Our Latest Look at Lyme

I recently sat back and thought about the past ten years during which I have been treating Lyme disease. In different situations I have used pulsed antibiotics, blood ozone therapy, herbal medicines and combinations of the three as a primary treatment beyond diet and lifestyle corrections. The results have been generally good (it's hard not to do better than the establishment doctors who, after giving a two-week course of antibiotics, pronounce the patient cured no matter what symptoms remain). However, too often antibiotics cause new trouble – a disruption of the gastrointestinal microbiome. This can lead to changes in digestion and even alterations in gut permeability ("leaky gut"), which leads to systemic inflammation and even autoimmune disease.

Another problem has been relapse, a return of symptoms in patients who had responded very well to earlier treatment. In those cases, we are finding that a few more blood ozone treatments restore the patient again. But still, there are people who just never get back to where they were before they acquired Lyme disease.

All doctors know the official story on the biology of Lyme disease [1]. First, a spirochete known as *Borellia burgdorferi* (*Bb* for short in the rest of this writing) is the cause of the disease. This microbe may be present in a variety of small mammals, birds and even amphibians. In most cases, these animals don't become ill from acquiring *Bb*. When the tick takes a blood meal from the carrier of the Lyme germ, the bacteria migrate to the mid-gut of the *Ixodes scapularis* tick and there steal some of the nutrients in the blood meal. After a while, the bacteria migrate to the salivary glands of the tick. The tick's saliva is now a reservoir for further transmission of the disease. When the tick later bites a deer, for example, the deer becomes a carrier of the germ. If it bites a human, depending on the immunological status of the person, they may come down with Lyme disease. That person may or may not know that they have been bitten. Of course, if they notice a "bull's-eye" rash and/or become ill – feverish, achy, weak – they will go to a doctor and get a prescription for a tetracycline drug and this will cure the infection before it has a hold on the person. However, not everyone so afflicted has a complete recovery from the typical fourteen-day course of antibiotics. Worse, the person bitten may not notice the tick or see a bull's-eye rash. They might not become ill right away. It may be weeks or months or even years before symptoms develop. And the symptoms don't always present in a medical textbook fashion.

When syphilis, a first cousin to *Bb*, was rampant in the 19th and early 20th centuries, it was called "the great masquerader" and it was said that "if you knew syphilis you knew medicine." [90] The statements were made to indicate the diversity and often confusing array of signs and symptoms that spirochetes could cause in an infected person. The Lyme spirochete can create an equally confusing picture. Strange neurological symptoms may occur: tingling, numbness, "crawly feeling," joint pain, muscle pain, joint swelling, intermittent fevers, brain fog, profound fatigue, heart rhythm disturbances, unusual rashes, etc.

A doctor has to think of a diagnosis in order to make it. As always, the patient's story is most important. The laboratory can also be of help. A number of antibody tests can be used, notably the measurement of antibodies against various borellial proteins in the patient's blood. The most

thorough of these antibody tests is known as a Western blot. But there is a problem with this testing: if a patient shows positive antibody titers against proteins of *Bb*, it indicates that the person has been exposed to the germ, but it doesn't necessarily establish that the patient's present symptoms are a result of an active Lyme infection.

On average, my patients have been ill for months or years. They have often consulted ten or more physicians in a number of specialties. They have numerous complaints and various diagnoses. Very often no definitive diagnosis of their condition has been made. Is it Lyme disease? Chronic fatigue syndrome/fibromyalgia? Endocrine dysfunction? An autoimmune disease? Multiple body systems appear to be malfunctioning. Our clinic has worked hard over the past 35 years to try to understand what has befallen patients with complex presentation and what to do to help them. We obviously look at all potential causes of their symptoms – dietary and digestive problems, adrenal, thyroid and sex hormone imbalances, deficiencies of essential nutrients, toxic metal accumulations, allergies and environmental sensitivities, autoimmune processes and, of course, occult infections.

That brings us back to the evaluation and potential treatment of Lyme disease as one of the dominant factors causing the presenting illness. Because Lyme disease can be so confusing to diagnose and difficult to treat, I decided to look at the basic biology of its causative agent, *Bb*, and that of the tick, *Ixodes scapularis*, that carries it [2]. I also reviewed what science knows about what happens to a human being when the germ enters their body from the tick's saliva and what defenses the victim erects to stop the germ from making them ill [3]. As described above, the Lyme bacterium develops in the mid-gut of the *Ixodes* tick where it "shares" the blood meal the tick siphons out of an animal. After the spirochetes develop in the gut, they migrate to the tick’s salivary glands and are secreted into the puncture wound of the next host to start a new life, (hopefully, from the spirochetes’ viewpoint), in their unfortunate victim.

