

# The Complexities of Lyme Disease

(A Microbiology Tutorial)

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(An excerpt from the Lyme Disease Survival Manual 2000, Duluth, MN, USA)

Lyme disease is a multi-system disease which can seemingly affect virtually every tissue, and every organ of the human body. It is a disease which can be mild to some, and devastating to others. It can cripple and disable, or fog your mind. It can affect men, woman, and children, and even your family dog and can be devastating to horses and cattle. (1-5,7-19) You may test negative for the disease, and still have it, or test positive and be symptom free. Some will get symptoms within days of a tick bite, while others may have it for years before they are even diagnosed. Some Lyme patients are told they have fibromyalgia, chronic fatigue syndrome, depression, MS, ALS or some other disease of unknown origin. (See abstracts of the 1996 International Lyme Conference) There are some studies which support the theory that the infection can be transmitted from mother to the unborn fetus, and may even cause still birth and has been implicated in some SIDs deaths. (MacDonald-20,52; 45,53)

**Why** is Lyme disease such a mystery? Why does it mimic so many other disease? Why is it so difficult to detect? The reasons come from the microbiology of the bacteria that causes Lyme Disease. This paper will look at the biology of this bacteria and the consequences of the organism's unique microbiology on human victims.

Lyme disease is caused by a spiral shaped bacterium known as a spirochete. Diseases that are caused by spirochetes are notorious for being relapsing in nature, difficult to detect, and great imitators of other diseases. Syphilis, Tick-Borne Relapsing Fever, and Leptospirosis are other examples of spirochetal diseases. Lyme disease is caused by a bacteria called *Borrelia burgdorferi*, named after the man who isolated it from a Deer Tick in 1981, Dr. Willy Burgdorfer. The following is a tutorial to help explain away the mysteries of this bacteria, and the why it causes so much controversy between patients and the medical community. (1)

## The Structure of the Lyme Bacteria

The structure of the Lyme spirochete, is unlike any other bacteria that has ever been studied before. It is one of the largest of the spirochetes (0.25 microns x 50 microns) It is as long, as a fine human hair is thick. *Borrelia burgdorferi* is a highly motile bacteria, it can swim extremely efficiently through both blood and tissue because of internal propulsion. It is propelled by an internal arrangement of flagella, bundled together, that runs the length of the bacteria from tip to tip. Like other *Borrelia* bacteria *Borrelia burgdorferi* has a three layer cell wall which helps determine the spiral shape of the bacteria. What makes this bacteria different from other species, is that it also has a clear gel-like coat of glyco-proteins which surround the bacteria. This extra layer is sometimes called the Slime Layer or S-layer.

(See diagram 1) (45,46,59) Flagella runs internal from tip to tip DNA containing BLEB, newly formed - Shed BLEB - Glyco-Protein Slime Layer (exaggerated In the example for illustrative purpose) - Receptors in tips -

**This means:** This extra layer of glyco-proteins (exaggerated in thickness here) may act like a stealthy coat of armor, that protects and hides the bacteria from the immune system. The human immune system uses proteins that are on the surface of the bacteria as markers, and sends attacking antibodies and killer T-cells to those markers, called outer surface protein antigens (OSP antigens). This nearly invisible layer is rarely seen in washed cultures,

but can be seen regularly in tissue biopsies.(46)

The Lyme bacteria is different from other bacteria in its arrangement of DNA. Most bacteria have distinct chromosomes that are found floating around inside the cytoplasm. When the bacteria starts to divide it forms a new cell wall in the middle and begins to split in two, the chromosomes also divide, and the new copies of the chromosomes enter the new cell. The arrangement of DNA within *Borrelia burgdorferi* however; is radically different from other bacteria. It is arranged along the inside of the inner membrane of the cell. It looks something like a net embedded just underneath the skin of the bacteria. (46)

**This means:** We really don't understand the mechanisms of how Bb regulates its genetic material during its division.

The bacterial DNA is uniformly embedded inside the inner membrane of the Bb bacteria, like nylon stocking.

Another unique feature to *Borrelia burgdorferi* are Blebs.

This bacteria replicates specific genes, and inserts them into its own cell wall, and then pinches off that part of its cell membrane, and sends the Bleb into the host. Why it does this we don't know? But we do know that these blebs can irritate our immune system. Dr. Claude Garon of Rocky Mountain Laboratories has shown that there is a precise mechanism that regulates the ratio of the different types of blebs that are shed. (46) In other bacteria the appearance of blebs often means the bacteria can share genetic information between themselves. We don't know if this is possible with *Borrelia* species. There have been reports of a granular form of *Borrelia*, which can grow to full size, fully autonomous spirochetes and can reproduce. These granules are so small that they can be filtered and separated from live adult spirochetes by means of a micro-pore filter. The granular/spore form of *Borrelia burgdorferi* is still being debated. (Stealth Pathogens Lida Mattman Ph.D 66, Phillips/Mattman 98, Preac-Mursic)

The division time of *Borrelia burgdorferi* is very long. Most other pathogens such as *Streptococcus*, or *Staphylococcus*, only take 20 minutes to double, the doubling time of *Borrelia burgdorferi* is usually estimated to be 12-24 hours. Since most antibiotics are cell wall agent inhibitors, they can only kill bacteria when the bacteria begins to divide and form new cell wall.(35,59-62)

**This means:** Since most antibiotics can only kill bacteria when they are dividing, a slow doubling time means less lethal exposure to antibiotics. Most bacteria are killed in 10-14 days of antibiotic. To get the same amount of lethal exposure during new cell wall formation of a Lyme spirochete, the antibiotic would have to be present 24 hours a day for 1 year and six months!

