is needed as regards something highly contagious. My colleague Dr. Monnickendam knows about notifiability, I'll ask her to comment.

Dr. Monnickendam, HPA: There are several infectious disease reporting systems. Oldest is notification and this is 100 years old and relates to easily spread diseases. It gives a legal requirement on doctors. Other systems for reporting are: Laboratory reports (voluntary) from microbiology labs, and one example of this is Lyme disease (i.e. Not infectious to others). Reporting is an effort to get Information.

Dr. O'Connell: No Disease Register as such in the US. In US, some compulsory system and statistics to CDC. Recently changed slightly and will look at serious manifestations as a sentinel for what is going on in highly endemic states. In the US, Lyme disease is focally endemic, i.e. Not present to a high degree in all states, some States have low incidence.

ID consultant 1: – Main message. There is a case definition crisis. There is no register, so we cannot register cases. Long term chronic patients - big problem - no case definition. What does one mean by chronic Lyme? I refer you to the Oxford criteria - which is a set of case definitions for research purposes.

Mr Clarke (Mel Clarke's father): We've heard a lot of very clever medical people, I'm just a lay person but to me it is strange what I have heard - it does not affect us directly because luckily Mel was in the US, but there is a lady in Norwich, a headmistress who was going from doctor to doctor. She saw Mel in the paper and then she was diagnosed with Lyme disease. It seems people have to push and push and eventually, against reluctance, they get diagnosed. Pushing against reluctance, to accept it exists. Clinicians should listen to patients.

Mr Swire asks the Panel of Speakers for their final summaries.

Miss Mel Clarke: - I was in a room and there were 3 or 4 possible diagnoses. They said that to me. I am glad they found the right one. I am doing OK now, so far, thank you.

Dr David Owen: At present there is no gold standard test, there is no certainty how good current testing is. Western blot is at best 50% . This is causing big problems and yes, false positives occur, and in someone who is otherwise well. At present Lyme should be a clinical diagnosis.

Dr. Sue O'Connell: In well validated studies that have been done, in patients with early Lyme - the antibody test is not good. It is only identifying 50% in early Lyme. But after that, later infection, it is not the same, good studies show that actual pick up rate of cases is good. Professor Wilske, who is pre-eminent in the world in this field says that in excess of 99% late stage Lyme disease cases are seropositive. I do take the points. New ways of reaching to clinicians to raise awareness of Lyme. GPs to take part in a tick bite study - will help quite a lot to highlight the problems and risks with the general public - to be aware of ticks and their risks. The risk of tick exposure is what we want people to be thinking about.

Mrs Stella Huyshe-Shires: I note Dr O'Connell says that further studies into persistent infection are needed. And we need UK guidelines. I hope that we don't make the US mistake by only including on the panel those

who only have one point of view. We have not raised that matter today but I hope the UK will have a better science-based position than that.

Professor Sarah Randolph: We haven't had the opportunity to talk about underlying causes for the increase in cases of Lyme disease and other diseases. Changing practices is relevant for the government to take on board and address.

Mr Swire read out the current EDM signed by 88 MPs.

Mr Swire thanked the speakers and closed the meeting.