Clearly, it is important to understand your microbial enemy to mount a defense against it. There seems to be a lot of confusion as to what *Bb* uses for fuel in both the tick's and the human's bodies. People tell me they read that when we lose weight, the germs gorge themselves on our fat, or that they eat up our cartilage or brain cells. It is easy to put those ideas to rest. The truth is that the Lyme spirochete is an extremely simple creature [4]. It lives primarily on glucose and other sugars that it ultimately converts into glucose. This is the sole fuel it uses to make energy. It has no mitochondria, doesn't have an oxygen-dependent electron transport chain, and it can neither synthesize nor burn fatty acids [5]. It can't even manufacture the components of its own DNA, the nucleotides. It isn't able to synthesize amino acids. The extent of its processes and machinery is that it ferments sugar to make energy; it sequesters from its host all the amino acids it needs to make its own proteins. It salvages the host’s nucleotides to make its RNA and DNA. It uses fatty and proteinaceous material that it acquires from its host to construct its phospholipid membranes, genetic material, and its locomotor apparatus – the flagellum [6]. It is a parasite in the truest sense of the word. Later, I will explain how understanding its needs and capabilities can help us plan treatment.

After the bite, the host’s immune cells are called into action. Cells belonging to the innate immune system, such as macrophages and neutrophils, generate large quantities of reactive oxygen species (ROS) to kill invaders [2, 3].The principal ROS is known as superoxide anion.

This is then reduced to hydrogen peroxide. These oxidants add to the level of the ones constantly being created as waste products of normal metabolism. The mitochondrion, where 90% of our body's energy is produced, is the biggest source of our ROSs in a non-infected, healthy state. Between the oxygen free radicals produced in the mitochondria and the ones produced by the upregulated immune cells in the event of an immune response, dangerous, tissue-damaging levels of the reactive molecules can accumulate. Normally, these radicals are neutralized by antioxidants such as vitamins C, E, beta-carotene and the polyphenols from the plants in our diet. We also manufacture endogenous antioxidant enzyme systems such as catalase and superoxide dismutase (SOD), and possess a complex system of detoxification based on the tripeptide glutathione (GSH). Thus, during the oxidative storm initiated by the infection, the antioxidant system is overwhelmed, and glutathione, the central player in neutralizing free radicals and other toxins, is exhausted. The elevated ROS levels activate the central inflammatory pathway known as NFκB. This nuclear factor turns on genes that make cell-signaling molecules called proinflammatory cytokines, such as IL-1, IL-6, TNFα etc., and these molecules lead to an exacerbation of the oxidative stress and more intense inflammation. The result is damage to various biomolecules: the fatty acids in cell membranes, proteins of all kinds, and the genetic material itself. Worst, the mitochondria themselves are injured and their ability to make energy is compromised. At this point, the patient is very ill.

So why doesn't this storm of inflammation destroy all the spirochetes and stop the disease in its tracks? *Bb* is very unique; it contains no intracellular iron [7]. This is important because when a lot of hydrogen peroxide (H_2O_2) is generated in the presence of iron, a very nasty free radical known as hydroxyl radical is formed, which damages the DNA of bacteria. So, in the case of *Bb*, the absence of intracellular iron means that DNA is not a target for the free radicals being produced. Further proof of this is that *Bb* also lacks DNA repair enzymes, which further indicates that free radical damage to DNA is not a significant aspect of host immune defense against *Bb* as it is in defending against other bacteria [7].

But excess free radicals also damage lipid membrane structures, so is this a route we use to destroy spirochetes? *Bb*, remember, does incorporate fatty acids from the host environment into its membranes. In most bacteria, free radical damage to lipid membranes is minimal because their membranes lack polyunsaturated fatty acids. In contrast, *Bb*'s cell membranes contain significant amounts of unsaturated fatty acids acquired from their host. When lipid-directed oxidants are added, the highly essential fatty acid linoleic acid is reduced 50-fold, so *Bb* membranes are indeed targets for ROSs. Following oxidant exposure, the fatty acid content goes down, and the damage products, known as MDA (malondialdehyde), go up. Under the electron microscope, obvious membrane damage can be seen [7].

The other fact about *Bb* is that, like most invasive microorganisms, they grow best in very low-oxygen environments. If they are grown in oxygen-rich environments, as shown in the above-cited study, they are unable to multiply, and show the same damage as seen when they're exposed to oxidants. In the study the author concludes:

> "this indicated that (*Bb*) cells grown aerobically (high or even low oxygen culture conditions) had significant damage compared to cells grown anaerobically (no oxygen)."

Bb also possesses no enzymes to break down fuel in the presence of oxygen like we do, so any oxidants they are exposed to come from the actions of the host trying to destroy them. In addition, *Bb* lacks a complex antioxidant system to defend itself from host-derived oxidants.

But, as Paracelsus said 500 years ago: "The poison is in the dose." So, we will discuss methods to increase oxygen and oxidants to inhibit the proliferation of *Bb* or kill them outright without harming our own cell membranes, proteins and DNA.

Thorough scientific analysis reveals that *Bb* doesn't cause disease in animals but does in humans due to our immunopathological response. *Bb* makes products to survive and replicate but not virulence factors like other germs. One author said:

"*Bb* did not evolve to cause disease in animals." [2]

However, it does make lipoproteins that do trigger components of the mammalian innate immune system. In general, our immune system recognizes and mounts various immune responses to proteins and lipoproteins that it doesn't recognize as "self." Thus, it would be expected that *any* foreign protein could trigger antibody formation, since we can measure them via antibody assays against the milk protein casein, gliadin, fruit or vegetable proteins, and even against our own proteins when they are exposed to the immune system during trauma or infections. So we, like the tick, do suppress *Bb* when we are invaded.