*Staphylococcus* Lyme spirochetes

\* *Note:* Antibiotics kill bacteria by binding to RNA rich organelles inside the bacteria called ribosomes\*, and interrupting the formation of cell wall proteins, or proteins involved in cell metabolism. (See LD Survival Manual) Some newer antibiotics kill by disrupting DNA/RNA synthesis. (Cipro and other quinilones interrupt DNA gyrase and enzyme that unwinds DNA for replication)

If a bacteria is in a non-metabolic state (dormant) no antibiotic is effective. To be lethal the

antibiotic must be absorbed and processed through the bacteria's metabolic machinery and cause a disruption of metabolism.

Unlike antiseptics, antibiotics don't kill on contact. If there are any dormant bacteria hidden in sequestered sites, then regardless of the length of treatment, antibiotics can fail until the bacteria become metabolically active. (The Forgotten Plague see reference to Tuberculosis)

A ribosome translates messenger RNA into proteins. In other words, cellular genes are expressed as proteins that are created at the site of the ribosomes.

Ribosomes are protein creating factory assembly lines. Like other spirochetes, such as those that cause Syphilis, the Lyme spirochete can remain in the human body for years in a non-metabolic state. We know this because patients with ACA rash for years are often culture positive when the skin is biopsied and cultured. Non metabolic bacteria is essentially suspended animation. The bacteria does not metabolize in this state, antibiotics are not absorbed or effective. When the conditions are right, those bacteria that survive, can seed back into the blood stream and initiate a relapse. It is a beautiful and patient survival mechanism. (59-62,70)

**This means:** Just because a person is symptom free for long lengths of time doesn't mean they aren't infected. It may simply be a matter of time before the re-emergence of sequestered non-metabolic bacteria. Whereas viral infections often impart a lifelong immunity, and may suppress subsequent relapses or reinfections. Lyme like other bacterial infections, does not impart an active immunity for long a period of time. People are often reinfected with Lyme. A relapse of symptoms could actually be thought of as a reinfection or a reseeding of infection from immune privileged sites.(96)

**POLYMORPHISM:** The ability of a bacteria to change its structural identity. During cell division this bacteria has the ability to change its cell wall structure, and surface antigens thus making it more difficult for the human immune system to recognize. Like its cousins, the RELAPSING FEVER

**SPIROCHETES** , the Lyme spirochete has a sequence of surface antigens it can choose to express or not express. There are more than two dozen species of Relapsing Fever Borrelia bacteria which have been clearly identified. We are now beginning to see a similar diversity within the Lyme spirochete family as well. Polymorphism makes recognition and identification more difficult, it is like a criminal putting on a new disguise after every time he has committed a new crime. While there are four generally accepted genospecies of Lyme disease Borrelia burgdorferi, afzellii, garinii, and lonstarrii, there are hundreds of identified strains of the first three species. Borrelia spirochetes are polymorphic because they have built in genetic mechanisms to vary their antigens.

**This Means:** Just as the immune system recognizes the bacteria and tries to kill it. The bacteria changes its clothes and fools the immune system and survives a little longer. Soon the bacteria finds safer areas of the body to hide in and the immune system stops looking for it. But another aspect of polymorphism is that once the cell changes it may become even more lethal to some cells. For example when Borrelia burgdorferi was introduced into the mouse via the blood stream, the bacteria traveled to the brain. But the bacteria recovered from the brain was more adapted to the brain and could no longer be killed from antibodies in the bloodstream. Polymorphism is a clever way to survive and may offer reasons to multiple symptoms.

**CELL WALL DEFICIENT SPIROCHETES:**

The nice clearly definable spiral shape of the Lyme spirochete is formed by the presence of the bacteria's cell wall. Without this cell wall to determine its shape, the bacteria only has a thin pliable membrane to hold its structure together. When the bacteria turns off its genes that govern cell wall synthesis, the bacteria can change from a spiral shape, to a sphere. These spherical forms are known as L-forms or Cell Wall Deficient (CWD) forms. They represent a new hazard in the diagnosis and treatment of common diseases.

Many doctors and microbiologists have a hard time understanding that spirochetes can actually be fuzzy blobby looking spheres, but they are a reality. As a defense mechanism to mammalian immune systems, the Lyme spirochete has learned to turn off its group of genes that result in cell wall formation. This also eliminates all associated cell wall antigens.

