

Letter to the ME/CFS/FM community in response to comments under the heading "Lyme disease - let's dispel the myths", by Dr D. Ho-Yen, October 2006 ME Essential, published by the ME Association, UK.

Mists and Myths swirl around Inverness

By Annie Drummond

Scotland is a land of mists, mountains, and malicious ticks. Sorry Scotland, I love your beautiful country and your hospitable, friendly people, but it is where I was bitten by a tick which gave me Lyme disease (also known as borreliosis.)

Several researchers have found that many patients diagnosed with myalgic encephalomyelitis (ME), Chronic Fatigue Syndrome (CFS), Fibromyalgia (FM) (1,2,3) and Multiple Sclerosis (4,5,6,7) have borreliosis, as do a certain proportion of psychiatric patients (8,9,10).

Scotland has its very own Lyme diagnostic laboratory at Raigmore Hospital in Inverness, while the rest of the British Isles relies on one reference laboratory at Southampton in England. At Raigmore, Dr D. Ho-Yen is the chief microbiologist and has been interested in ME for many years. In fact, he published the first "How to treat ME" book in 1985. He maintains that only a small minority of ME/CFS patients could have Lyme disease as the cause of their illness (11). But is he right?

Lyme disease was brought to worldwide attention in 1975, but its history goes back further (12). However, Ho-Yen in 2006 still feels that he must call Lyme an "emerging disease". Perhaps the pandemic levels (13) that have now been reached have allowed the illness to "emerge" from the cloak of silence that has covered the spread of the disease in the UK. Yet as far back as 1989, i.e. over 17 years ago, the World Health Organisation was aware that the whole of the British Isles, plus Scandinavia, Germany, Austria, half of France, California, areas South of the Great Lakes, and other areas, were endemic for Lyme disease (14).

Ho-Yen has recently admitted that his laboratory missed 33% of Lyme cases (15). He retested old serum samples for the year 2003 to 2004, using different methods of interpretation, and found that previous negative tests were becoming equivocal or strongly positive. One is left to speculate how many suspected victims over the last 30 years have been retested, if any, using these new criteria, and how many patients have been recalled for further investigation. It is admirable that Ho-Yen has published these results, but they sit uncomfortably with his latest pronouncements on the ME/Lyme question.

The ME charities, Action for ME, the ME Association and the TYMES Trust, have relied on Ho-Yen to inform the ME community on the relationship between Lyme and ME in the October and November 2006 issues of their recent magazines. Many scientists and commentators, while not disputing his personal findings and his integrity, would wish to respond to some of the statements he has made in these articles.

There are 6 so-called "myths" that Ho-Yen identifies as current in the Lyme world; each one will be discussed in the light of knowledge available. A very different picture from the one he paints will emerge.

Myth 1: The Internet has the best information on Lyme disease. Verdict: True. This is not a myth. The Internet is the source of millions of archived peer-reviewed scientific reports. We all use the Internet; most of us would be lost without it. The data is more accessible and available to be used more readily; researchers no longer have to physically retrieve dusty documents from medical or university libraries.

To be fair there is a lot of rubbish on the World Wide Web, but it is the easiest place to look for the very latest research. Ho-Yen suggests that it is almost impossible to discern the rubbish from the good material, and at first it can be difficult. However, a recent peer-reviewed paper from 2005, authored by several of the most experienced doctors and scientists working in the Lyme field (16), gives a very useful overview of the data available on the Internet and how this relates to their clinical experience.

Myth 2: Doctors are ignorant of Lyme disease.

Verdict: True. This is not a myth and is definitely true in Britain. Please ask your GPs, whether rural or urban [(Richmond Park, as well as other London parks, has been found to harbour Lyme-carrying ticks (17)] if they have heard of Lyme, or of borreliosis, or of the latest infection rates being reported in Europe?

Most doctors, and members of the public too, think of it as an American disease, (that is, if they have heard of it at all!). But the increasing number of cases across Europe is a cause of concern. For example, in Holland (18), the incidence of the "bull's eye" rash, Erythema Migrans, (EM), which is pathognomic for Lyme disease, was estimated at 39 per hundred thousand in 1994, which doubled to 74 per 100,000 in 2001, and tripled to 103 per 100,000 in 2005. In southern Sweden (19), the mean annual incidence rate in 2005 was 464 cases of EM per 100,000 inhabitants. The incidence was significantly higher in women than in men, 505 and 423 cases per 100,000 respectively.