Also of interest is the observation that the flagellum of *Bb* is hidden beneath its outer membrane to hide the evolutionarily-conserved 41 kD protein from our immune system. Many microorganisms manufacture this protein for their locomotor functions. It would stand to reason that we can mount a defense against this protein when the immune system sees it. Band 41 on the Western blot test demonstrates exposure of the patient to this protein, but it does not say it specifically comes from exposure to *Bb*.

Another important factor to consider regarding *Bb* is that it has a very small genome, indicating that it is an obligate parasite [2]. These types of microbes don't want to kill us, only use us. In fact, since we have become so sanitary, we no longer harbor helminths (worms) and leading immunologists believe that the rise of allergic and autoimmune diseases appeared because of the lack of diverse creatures in our intestines with which we used to live in harmony [8]. Maybe our ecology is just out of whack and *Bb* has become a much more serious pathogen, as will be discussed below.

As stated above, humans and our dogs (who eat the same processed foods we do in modern times) are the rare animals who become ill after exposure to *Bb*. Rabbits, for example, get a rash but clear the infection [2]. Scientists have shown that wild mice show no sign of disease but can become persistently infected [2]. Some mouse strains in the laboratory, however, do develop ankle swelling and inflammation resembling the arthritis of Lyme disease. The authors of a review paper entitled "Biology of Infection with Borrelia burgdorferi" conclude:

> "These data suggest that disease is a consequence of host immunopathology, rather than a strategy of the bacterium to facilitate its persistence or transmission [2]."

Our immune system does mount a powerful response that does suppress the infection. The innate immune system's complement proteins bind to the spirochete, which then facilitates our phagocytic cells to be able to engulf and destroy the bacteria. In addition, we have cells that recognize molecular patterns of the bacterium's lipoproteins and then pass this information to cells which then make specific antibodies against these bacterial surface proteins. Attachment of antibodies to the spirochetes either kills them directly or sets them up for destruction by other immune system cells such as natural killer cells.

This is how the human body defends itself, but sometimes the strategy goes awry. As mentioned above, the patterns of microorganisms recognized by our own immune system can be similar in structure to some of our own proteins, and thus, "autoimmunity" can result. I believe the German term for this phenomenon is more descriptive: "Autoagressiv."

So, in summary, *Bb* doesn't cause disease in other animals. We get sick due to our immune system's response to *Bb*. *Bb* makes products to survive and replicate, but does NOT make virulence factors (toxins or poisons) like other germs do. As a preliminary to later conclusions drawn from studying the medical and biological literature on *Bb* and Lyme disease, I believe some people get so ill because they are already in a state of increased oxidative stress and inflammation, due to a myriad of other modern factors in our lives.

I even wondered: "Does the tick get sick by harboring *Bb*?" It turns out that the tick's immune system keeps the spirochete population at a very low level and uses various methods to kill them in all areas of their body except the gut, where they develop, and the salivary glands, from whence they enter the next host. It might even be possible that the spirochete aids the tick's blood meal acquisition by factors it manufactures and releases into the wound from the bite. Thus far, it appears that the tick and the spirochete are both doing just fine at our expense. And to reiterate an earlier point, it appears that most animals escape serious harm as a result of infection by *Bb*.

So why DO we humans sometimes get so ill after *Bb* enters our body? A great insight into that question was attained from a study of how the antibiotics doxycycline and minocycline affect human cells' response to infection with *Bb* [9]. These antibiotics suppress the growth of *Bb* by inhibiting their ability to make protein. They don't kill spirochetes, they just slow them down. These are interesting agents which have been shown to have many other effects besides antimicrobial ones [10-13]. They have been shown to ameliorate the symptoms of a number of neurodegenerative and autoimmune diseases, and they do so by down-regulating the very inflammatory pathways that are turned up by Lyme and other infections. They lower the activity of that master regulator of inflammation known as NFκB, and the associated inflammatory signals like IL-1, IL-6 and TNFα. These molecules are known as cytokines, which means that they signal cells to participate in the immune response in specific ways. In a very revealing study on brain abscesses in mice caused by infection with the Staphylococcus bacterium, minocycline reduced the brain inflammation and abscess-associated death rate and improved brain survival

significantly [14]. This is of great importance, because the strain of Staphylococcus used is totally resistant to minocycline! Thus, the drug worked solely via its anti-inflammatory effects. Another study demonstrated that when microglia (a kind of brain connective tissue cell with immune function) were exposed to a primary lipoprotein of the Lyme outer membrane, Osp A (Band 31 on the Western Blot test), there is a huge increase in the release of the pro-inflammatory cytokines IL-6 and IL-8. Doxycycline markedly attenuated their release [9]. The authors of this study argued that patients who had been treated for Lyme disease and were still suffering from fatigue, cognitive dysfunction and musculoskeletal complaints months or years after the original treatment often have no evidence for continuing active spirochaetal infection. In these cases, the beneficial effects of doxycycline, in the authors' words "may not be confined to the antimicrobial properties of this antibiotic but may include an anti-inflammatory component." Interestingly, both minocycline and doxycycline have also been used to treat autoimmune diseases like rheumatoid arthritis [15] and multiple sclerosis [16, 17], both of which have been linked to *Bb* and other infections.