**How** does a microbiologist recognize *Borrelia burgdorferi* once it is no longer a spirochete? In order to prove that these spheres floating around in human blood are actually spirochetes is difficult because they do not culture well. Instead a microbiologist will make a wet mount of the infected blood on a slide, and then add acrodine orange stain to stain the nucleic acids. Then a second stain that is specific for *Borrelia burgdorferi* is added. It is prepared by first making a monoclonal antibody specific to a *Borrelia* membrane antigen. Then that monoclonal antibody is tagged with a fluorescent dye. When this dye is added to the wet mount slide it stains only the *Borrelia* species of bacteria. Suddenly what was once totally invisible in blood by normal staining techniques, becomes visible. Spirochetes can in fact become cell wall deficient spheres.

Another technique to identify spheroplasts as being *Borrelia* bacteria is to take antibodies unique against *Borrelia* and tag them with inert gold spheres. Then culture the L-forms with the antibody-tagged-gold. When these cultures are viewed under electron-microscopes, the gold can clearly be seen attached to the membrane indicating that the antibody has attached to a protein specific to *Borrelia*. Therefore the spheroplasts must have once been spirochetes.

The most compelling evidence of spirochetes reverting from its classical form to L-forms and back to the classical form, is sometimes seen in live wet mounts. Occasionally L-forms can be observed producing a classical form spirochete that is actually in the process of being extruded from the membrane of the L-form. In other words the bacteria can revert back and forth from L-forms to spirochetes by a method other than normal binary fission. It appears that the membrane its self can yield an intact spirochete without creating the normally obligatory process of binary fission. Binary fission starts with the host cell splitting itself in half with a cell wall, and then creating an identical clone cell, but when L-forms reproduce they don't always form identical clones. (Lida Mattman, *Stealth Pathogens*, Detroit 1997 lecture and video, Mattman/Phillips 98)

**This means:** Cell wall inhibiting antibiotics such as Rocephin and amoxicillin, are ineffective since they depend on inhibiting cell wall formation to induce cell lysis. This means most antibiotics used in treatment of Lyme disease may have a built in deficiency when confronting L-forms. Other antibiotics such as doxycycline and clarithromycin which are protein inhibitors, may have to be used when cell wall agents fail. Diagram: The Cell Wall Deficient form of *Borrelia burgdorferi*, or the L-form lacks its normal spiral architecture due to the lack of structural rigidity that is maintained by the structural presence of a cell wall. The bacteria reverts back to a simpler spherical form.

The bacteria is held together by a much more fragile 3 layer membrane stains semipermeable 3-layer membrane. Just beneath this membrane with acrodine orange is the bacteria's genetic material, from which new cell synthesis seems to originate from a simple amorphous membrane, the bacteria can give rise to the classical cell wall spiral shaped bacteria.

A Classical form arising from an L-form: Membrane antigens used to create monoclonal antibody stain.

## Cell Walled Classical Form (Gold tagged antibody to *Borrelia burgdorferi*)

In what form does the bacteria exist in the human body? A pioneering study on L-forms of spirochetes, was done on tissues from a tertiary syphilis patient. A syphilitic aorta from the heart of a human patient was dissected and analyzed for the presence of L-forms. What was seen was that within the lumen of the artery or within the bloodstream, the classical form was predominant. As you traveled into the vessel through the endothelium and into the basement membrane, you found a progression of morphogenic forms. The spirochete slowly went through a transition from a spiral shaped bacteria to a small sphere.

**This means:** The preferred form of the bacteria may be dependent on its physical surroundings. In some tissues it prefers the classical form, in other tissues it reverts to a cell wall deficient form. While such a dimorphism has long been accepted for yeast and fungal infections such as *Candida* infections. It is only just now being accepted as occurring in *Borrelia* species. (A yeast can also have a separate rhizome fungal form and a fungus can revert to a spore forming form!) Motility: How does the Lyme bacteria travel from the bloodstream to other tissues? While we have known for a long time that the Lyme spirochete can show up in the; brain, eyes, joints, skin, spleen, liver, GI tract, bladder, and other organs, we didn't understand the mechanism by which it could travel through capillaries, and cell membranes. (Abstract 644) Then Dr. Mark Klempner presented at the 1996 LDF International Lyme Conference an interesting paper that gave us part of the answer.

Many researchers have observed that the Lyme spirochete attaches to the human cells tip first. It then wiggles and squirms until it enters the cell. What Dr. Klempner showed was that when the spirochete attached to the human host cell, it caused that cell to release digestive enzymes that would dissolve the cell, and allow the spirochete to go where ever it pleases. This is very economic to the bacteria to use our own cell's enzymes against us, because it does not need to carry the genes and enzymes around when it travels. Dr. Klempner also showed that the spirochete could enter cells such as the human fibroblast cell (The skin cell that makes scar tissue.) and hide. Here the pathogen was protected from the immune system, and could thrive without assault. More importantly when these Bb-fibroblast cultures were incubated with Rocephin (ceftriaxone), two thirds of the cultures still gave rise to live spirochetes after two weeks, and in later experiments for more than 30 days.