These are epidemic rates of infection. Britain's approximate incidence figures, quoted from the Health Protection Agency (20) are no greater than 1.1 per 100,000. It is difficult to rationalise figures that are 2 orders of magnitude lower than those in Holland for example. The island status of the UK will not have protected it from migratory birds, which are well-documented carriers of Lyme-infected ticks (21,22,23,24). It is also not necessarily true that rural doctors are aware of Lyme disease. There have been several cases in my own rural area of the so-called "well recognised" EM rash being labelled as ringworm and others have been told that they were suffering from shingles or allergies. How many GPs will recognise the condition Acrodermatitis Chronica Atrophicans (25), which is a skin disease associated with Lyme?

Ho-Yen has stated himself that the number of cases in Scotland is underestimated by as much as a factor of 1 in 10. The point is

- if Lyme is continually labelled as one of "those obscure foreign diseases" doctors will not even bother to test for it. The head of the UK's Lyme reference lab continues to inform the medical world that the disease is rare in Britain (26) and that positive tests are to be ignored in non-endemic areas.

With the exception of Scotland, Lyme is yet to be made a notifiable disease in Britain. Currently the Health Protection Agency (HPA) website (20) gives the

estimated incidence as 1000 to 2000 additional cases per year. This is to be added to the figure for the lab reports for the year, which was 585 cases in England and Wales. The true incidence is unknown.

If the laboratories testing for Lyme are not aware of the many reasons for negative antibody tests in the presence of the disease, and do not inform consultants that the patient could still have Lyme, despite the serology being negative, then the situation is perpetuated.

Myth 3: Most ME is Lyme disease.

Verdict: Open. But it is likely to be true for a high proportion of ME/CFS/FM cases, and not a myth at all, according to many Lyme specialists (27,28,29). Most open-minded people agree that not all cases of ME/CFS/FM would be due to Lyme but there are now thousands of people with these conditions who are finding out that they have Lyme borreliosis or other tick-borne infections.

Recent research in the UK points to the fact that biochemical and immunological markers are very similar in Lyme and ME. In a presentation to the Edinburgh ME group in September 2005, Professor John Gow of Glasgow University stated that gene expression regulation in those with ME is identical to that seen in Lyme patients.

In contrast to Ho-Yen's assertion that the EM rash of Lyme is an easily recognised indicator, half of those bitten do not show the rash and those that do may have atypical presentations (30,31). Seventy percent of Lyme patients who responded to a poll by the Internet group EuroLyme stated that they were previously diagnosed with ME/CFS. The UK government has stated that Lyme can cause Chronic Fatigue Syndrome, but has not broadcast this statement as an important issue. While there is a heated dispute between specialists who believe that Lyme infection is easily cured by a short course of antibiotics and those who say it persists, nevertheless, both sides agree that the "post Lyme syndrome" often presents as fibromyalgia and chronic fatigue syndrome. However, many studies have shown that there is persisting infection, and that this is treatable (32,33,34,35).

Late Lyme is also hard to distinguish from many other diseases, and is more often under-diagnosed than over-diagnosed (36,37,38,39). Most importantly, although Ho-Yen has listed cardiac, joint and skin manifestations of Lyme, he has omitted to mention the devastating neurological symptoms manifest both in ME/CFS/FM and Lyme (40), unless he is implying that the term "fatigue state" encompasses all of the central and peripheral nervous system deficits that may occur in neuroborreliosis, (e.g. encephalopathy, facial paralysis, vertigo, light and sound sensitivity, tinnitus, meningitis). Ho-Yen fails to state the source of his belief that only 10% of late Lyme patients show this "fatigue state". Most people with late Lyme are crippled by a "fatigue state", as are most people with ME/CFS/FM.

Ho-Yen contends that only 5% of Scottish ME patients studied by him had Lyme. However, he does not state which criteria were used for diagnosing Lyme (as mentioned earlier, blood tests cannot be relied upon to rule out Lyme.) Neither does he mention the length of time of follow up of these patients, despite the fact that Lyme, like ME, is known to be a relapsing-remitting disease (41).