The macrolide group of antibiotics include clarithromycin and azithromycin. These agents also don't directly kill bacteria, but suppress their growth. These agents also dampen the production of inflammatory cytokines such as IFNγ, TNFα, and IL-8, and inhibit the central inflammatory regulating pathway known as MAPK [18]. These drugs have shown efficacy for various inflammatory diseases, psoriasis and arthritis. Interestingly, the inflammatory bowel condition called Crohn's Disease has responded to a combination of a macrolide and a rifampin class drug [19] – a combination that has been successfully used to treat *Bartonella* infection, a coinfection transmitted by ticks. The same authors cite studies showing the clarithromycin also inhibits various other viruses known to be transmitted by Lyme ticks.

In another review of the effects of macrolides in chronic inflammatory skin disorder, the authors point out that in reference to the therapeutic effects of the drugs:

> "It must be pointed out that immune modulation is the suppression of inflammation and immune hyperactivation without causing immune depression (immunosuppression) [20]."

In other words, these drugs reduce inappropriate inflammation, inhibit bacterial growth but don't suppress immunity.

Finally, another bacteriostatic antibiotic, clindamycin, has been shown to protect neurons better than the bactericidal agent ceftriaxone, during bacterial meningitis [21]. This drug also suppresses *Bb*, a bacterium that has profound effects on brain tissue.

That brings up a very important question: can infection with the Lyme bacterium lead to autoimmune processes? In Yehuda Schönfeld's monumental book entitled Infection and Autoimmunity [22], he and his co-authors presented a vast array of studies showing that viral, bacterial, fungal, and protozoan infections can precipitate various autoimmune diseases. In fact, the first scientific article linking *Bb* to autoimmunity was published in 1989 [23], only seven years after Dr. Willy Bergdorfer proved that the etiology of the disease first described in Lyme, Connecticut in 1977 was in fact *Borrellia bergdorferi*. There are more than 80 peer-reviewed

publications showing a connection between *Bb* and host-directed (autoimmune) damage to proteins in the joints, muscles, brain and heart [23-26]. It turns out that viruses and bacteria may have a protein containing an amino acid sequence that is very similar to that of a human protein. After an infection occurs, certain lymphocytes "read" the amino acid sequences of the invaders' proteins and pass the information on to other types of lymphocytes, which then begin to produce antibodies against the invader's proteins to kill them. Even after the infection is brought under control, the antibody-producing cells may continue the attack, and human proteins, which appear to the body to be the invading germ, may become the target [27, 28]. This phenomenon is known as "molecular mimicry." [26, 29]. Usually, after an infection is brought under control, the immune cells that had been activated to mount the attack are given instructions by regulatory lymphocytes (T-regs and B-regs) to cease their activities. In certain genetically susceptible individuals, the system fails and the attack continues. Unfortunately, destruction of human tissue is the result. If the "self" protein is in the synovial membranes of a joint, inflammatory arthritis occurs; if it happens to be a myelin sheath protein covering brain cells, the patient develops multiple sclerosis. If the proteins of the microbe have molecular similarity to skin proteins, psoriasis or other skin disorders ensue. One recent study from the University of Rome revealed that a patient with long-standing fatigue and cognitive abnormalities was found to have auto-antibodies against a brain enzyme that is necessary for energy production [30]. This protein, gamma-enolase, was found to be a molecular mimic of an enolase found in *Bb*.

This enzyme protein is necessary for making energy through a process known as glycolysis, the preferred way to make energy in the human brain and the only way to make it for *Bb*. This is the pathway by which glucose is metabolized. It is easy to understand why these patients have cognitive problems. This finding is not only revealing in our understanding of why Lyme patients have neurological symptoms long after they have been treated for Lyme disease, but also gives us insight into methods to treat such patients: notably, the ketogenic diet.

Remember that *Bb* can't use fatty acids to make energy. We, on the other hand, are well-adapted to being without food for days or weeks. It occurred often in our history when food was scarce. There is only about one hour's worth of glucose in our blood stream at any one time, and only about a day's worth of stored starch in our liver and muscles. After that, if we are to make energy, we have to burn fat. We can. *Bb* can't. We flourish. They founder. This gives our immune system an advantage in destroying the spirochetes if there is an active infection – if not, this metabolic state, ketosis, has been proven to help diseases from chronic fatigue syndrome to cancer to epilepsy [31-33].

At this point, there are only anecdotal reports of people using the ketogenic diet to treat their Lyme disease. But there are numerous scientific studies showing that this diet improves energy production (burning fat gives more energy and fewer damaging waste products than burning glucose). In addition, the highly inflammatory cytokines mentioned above are reduced, memory is enhanced, pain is dampened, and markers of damage to DNA, proteins and membrane fats are reduced. This is a win-win for the victim of *Bb*: reduced ability of the germ to proliferate, and enhanced energy and defense systems to fight the germ.