If we can't kill it in a test tube at these high concentrations of Rocephin in four weeks, how can we hope to kill it in the human body? (22,48,79,80,)

**This means:** The infection can enter the best tissue that is optimal for its survival. Once it gains an intracellular position, it may evade the immune system, and antibiotics therapy, by remaining sequestered away from these hostile environs.

Another interesting observation about this bacteria is how it interacts with our body's immune system; Dr. David Dorward of Rocky Mountain Labs made a video tape of how *Borrelia burgdorferi* acts when surrounded by B-cells. (The type of white blood cell that makes antibody.) The spirochete attached tip first, entered the B lymphocyte, multiplied and ruptured the cell. It repeated this process for three days until the B-cells were able to come to an equilibrium. A matter of concern was that some of the spirochetes were able to strip away part of the B-cell's membrane, and wear it like a cloak. (Dorward, Hulinska 1994 LDF Conference Vancouver BC)

**This means:** If this spirochete is evolved enough to attack our B-lymphocytes, then it may also be evolved in other ways that we do not yet understand. It is for certain that

its ability to kill B-lymphocytes, evolved as part of a defense mechanism to evade its own destruction. The observation that it can use the B-cell's own membrane as camouflage, indicates that it may be able to go undetected by our immune system.

Receptors:

It now appears that there are specific receptors in the Lyme spirochete to attach to endothelial cells, N-Acetyl-glucosamine, B-cells, glial cells, nerves, and neurons.

The way our immune system is supposed to work, is that it recognizes foreign invaders as being different from self, and it attacks the infection. Unfortunately the immune system sometime attacks our own cells. This called autoimmune disease. If a foreign invader has a chemical structure similar to our own tissue antigens, our bodies sometimes make antibodies against our own tissues. In people with Lyme disease scientists have discovered auto-antibodies against our own tissues including: (23,28,38-40,43,45,56,57,60,88)

- \* Nerve Cells (Axons)
- \* Cardiolipid
- \* Myelin (also seen in MS)
- \* Myelin Basic Protein (also seen in MS)
- \*Neurons (brain cells)

When the immune system finds a foreign invader, it tags that invader in a number of ways. A cell called the macrophage can engulf the bacteria, and then communicate to other immune cells the exact description of the bacteria. Another cell might mark the cell with antibody which attracts killer T-cells. Some types of T-cells communicate to other cells what to attack, and regulates the immune assault. But sometimes the body can produce a type of antibody that doesn't attack or help. A blocking antibody will attach and coat the intruder, but it won't fix compliment, and it shields the bacteria from further immune recognition. In Lyme we have seen quantities of IgG4 blocking antibody such as is seen in some parasitic infections. (Tom Schwann RML 92 LDF Conference)

\* *Note:* Compliment is a term used for a series of 18 + digestive proteins that are only activated by signals from our immune system, such as compliment fixing antibodies that attach to foreign antigens.

In order for the immune system to make an attacking antibody, the immune system must first find an antigen which it can attack. Unfortunately as seen by freeze fracture electron microscope, photographs of the Lyme bacteria, show that most of the antigens are on the inside of the inner membrane, and not on the outside. (60) This makes the bacteria less visible to the immune system and more difficult to attack. The most intriguing fact about *Borrelia spirochetes*, is their well documented ability to change the shape of their surface antigens when they are attacked by the human immune system. When this occurs it takes several weeks for the immune system to produce new antibodies. During this time the infection continues to divide, and hide. (1,47,63,66)

It appears that *Borrelia* are able to change their surface antigens many times, and can do it quickly. In one study by Dr. Andrew Pachner MD, he infected mice with a single strain of *Borrelia burgdorferi*. After several weeks he was able to isolate two slightly different forms of the bacteria. The bacteria from the bloodstream was attacked and killed by the mouse's immune sera, but the bacteria isolated from the mouse's brain was unaffected by the immune sera. The bacteria isolated from the mouse's brain had a new set of surface antigens. It appears that contact with the CNS caused the bacteria to change its appearance. Since the brain is isolated from the immune system, and is an immune privileged site, the bacteria became its own separate strain. (47,97) This means: Infections of the bloodstream may be different from the infections that are sequestered in the brain. While we continue to

have active immunity in the bloodstream, the brain has no immune defenses except for circulating antibodies. So if those circulating antibodies are ineffective to attack the bacteria in the brain, then the brain is left without any defenses, and the infection goes unabated.