Myth 4: Antibiotics can cure Lyme disease.

Verdict: True. This is not a myth. Antibiotics and other drugs in combination or in series can cure many cases of Lyme disease. The treatment needs to be under the supervision of an experienced Lyme specialist and sometimes must be carried out for months or even years.

According to Ho-Yen "the very need for such prolonged treatment with antibiotics suggests that the success rate is not good". Applying his criteria we would refuse to treat TB patients and leave them to their misery. The longer that Lyme disease remains untreated or under-treated, the worse the potential for permanent damage. In some cases, antibiotics may merely lessen the progress of the disease. However Lyme patients across the world who can access appropriate medical care may recover their health or at least have partial remission. (42).

Ho-Yen states "Indeed, it is difficult to separate the natural improvement that occurs with chronic disease from the effects of antibiotic treatment". His solution is to treat ME/CFS as if it were a viral illness, but this is not appropriate knowing the bacterial causation of Lyme. Viruses and bacteria are quite different biologically, needing completely different treatment approaches.

Myth 5: All laboratories produce dependable results. Verdict: False. This is perhaps the only myth on which we have a point of agreement: if all laboratory tests were reliable, Ho-Yen would not have published his 2005 paper, saying that his lab had had to reinterpret a third of its own tests.

Two comprehensive reviews of the accuracy of standard tests for Lyme, in Europe (43) and the US (44), showed that the same sample of blood could test positive or negative depending on which lab it was sent to, or even if tested again in the same lab. Worse still for those with suspected *Borrelia* infections, the Polish National Institute of Health has reported that patients with low or negative antibody levels have tested positive using other more sensitive techniques. Specific DNA capture and culturing showed that there were live bacteria in their body fluids (45) indicating that those with negative blood tests could be even more ill than those who have circulating antibodies. The problem of co-infections with other organisms is another complicating factor.

In 2003 Dr Lowes, head of microbiology at Southampton, where the Lyme reference laboratory is housed, promised that an internal audit would be conducted into the lab's operations. He made that promise following complaints that inaccurate testing and interpretation procedures were being carried out at the Lyme lab. The results of that audit have never been made public to this day.

We agree with Ho-Yen that commercial motives could compromise the quality of lab diagnostics. However, nowhere is this more reflected than in the vested interests of the Lyme committee of the Infectious Disease Society of America (IDSA), which as mentioned below, is currently the subject of an anti trust investigation by the Attorney General in Connecticut, where there is one of the highest rates of Lyme infection in the world.

Dr Susan O'Connell, the head of the UK'S Lyme Reference Laboratory, was a consultant to that committee, and both she and the Department of Health promote its viewpoint as a model for diagnostic and treatment policy in this country. Ho-Yen's recent article demonstrated that he too has adopted much of that view.

Myth 6: There is misleading expert comment

Verdict: True. This is definitely not a myth. As alluded to earlier, in November 2006, Connecticut Attorney General Richard Blumenthal ordered a Civil Investigative Demand under the anti-trust laws concerning the recently published guidelines produced by the Lyme committee of the IDSA. This group of 14 scientists have been the most vociferous in stating that Lyme disease is never chronic and that treatment, beyond a few weeks of antibiotics, is not indicated. (46).

In a press interview (47) Blumenthal voiced his fear that the guidelines were being used by the powerful US insurance industry to deny health coverage to

Lyme patients. In addition to the close ties with the insurance industry held by some members of the committee, a number of them have significant conflicts of interest due to their involvement with companies producing Lyme vaccines or test-kits.

Two of the members, Gary Wormser, lead author of the guidelines, and Allen Steere, admit to receiving money from the multi-national Baxter corporation, which is currently developing a vaccine for the European market. A restrictive approach to Lyme diagnosis serves the interests of vaccine manufacturers as it can cover vaccine failure. It is also difficult to conduct clinical testing of vaccines without using antibody tests to rule out the disease. However, all the evidence indicates that the tests are not sensitive enough to be used in this way. The end losers are the patients.

Clinicians associated with the International Lyme and Associated Diseases Society (ILADS) oppose the IDSA, and treat thousands of patients in the US and across the world with long-term antibiotics if necessary (48).