Even a drastic reduction in sugar and starch intake with an increase in the consumption of unprocessed vegetables, berries, nuts, and a switch to organic meat results in improvement in

immune function and a reduction in symptoms. A ketogenic diet is one of very low carbohydrate, high fat and moderate protein content. The total carbohydrate content of the diet is limited to 20-30 grams per day. The ratio of fat-protein-carbohydrate calories is 80-10-10. This diet gives enough protein to prevent muscle breakdown, but forces the body to shift over to burning fat as its main source of energy. Basically, we only have enough glucose in our blood at any one time to last about one hour in providing energy in the fasting state. The starch stored in the liver and muscle can also be converted into sugar and burned for energy, but after one to two days, this source of glucose is exhausted, and the body is forced to burn fat. This fat, which is converted into ketones, a fuel which *Bb* is unable to use, can come from fat storage or from dietary fat. *Bb* is unable to use anything except glucose to make energy, so once a person's metabolism shifts into burning ketones derived from fat, the blood sugar drops, and there is a dramatic reduction in glucose available for *Bb* to convert into energy.

Now that we have set the stage for a method to inhibit the growth of the Lyme spirochete with diet and bacteriostatic antibiotics, we can look at other maneuvers that can further suppress and eliminate the invader AND possible autoimmune processes it can initiate. We detailed above a dietary method to exploit the primitive glucose-fermenting metabolism of *Bb*. Another weakness of this germ is its intolerance of oxygen. Studies show it can't multiply in even low-oxygen environments [7]. In addition, it doesn't have good antioxidant systems. Free radicals damage its phospholipid membranes. We, on the other hand, have very sophisticated antioxidant defense systems. These work very well under normal circumstances to protect us from free radicals manufactured during maintenance metabolism. However, in the present day and age, our capacity for antioxidant defense is limited. We are already so weakened and inflamed that an attack by Lyme can put us over the top and overwhelm our defense systems. That is why Lyme patients feel so ill – no energy, pain, brain fog and the myriad of symptoms that come with long-standing Lyme disease.

To capitalize on *Bb*'s susceptibility to high oxygen levels, we are able to administer a treatment developed in Germany 50 years ago. It is known as major autohemotherapy (MAHT) with ozone. To perform this treatment, a given amount of blood is removed from the patient and an exact dose of an oxygen/ozone gas mixture is added to the blood. The blood is then re-infused into the patient. The biological effects of this treatment are better documented than those of almost any other standard or alternative treatment for human ailments. There are over 2500 peer-reviewed scientific studies indexed at the National Library of Medicine (pubmed.org). A number of scholarly books on the mechanisms of action and efficacy of ozone therapy have also been published.

In reference to the treatment of Lyme disease, the following effects of ozone therapy are relevant [34-36]:

*Delivery of an oxygen/ozone mixture to blood causes an increase in the release of oxygen from the red blood cells (hemoglobin) at the cellular level, and thus, increased oxygen is delivered to the mitochondria, where 90% of our energy is made. This improves the human cells' energetics while it creates an environment that is inhospitable for *Bb*.

*The compounds formed as a result of the interaction of ozone with body proteins and fats act as

signals to our DNA and result in increased synthesis of antioxidants to protect us from free radicals.

*Those compounds also up-regulate the production of growth factors, which promote tissue healing.

*There is a direct effect on viruses and bacteria when ozone is mixed with the blood. The damaged molecules of the killed-on-contact germs act as immune stimulants to the native immune processes of the body.

*Glutathione (GSH) production is increased. This simple protein is the main antioxidant and detoxification agent produced in the human body. Besides neutralizing free radicals, it attaches to various chemicals and damaged proteins which contribute to the total load of illness causation, and escorts them from the body via the liver and the kidneys. Finally, GSH is a chelating agent which removes poison metals like mercury, lead, cadmium and arsenic, also via the liver and kidneys. Every disease process studied by science has been shown to result in the exhaustion of the GSH supply. This then leads to more damage, and a vicious circle is created. Raising GSH is an integral component of the treatment of Lyme disease that will be discussed below.

As indicated above, *Bb* stimulates the immune system to produce numerous pro-inflammatory cytokines and oxygen free radicals. The purpose of this reactivity, of course, is to destroy the invaders. Unfortunately, the host's molecules experience collateral damage. Studies have shown that these phenomena can be dampened through the use of certain herbal medicines [37]. These include polyphenols such as quercetin, curcumin, EGCG and Boswellic acid. One study showed a synergy between certain phytochemicals, iodine, vitamin C, vitamin D and monolaurin in inhibiting *Bb* [38].

Beyond herbal products acting as antioxidant agents, there are numerous studies of specific herbs in treating Lyme infections. These studies not only looked at whether the herbal products were effective in suppressing *Bb* directly, but also the mechanisms by which they worked. It turns out that some of the principal herbal ingredients of specific plants do have the ability to suppress the spirochetes directly [39, 40]. More importantly, many of these herbal medicines modulate the immune system in a favorable way. Some of them increase the killing power of our natural killer cells [41]. Others increase immune cell production of antibodies against bacteria, including *Bb* [42]. They also have immune-enhancing properties against viruses, fungi and protozoa [43] – microbes which are also found in ticks' salivary glands and transmitted to hosts along with the Lyme organism. We will discuss some of the herbal medicines we use in the treatment protocol at the end of this article.