Another peculiar observation of this bacteria is seen inside the bacteria. When the genetic control mechanisms of this bacteria are inhibited with antibiotics known as DNA Gyrase Inhibitors (ciprofloxin) the bacteria start to produce bacterio-phage. A phage is a virus that specifically attacks bacteria. In this case there are two distinct forms. This means the Lyme bacteria at one time was attacked by viruses, it was able to suppress them, but the DNA to make the phage is still incorporated within the DNA of the bacteria. Perhaps activation of this phage could one day be beneficial to treating chronic Lyme patients? (JTBD 94)

### **What happens** when the infection gets to the brain?

In the case of Lyme disease every animal model to date shows, that the Lyme spirochete can go from the site of the bite, to the brain in just a few days. (41,60, abstract 644) While we know this bacteria can breakdown individual cell membranes, and capillaries, its entrance into the brain is too pronounced for such a localized effect. When the Lyme bacteria enters the human body, we react by producing several immune regulatory substances known as cytokines and lymphokines. Several of these act in concert to break down the blood brain barrier. (eg. Il-6, Tumor Necrosis Factor-alpha, Il-1, Transforming Growth Factor-beta etc. ) In addition to affecting the blood brain barrier, these cytokines can make us feel ill, and give us fevers. (54,60,) (JID 1996:173, Jan)

Since the brain has no immune system, it prevents infection by limiting what can enter the brain. The capillary bed that surrounds the brain, is so tight that not even white blood cells are allowed to enter. Many drugs can't enter either, making treatment of the brain especially hard. For the first ten days of a Lyme infection, the blood brain barrier is virtually non existent. This not only allows the Lyme bacteria to get in, but also immune cells that can cause inflammation of the brain. (41, see LDSM 95 for diagram)

*\*Note:* The breakdown of BBB was shown to occur by tagging WBCs, albumin, and other substances known not to cross the BBB with radioactive Iodine. The CSF was tested, and then the animals were infected with Bb. Then the CSF was tested everyday for several weeks. The result: No cross over of Iodine in the control group, 100% crossover in the infected group for 10 days. The infection had the same result on the BBB, as if you were injecting the radioactive iodine directly into the brain. (60)

When the human brain becomes inflamed, cells called macrophages respond by releasing a neuro-toxin called quinolinic acid. This toxin is also elevated in Parkinson's Disease, MS, ALS, and is responsible for the dementia that occurs in AIDS patients. What quinolinic acid does, is to stimulate neurons to repeatedly depolarize. This eventually causes the neurons to demyelinate and die. People with elevated quinolinic acid have short term memory problems. (27,29-37,40-42,74,75, 82-84,87-90)

**This means:** If we think of all of our brain cells like telephone lines, we can visualize the problem. If all of the lines coming in are busy we can't learn anything. If all of the lines going out are busy, we can't recall any memories. Our thinking process becomes impaired. A second impairment to clear thinking that Lymies experience, is the restriction of proper circulation within the blood vessels inside the brain. Using an instrument called the Single Photon Emission Computer Tomography scanner ( SPECT scans), we are able to visualize the blood flow throughout the human brain in 3-D detail. What was seen in the brains of chronic neurological Lyme patients was an abnormal "Swiss-Cheese" pattern of blood flow. The cortical or thinking region of the brain was being deprived of good circulation, the occipital (eyesight) regions had an increase flow. This could help explain why most Lyme

patients complain of poor concentration, and overly sensitive eyes. (91)

## Lyme Tests

There's a Lyme test, **so what's the problem?** There are several Lyme tests, but most of them are dependent on the body's ability to make antibody against this bacteria. As we have seen this may be a problem. There is the S-layer protecting the bacteria, the surface antigens are not readily exposed, there may be a blocking antibody, the bacteria might be inside a human cell, the bacteria might be down regulating the immune system through cytokines, the bacteria might have altered its antigenic appearance to fool the immune system, the bacteria might be cloaked in B-cell membrane, the bacteria might be hiding in joints, tendons, white blood cells, skin cells, and the brain, and finally the bacteria may have shed its cell wall making rendering it in effect invisible. Remember if even just one spirochete survives, it could cause a relapse. Then there is another problem, the tests that detect antibody can only detect free uncomplexed antibody. (23,25,55,70)

When an antibody is formed it is meant to latch on to something and never let go until it is destroyed. Like a lock and key, antibodies fit their associated antigens. Once the antibody attaches to the antigen it is no longer a detectable antibody, because it has now become an antibody-antigen complex. This complex is not measurable using today's commercially available tests. Also as the amount of antigen increases, the amount of antibody can decrease because the antigen will trap out the available antibody and sequester it. So a person who has a bad infection, but is making a limited amount of antibody, can be overwhelmed by antigen thus making antibody detectable only if you can detect the complex.

Ab + Ag = Ab/Ag-complex  
Antibody + Antigen = Antibody/Antigen---complex--  
(free) (free) (complexed)

Free antibodies are detectable with the current Lyme tests, but antigen/antibody complexes are undetectable using either the ELISA or Western Blot tests.

**This means:** People who have the worst infections may have the lowest antibody titers, and test negative because the bacteria "load" overwhelms the antibodies present.