How many Infectious Disease experts in the UK know about the many reasons (49) why both chronic and early Lyme disease can show no antibodies in blood tests (seronegative)? Why does the Health Protection Agency's Lyme Reference Laboratory inform doctors that a negative ELISA test rules out Lyme in all but the earliest stages, when there is documented evidence (50) that this is not the case?

Conclusion

A combination of the facts above, and the lack of openness surrounding the topic of Lyme borreliosis, has left many thousands of Lyme patients undiagnosed and untreated.

There are many people who suffer for long periods of time, decades in some cases, who have never been tested for Lyme or who have had negative tests. Years later, they find that the antibodies can be seen in their blood or that other more precise tests reveal the DNA of borrelia in their bodies.

A Lyme diagnosis means virtually nothing here in Britain since there are very few doctors who know how to proceed. The persistence of borrelia infections (51,52) means that antibiotic therapy must be extended in order to reduce the bacteria to a low enough level for the immune system to take over.

There is also the problem of co infections, with growing evidence that many Lyme patients may be infected with anaplasma, babesia, bartonella and mycoplasma species (53,54,55,56).

If the patient has been ill for years, thousands of generations of bacteria will have multiplied and spread throughout the body. They may then lie dormant until the immune system is challenged by other events - perhaps by toxicological insult from organophosphates and other poisonous chemicals in the environment, or by catastrophic life events such as automobile accidents etc.

In other patients, the bacteria may rampage continuously and may cause ME/CFS/FM, heart disease, arthritis, MS, ALS, thyroid disease, and visual defects. They may endure pain and vertigo and brain fog, arthralgia and arthritis, endocrine problems, endometriosis, irritable bowel and bladder disease, skin rashes, rapid heart beats, heart failure, hearing loss, seizures, temporary or permanent paralysis, muscle spasms, tendonitis, memory loss and panic attacks. There is even some evidence to suggest that borrelia infection may lead to bipolar disorder, schizophrenia and Alzheimer's disease (6, 57,58).

On and on the list goes, making many doctors certain that it is an impossible mixture of symptoms to have and therefore must be all in the patient's mind. Victims of Lyme disease, like those with ME/CFS/FM, have consequently been

called over-emotional yuppies with personality problems, stressed-out under-achievers, or over-anxious and depressed individuals.

Now Ho-Yen has exacerbated this situation by accusing British Lyme patients of hysteria. Lyme victims are hysterical, and demand antibiotics. They are hysterical, and say they know more than doctors. Worse still, people with ME/CFS/FM are catching the hysteria, and phoning him up in hundreds to ask if they have Lyme.

Patients with ME/CFS/FM are advised to beware of this hysterical label and to remember how the two hundred or so nurses, doctors and patients in the Royal Free Hospital came down with a nasty epidemic of so-called "hysteria" in 1955. Many of them never recovered from the disease, and never recovered from the stigma attached to that label.

Over the last 30 years Lyme patients have received the same sort of treatment as people with ME/CFS/FM, - ridicule, contempt, disbelief, denial of investigations and treatment, and the ignominy of a psychosomatic label.

Unfortunately, over the last 20 years, there has been a concerted effort by a small but very influential group of psychiatrists to inundate both the scientific literature and the ordinary press with tales of "psychosocial" causes of ME/CFS/FM (59).

We are all being confused by myths, according to Ho-Yen, but is it possible that he has himself been myth-taken? His suggestions that "fatigue" is only shown by the minority of Lyme patients; that antibody tests can rule out the disease; and that chronic Lyme responds to palliative rather than antimicrobial therapy, are all unproven. They are especially unhelpful in the present situation.

Now the common sense of decent people and the integrity and honesty of certain doctors and scientists, such as Kenneth Liegner (60), will unearth the truth about the causes of ME/CFS/FM. These may be multiple. However, in every case, patients are entitled to full information about their diagnosis and prognosis.

Ho-Yen concludes with "In the end, it is a matter of what makes you better" and urges patients to take responsibility for their own illness. We contend that ME/CFS/FM patients struggle heroically to cope with their condition and are forced to take responsibility for their illness every day. Patients will never get better until there is clarity (61) over the issues surrounding Lyme, ME/CFS/FM and other chronic infections.

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