Of course any dietary directions given to help combat Lyme disease will be accompanied by attention to related issues, i.e., deficiencies of essential nutrients needed to combat invasions, repair cellular structures, digest food and coordinate inflammation. The latter include the interactions between the brain, gut, endocrine glands and every cell of the body. We measure and correct deficiencies of vital minerals, vitamins, essential fatty acids and accessory substances needed for healthy structure and function of all systems.

In particular, some scientific work done in Poland [44] showed that patients suffering from Lyme disease had significantly less of the amino acid L-carnitine in their blood than healthy controls. In fact, the study analyzed three patient groups: 1) acute Lyme infections with the erythema migrans (EM) rash, 2) Lyme neuroborrelliosis (LNB) patients (patients with central nervous system involvement), and 3) "post-Lyme disease" patients who were thought to be adequately treated but were still very ill with a variety of symptoms. The lowest levels of carnitine were found in the second group, followed by the "post-Lyme" group. The levels in the EM group were higher than the other two, but still significantly lower than the carnitine level found in healthy control patients.

This is a very important finding for at least two reasons. First of all, L-carnitine is needed in the transfer of fats into the mitochondrion for burning into energy. L-carnitine also has a number of other housekeeping functions in cells as a regulator of energy production, in maintenance of salt and fluid balance, as an antioxidant, in neurogenesis (the process whereby brain cells make new connections or repair damaged ones), and as a neurotransmitter. It is hard to imagine how a person could successfully fight Lyme disease when L-carnitine supply is inadequate.

The second consideration from this study is: “what came first, the chicken or the egg?” This is, in a way, a rephrasing of the debate between Louis Pasteur and Antoine Bechamp when the argument was phrased "Seed vs. Soil.” Pasteur argued that the seed (the germ) was of most import in causing disease while Bechamp said it was the condition of the soil; that is, the health of the body. A germ could not grow in a patient with robust immune defense – his "soil" was inhospitable to the germ. While Pasteur won that argument at the time, we are beginning to see that Bechamp was actually correct. [91] Is it possible that the L-carnitine levels in the patients in the study were *already* low when they became infected with *Bb*, and thus they were already in a state of susceptibility? It would be hard to design a study that could unwind this question, but it is clear that having an inadequate carnitine level is undesirable, especially during the demands of fighting a dangerous invasion. Replacing carnitine will obviously be part of our Lyme disease protocol. Of course, we will also direct our attention to digestive issues, especially promoting a healthy microbiome, and to identifying and correcting inadequacies in thyroid, adrenal and sex hormone biology.

Also, remember that the gastrointestinal tract is the home of most of our immune system. It is lined with immune cells which identify any foreign antigens that could find their way into the blood, and they both make antibodies to block the invaders, and send messages to the regional lymph nodes and liver, both of which communicate with immune cells, the endocrine system and the brain. Together, all these players orchestrate a coordinated defense against all types of invasion.

In addition to the Lyme patients having a deficiency of carnitine, they have an increased need for glutathione [45], as mentioned above. This is a molecule that is made in every cell of the body, but this most important detoxification agent becomes exhausted in states of high inflammation, such as a Lyme infection. To ensure that there is an adequate supply, we often prescribe a highly absorbable form of this antioxidant. If a person ingests the typical form of glutathione, it is rapidly broken apart in the digestive tract and thus doesn't do any good in neutralizing toxins. Fortunately, a special preparation has been created by an integrative practitioner named Tim

Guilford, M.D. He produces GSH that has been inserted into little fatty envelopes called liposomes. The GSH-liposomal particles have been proven to cross the gastrointestinal barrier intact, and enter both the lymphatic and blood compartments and thereafter be distributed to the entire system [46]. A number of peer-reviewed scientific studies have been published that demonstrate that Dr. Guilford's preparation is absorbed intact and, more importantly, results in positive effects on the immune system in serious diseases such as tuberculosis and HIV/AIDS [47]. The administration of liposomal GSH has been shown to enhance cell-mediated immunity and reduce inflammation [48]. The treatment has also been demonstrated to decrease free radical activity and immunosuppressive cytokines [47, 49]. Without an ongoing GSH supply, energy production falters and destruction of biomolecules marches forward.

Now that we have an overview of the nature of Lyme disease – its lifecycle, transmission and the effects it has on the human host as it defends itself, we can summarize the treatment protocol we have developed at the Waters Center for Biological Medicine. This is an eight-pronged program that covers suppression and destruction of the spirochetes, the dampening of the excessive inflammation created by the body's defense system; the support of the interventions via correction of troubled digestive, endocrine and neurological systems; the repair of damaged structures and a method to balance the immune system, both through eliminating allergies; and, most importantly, reversing the autoimmune processes that *Bb* and possibly other microorganisms have triggered during the course of the illness.

1) The first step is to deprive the spirochetes and other microbes of an energy source. This is done with a ketogenic diet, calorie restriction diet or a very low carbohydrate diet. It is important that the diet is doable for the patient, so we guide people in choosing and maintaining a diet that will work.