\* *Note:* It takes four weeks from the day of the tick bite to test positive.

There are two main categories of Lyme tests, the most common and least specific is the Enzyme Linked Immune Sera Assay or ELISA, the other is an Immuno Blot or Western Blot. The Western Blot essentially makes a map of the different antibodies we make to the bacteria. The map separates the antibodies by size and weight and is reported in units called kilo daltons or kDa. For example a Western Blot may report bands at 22, 25, 31, 34, 39, and 41 kDa. Each of these bands represents an antibody response to a specific protein found on the spirochete. The 41 band indicates an antibody to the flagella protein, and is non specific. The 31 kDa band represents the OSP-A protein and is specific for Borrelia, as is the 34 band OSP-B, and 25 kDa OSP-C.

In 1994 the NIH decided that there should be consistency between labs reporting Lyme Disease Western Blots, and that a specific reporting criteria should be established. This sounds good, but one could argue they made a bad situation worse. The consensus of the Dearborn MI. committee decided to set the standards for a positive test based on the number of specific bands that appear, and where as every lab prior to this hearing had accepted bands 25, 31, and 34 as specific and significant. The NIH without any clear



reasoning disqualified those bands as even being reportable. The result was, what had been a fair-good test had now become poor or even useless. Many labs stopped reporting the actual bands and simply reported the test as positive or negative, thus preventing any further interpretations. (90)

(Diagram of Western Blot) Band 41 kDa Flagellin  
OSP-B Antigen 34 OSP-A Antigen 31 kDa  
OSP -C Antigen 23

**How** badly did the NIH boot strap this test? The following is an analysis of the new guidelines presented as an abstract and lecture at the 1995 Rheumatology Conference in Texas. 1995 Rheumatology Symposia Abstract # 1254  
Dr. Paul Fawcett et al.

This was a study designed to test the recently proposed changes to Western Blot Interpretation. The Second National Conference on Serological Testing for Lyme Disease, sponsored by the NIH. The committee proposed limiting the bands that could be reported in a Western Blot for diagnosis of Lyme Disease. A IgG Western Blot must have five or more of these bands: 18, 23, 28, 30, 39, 41, 45, 58, 66, and 93 kDa. An IgM Western Blot, must have two or more of the following three bands: 23, 39, 41.

Conspicuously absent are the most important bands 22, 25, 31, and 34 which include OSP-A, OSP-B and OSP-C group antigens. The three most widely accepted and recognized antigens. These antigens are so immuno reactive that they were the antigens chosen for human vaccine trials. Yet they are not considered important enough to include in the diagnostic criteria?

#### **Why?**

This abstract showed that under the old criteria, all of 66 pediatric patients with a history of a tick bite and, Bull's Eye rash who were symptomatic, were accepted as positive under the old Western Blot interpretation. Under the newly proposed criteria only 20 were now considered positive. That means 46 children who were all symptomatic, would probably be denied treatment! That's a success rate of only 31 %.

66 Children with Bull's Eye rash Old W. Blot Criteria 100 % positive  
New NIH Criteria 31% positive  
The number of false positives under both criteria was ZERO %

\* Note: A misconception about Western Blots is that they have as many false positives as false negatives. This is not true. False positives are rare.

The conclusion of the researchers was: "the proposed Western Blot Reporting Criteria are grossly inadequate, because it excluded 69% of the infected children."  
" The Accuracy of Laboratories Using the ELISA/EIA Lyme Tests

We are told by manufactures, health departments, and clinics that the Lyme ELISA tests are good, and that they are useful, but in two blinded studies that tested laboratories accuracy, they failed miserably. In two studies by Lorie Bakken MS/MPH she showed that there was not only inaccuracy and inconsistency between competing laboratories, but also between triple identical samples sent to the same lab. In other words identical samples often resulted in different results! In the latest study by the College of American Pathologists, 516 labs were tested. The overall result was terrible, there were almost equal numbers of false positives as false negatives. Overall the labs were 55 % inaccurate! You are actually better off to flip a coin!

(98, 99) 98- Bakken LL, Callister SM, Wand PJ, Schell RF. Interlaboratory

Comparison of Test Results for the Detection of Lyme Disease by 516 Participants in the Wisconsin State Lab of Hygiene/College of American Pathologists Proficiency Testing Program. J Clin Microbiol 1997; Vol 35, No 3:537-543

Repeatedly there have been patients who are seronegative for antibodies, yet culture positive. Despite this our medical community is dependent on these tests and rely upon them as though they were 100 % accurate. No matter how bad the tests are, as long as we have them doctors will use them. This is why doctor Samuel Donta MD asked for a complete ban of the Lyme ELISA test at the 1996 LDF Lyme Conference, at least until the tests could be standardized and made reliably accurate. He found that in his long term treatment study, that some ELISA tests were more than 70 % inaccurate. Yet many doctors continue to rely upon these tests as though they were the last word in diagnosis, and all too often it is.

The worst problem for chronic Lyme patients is that after they are treated with antibiotics, they are told they are cured, even if they have a recurrence of symptoms. There is a persistent dogma in medicine that 28 days of IV antibiotics cures all Lyme Disease. In fact the on going six year old Nantucket Island Lyme Treatment Study, showed IV antibiotics to have the highest relapse rate in late Lyme disease! This was because doctors put too much faith in IV antibiotics, as being so powerful, that they did not follow up IVs with oral antibiotics. The key to treating late Lyme appears to be the length of antibiotic treatment, not the method. If IVs are followed up by six months or more of oral antibiotics, the relapse rate dropped to 13%. (Dr. Leslie Fein MD, MPH, Magnarelli MD, MPH 96 LDF Conference)

I have included in the references, several published studies, case histories and abstracts, that deal with culture positive patients who had been previously treated aggressively with antibiotics, often including Intravenous antibiotics. Most of these cases are patients who are seronegative for any Lyme antibodies, yet are culture positive. If we are repeatedly culturing this bacteria out of patients who have been treated, and who are negative by all other tests, we need to re-think our understanding of this disease! We need to treat symptoms not tests, we need to recognize that while Lyme is a treatable disease, it in some cases appears to be incurable. I would not like to be the doctor who under treats this disease, now knowing that relapses are potentially more dangerous than treating until the symptoms are gone. (4,6,42,49,67,68,70-96) Too often I have seen the word cured used in Lyme Disease Studies, only to find that the researchers have redefined the word cure to mean seronegative. Seronegativity is not synonymous with cure. The numerous culture positive cases in recent years should have negated that kind of logic years ago, and yet in 1997 researchers are still publishing studies that use antibodies, and PCR as the end point for cure. Its time to ask the patients one simple question: How are you feeling?

So lets say hypothetically you are bit by an infected tick, you get a rash, you get sick, and you have a positive test. So you get 2-4 weeks of antibiotics, and you get better, but then you get sick again. No problem you go back to your doctor and he says "Well, we better give you another Lyme test" and its negative? **Why?** Even though you have an active infection, the antibiotics cleared that infection from your blood stream. That is where your immune system is. The rest of the pathogens are hiding from the immune system inside your joints, your tendons, and your brain. Only now you don't have antibiotics to fight the infection, or any antibodies!

In a study by Dr. Musher MD, he looked at incompletely treated Tertiary Syphilis patients, and compared them to those Tertiary Syphilis patients that never got antibiotics. He found that the incompletely treated group went into dementia faster. Why? Because they had no natural immunity left. Their ability to make sufficient antibody was diminished, because the antibiotics eliminated the stimulus from the blood stream, but the infection was still hidden in the brain!

(35,61,62,65,74,83)

Conclusion: Lyme is an extremely complex disease that can cause long term chronic infections. Patients can be seronegative yet culture positive (even after aggressive antibiotic therapy). The infection enters the brain early in the infection (within days). The sequestered bacteria within the CNS can be so different from the initial infection that serum antibodies are ineffective. Incomplete antibiotic treatment of Lyme Encephalitis can harm the patient.

For a historical account of where the medical community got off on the wrong foot with the truth about Lyme disease, and why they continue to support the fallacies, read the history of Lyme Disease in the Lyme Disease Survival Manual, by Tom Grier

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88- Abstract # 1154 by Dr. Pamela E. Morrissey et al 1995 Rheumatology Symposia, This study suggests that Bb binds to a variety of tissues, and has a specific affinity to many tissue types. These specific affinities seem to be mediated by sialic acid, and glycosaminoglycans. Further specific enzymes that dissolve these compounds resulted in the inability of the bacteria to remain attached to tissues in vitro.

89- Neuroborreliosis: In the journal, *Annals of Neurology* Vol. 38, No 4, 1995 There was a brief article by Dr. Andrew Pachner MD, Elizabeth Delaney BS, and Tim O'Neill DVM, Ph.D. The conclusion of the article was simple and concise: " These data suggest that Lyme neuroborreliosis represents persistent infection with *B. burgdorferi*." The study used nonhuman primates as a model for human neuroborreliosis, and used a special PCR technique to detect the presence of *Borrelia* DNA within specific structures of the brains of five rhesus monkeys. The monkeys were injected with strain N40Br of *Borrelia burgdorferi*, and later autopsied for analysis. Accuracy of the Western Blot Using the New Suggested Criteria

90- Western Blot and False Negatives in Children: 1995 Rheumatology Symposia Abstract # 1254 Dr. Paul Fawcett et al. This abstract showed that under the old criteria, all of 66 pediatric patients with a history of a tick bite and, Bull's Eye rash who were symptomatic, were accepted as positive under the old Western Blot interpretation. Under the newly proposed criteria only 20 were now considered positive. That means 46 children who were all symptomatic, would probably be denied treatment! That's a success rate of only 31 %. 66 Children with Bull's Eye rash Old W. Blot Criteria 100 % positive New NIH Criteria 31% positive The number of false positives under both criteria was ZERO %

\* Note: A misconception about Western Blots is that they have as many false positives as false negatives. This is not true. False positives are rare. The conclusion of the researchers was: "the proposed Western Blot Reporting Criteria are grossly inadequate, because it excluded 69% of the infected children."