2) In conjunction with the diet, we identify and correct disorders of the endocrine glands and gastrointestinal function. This step involves detoxification interventions – correcting the microbiome, improving or replacing digestive secretions from the stomach, liver and pancreas, stopping the intake of inflammatory foods and, in some cases, the use of toxin-binding agents such as charcoal and cholestyramine. Getting all body systems in order sets the patient up to eradicate the Lyme infection and heal the damage.

3) The third step is judicious use of bacteriostatic antibiotics. There are two major categories of antibiotics – ones that kill bacteria (bactericidal) and ones that suppress their growth by inhibiting their ability to manufacture proteins. The latter are known as bacteriostatic. The ones that kill germs have now been shown to damage our cells' power sources – the mitochondria [50]. The use of antibiotics such as amoxicillin, Cipro, penicillin and others, while effective in killing germs, also can inhibit energy production and make the patient sicker than they were before. That is why we limit our use of antibiotics to the bacteriostatic variety.

It turns out, as mentioned above, that two groups of bacteriostatic antibiotics, the tetracyclines and the macrolides (zithromycin et al.) as well as the group which contains clindamycin, not only suppress spirochetes and other microbes, but also diminish excessive inflammation generated by the host's defense against the bacteria [9, 18]. In addition, there is now evidence that these drugs

also affect positive changes in lymphocyte populations – in other words, they have immunomodulatory effects [14, 21].

Despite these drugs being much safer than the bactericidal antibiotics, they can nevertheless cause a disruption in the microbiome. We are diligent in replacing the important symbiotic organisms such as lactobacilli and bifidobacteria, as well as using antifungal agents to prevent yeast overgrowth. In some cases it isn't appropriate to use antibiotics at all. This may be due to drug allergy or a prior history of antibiotics causing serious disruption of the gastrointestinal microbiome. Patients who have experienced such reactions are not interested in using or taking antibiotics at all and I'm very supportive of their position.

However, when the patient and I elect to use pharmaceutical antibiotics, we use them in a "pulsed" manner. We may, for example, use minocycline three days per week and then for only two weeks out of four. In truth, we and many patients would like to avoid the use of any pharmaceutical antibiotics if possible, which brings us to the premier treatment for Lyme disease and virtually all other infections.

4) The fourth approach is ozone therapy, or MAHT. As indicated above, a precise dose of ozone is mixed with the patient's anticoagulated whole blood and then re-infused into the patient's vein. This is performed once or twice weekly for a total of approximately 15 treatments. Blood ozone therapy is probably the safest therapy in our armamentarium, and besides helping the body kill germs and improve its capacity to heal, it has been shown to improve neurological function and microcirculation, and correct autoimmune disease [34, 36, 51]. A German colleague, Dr. Fahmy, directs an 80-bed rheumatological hospital where ozone therapy is central to treatment for disorders such as rheumatoid arthritis and multiple sclerosis. His book, Ozone Mode Action of the Immune System, describes his approach to autoimmune disease, and is a thorough review of immunology as well [52].

Even in patients with no medical complaints, a series of ozone treatments has been shown to improve the ability to make ATP energy through oxygen-dependent metabolism [53] is the most efficient mechanism for energy production and diminishes as we age. A series of ozone treatments represents a form of rejuvenation therapy.

5) An additional approach to treating Lyme disease and other infections is the use of herbal medicines. We will discuss the main four used in our Lyme protocol:

The first is resveratrol; this polyphenolic stilbene is found in grapes, berries, peanuts and Japanese knotweed. It is thought to work in helping to fight various infections, in part by inducing immunomodulatory effects [54]. Namely, it up-regulates the natural killer cells. It also promotes the proliferation of regulatory T-cells [55]. The latter is important in preventing the immune response from destroying the host’s tissues, and in preventing autoimmunity. In addition, this study shows that resveratrol also reduces production of inflammatory cytokines such as TNFα and IL-6, as well as markers of DNA damage. It must be understood that it is important for the body to mount an inflammatory response in an effort to defend against a microbial invasion, but this response can get out of control and damage the very body it is trying to preserve.

Resveratrol has been shown to possess antibacterial activity by inhibiting a protein necessary for *Bb* cells to divide, the Z-ring [56, 57]. This results in fragmentation of the germ's DNA, and thus, loss of the ability to divide and proliferate. Other herbs, such as berberine, also inhibit bacterial cell division [58]. We may add this and other herbs in particular cases for special purposes. Resveratrol also inhibits a capsid which viruses need to replicate [43], so this herb can be expected to help defeat the viruses also carried by the Lyme tick. While resveratrol inhibits free radical damage to the host cells, it also increases the production of the superoxide anion radical in phagocytic cells [59], thus enhancing their ability to kill germs.

In addition to its various actions against microbes, resveratrol also protects brain cells from inflammation and enhances the body's production of antioxidants [60]. As a bonus, it also prevents excess calcium entry into cells, a process that leads to cell death [61]. Resveratrol is a very versatile herbal medicine with virtually no side effects.

A second powerful herb in our fight against Lyme disease is *Andrographis paniculate*, via its major phytochemical andrographolide. This substance also increases the production of enzyme antioxidants in response to inflammatory/oxidative stress [62, 63]. It also improves white blood cell phagocytic response and increases the proliferation of lymphocytes and their ability to make germ-killing cytokines [64].