91- Abstract # D612- E.L. Logigian - SPECT Scans in LD and reversible Cerebral Hypoperfusion in Lyme Encephalopathy. SPECT scans in patients with Lyme encephalopathy showed decreased blood flow in the frontal sub-cortical and cortical regions of the brain. After IV Rocephin there was partial improvement, but not total reversal.

Abstract #626 - Kenneth Linger, SPECT Scans in Lyme Patients: SPECT scans revealed significant perfusion problems in Chronic Neurologic Lyme Patients, and may offer clinicians another tool to help assess brain function, and neuropathies.

92- Abstract # D647 - P.K. Coyle et al, North American Meningitis. Conclusion: North American Meningitis does not produce the marked inflammatory and immune changes reported in European cases. Lyme Meningitis can occur despite early oral antibiotics.

93- Abstract # D654 - J. Nowakowski, et al. Culture-Confirmed Treatment Failures of Cephalexin Therapy for Erythema Migrans. Two of six patients biopsied had culture confirmed *Borrelia burgdorferi* infections despite up to 21 days of cephalexin

(500 mg TID) antibiotic treatment.

94- Abstract # D655 - Nowakowski, et al, Culture-confirmed infection and reinfection with *Borrelia burgdorferi*. A patient despite antibiotic therapy had a recurring Erythema Migrans rash on three separate occasions. On each occasion it was biopsied, and revealed the active presence of *Borrelia burgdorferi* on two separate occasions indicating reinfection had occurred.

95- Abstract # D657 - J. Cimperman, F. Strle, et al, Repeated Isolation of *Borrelia burgdorferi* from the CSF of two patients treated for Lyme neuroborreliosis. Patient 1, was a twenty year old woman who presented with meningitis but was sero-negative for *Borrelia burgdorferi*. Subsequently six weeks later, Bb was cultured from her CSF and she was treated with IV Rocephin 2 grams a day for 14 days. Three months later the symptoms returned and Bb was once again isolated from the CSF. Patient 2 was a 51 year old female who developed an EM rash after tick bite. Within two months she had severe neurological symptoms, her serology was negative. She was denied treatment until her CSF was culture positive nine months post tick bite. She was treated with 2 grams of Rocephin for 14 days. Two months post antibiotic treatment Bb was once again cultured from her CSF. In both these cases the patients had negative antibodies, but were culture positive, suggesting that the antibody tests are not reliable predictors of neurological Lyme Disease. Also standard treatment regimens are insufficient when infection of the CNS is established, and Bb can survive in the brain despite Intra venous antibiotic treatment.

96- Abstract # D658 - F. Strle et al. Reinfection with *Borrelia burgdorferi* in endemic areas. Conclusion: Even despite high antibody titers as seen in ACA patients, 7 % of 2273 patients with previous Lyme disease, became reinfected and present with an EM rash and late symptoms after a recent tick bite.

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Abstract # 1256 by K.K. McCartney et al : This study showed that the using the newly proposed Western Blot criteria resulted in 60 % false negative results in children with both E.M. Rash, and Bell's Palsy. A total of 23 patients with both a bull's-eye Rash and Bell's Palsy were tested using the new criteria for Western Blot as proposed by the NIH committee. Only nine of the 23 patients were considered positive with the new criteria. This means six out of every ten Lyme Patients would be a false negative. This means flipping a coin is actually more accurate by a healthy margin of 10%.

Abstract # D601/D618 - Y.Li et al. Neuroborreliosis associated with Guillian-Barre' Syndrome. - Report of two patients in China who were previously diagnosed with Guillian-Barre' Syndrome who tested positive for Bb. Their symptoms responded to antibiotic treatment. This means they may have been misdiagnosed, or GBS is triggered by a spirochetal infection.

Abstract: # D644 - P.K. Coyle, Rapid Dissemination of Bb from the skin to the CNS. Conclusion: Bb can rapidly seed the CNS from the entry site in the skin, even prior to the formation of a rash. Therefore the traditional staging of Lyme disease based on symptoms, as either early or late stage may be a poor indicator of actual dissemination of the spirochete.

Abstract #D646 - P.K. Coyle, et al, Multiple Sclerosis vs. Lyme disease a diagnostic dilemma. Forty-seven patients were identified as possible MS patients. Many had brain lesions on their MRIs, consistent with MS 61%. CSF was constant with MS in 46 % of the patients. The final breakdown of the 47 patients was: 21 MS, 15 LD, 7 had findings constant with both LD and MS. Thirteen patients responded to antibiotics but only those who had CSF findings consistent with LD.