Andrographolide additionally inhibits cell-killing capacity of viruses [65]. Luckily, this wonderful medicine also has antimalarial effects [66], and thus can be used against other protozoa such as *Babesia* which is also transmitted in tick saliva. It has even been shown to upregulate the production of β-defensin, an antimicrobial peptide produced by cells of our innate immune system [67]. You see, we were equipped with our own arsenal of antibiotics long before the pharmaceutical industry created them – we just need to help our system to produce them again.

This herb also acts as a true adaptogen by increasing germ-killing cytokines and inhibiting excessive host tissue-damaging molecules, while increasing antibody production [68]. This herb also has neuroprotective properties. Finally, experiments have shown *Andrographis* to inhibit biofilm formation [69]. Like resveratrol, *Andrographis* is an amazing multifunctional and very well-tolerated herbal medicine.

The South American herb *Uncaria tomentosa* is also known as cat's claw. It has documented antioxidant, anti-inflammatory and immunomodulatory effects. Like other herbs used in treatment of infectious diseases, it enhances the killing of various germs, but reduces the most inflammatory substances like TNFα [70].

The final herb we will discuss here is *Panax ginseng*. Ginseng is probably the most versatile adaptogenic herb on the planet. It also improves the function of natural killer cells, and the ability of macrophages to engulf and kill invading microbes [71]. It increases the ability of the natural killer cells to make the antiviral compound interferon gamma (IFNγ) [72]. Ginsinosides (the bioactive molecules in the roots) have the capacity to improve the function of dendritic cells [73]. These cells, belonging to the innate immune system, identify alien proteins of invading germs and present the information to T-helper lymphocytes for them to use to direct the immune

response via numerous other cell types. At the same time, the ginseng is promoting multiplication of various immune cells, and thus, the increased production of inflammatory cytokines. It is also activating a protein, *FoxP*, which promotes the generation of immunosuppressive T regulatory cells [74], which dampen excess inflammation. Ginseng also increases the production of all three main classes of antibodies, IgG, IgM and IgA. These molecules attach to foreign structures and destroy them, or work with cell-based microbe-destroying processes.

Plant-derived medicines literally work with your body's defense system to protect you from invading microbes, but also to protect the nervous system, balance the endocrine gland function and improve energy metabolism. No wonder Asians come to Wisconsin to buy our ginseng!

We could mention many other herbs, such as Echinacea [75], *Stevia rebaudiana* [76], *Dipsacus* species (teasel) [77], and individual polyphenols such as berberine [78, 79], tannins and quercetin. It is also well-established that a number of these herbals can work together synergistically to support body defenses [80]. This is an ancient idea as evidenced by the formulations used in both traditional Chinese medicine and Ayurveda – medical systems in use for thousands of years. Finally, the great gift of herbs is in addition to the myriad of beneficial effects they offer: their safety margin is great and they are generally better tolerated than synthetic pharmaceutical agents.

6) As described above, the main antioxidant and protective agent of our body is the tripeptide glutathione (GSH). While the body is fighting all the inflammation and toxic free radicals generated during a microbial invasion, it is often not able to keep up with GSH production. We offer a highly effective, scientifically documented liposomal liquid GSH for daily use until the body is able to make a sufficient amount of its own.

7) The very important amino acid L-carnitine has been shown to be decreased in the blood of patients with Lyme disease, as discussed above. The more ill they are, the less they have. It is impossible to efficiently burn fats in our mitochondrial powerhouses without enough of this amino acid. In our practice, we use the form of it known as acetyl-L-carnitine. It has been documented to be better absorbed and utilized in mammalian systems [81]. It also removes toxic fatty acid metabolites in the mitochondria and plays a number of secondary roles as an immune system modulator, antioxidant, anti-inflammatory agent, and regulator of cell volume and fluid balance in tissues, including the nervous system. If an ailing system is going to be repaired, all the key molecular players must be present.

8) The last area that must be addressed in the treatment of Lyme disease is the "immunoconfusion" it can initiate as our immune system attempts to control it. As related above, within seven years after *Bb* was found to be the cause of Lyme disease, scientific reports began to appear describing autoimmune syndromes following infection with the Lyme spirochete. A number of articles in the 1990s to 2010s show definitively that in many patients with "chronic Lyme disease" or "post-Lyme syndrome," the following scenarios were present:

- No active Lyme infection could be demonstrated by culture or PCR (a technique that identifies bacterial DNA). These are patients who have been aggressively treated with

antibiotics. In one study [82], there was no difference in the clinical outcome of chronically ill Lyme patients treated with three months of antibiotics compared to a group of such patients treated with a placebo. Both groups of patients were still sick with fatigue, cognitive problems and joint/muscle pain.

- A number of studies have shown that in patients with neuroborelliosis (brain involvement from Lyme disease), monoclonal antibodies against specific brain proteins such as myelin are found in the cerebrospinal fluid or in the brain tissue of such patients at autopsy. The telling finding here is that these antibodies cross-react with an outer surface protein (OspA) of *Bb* (band 31 on the Western Blot test). Interestingly, this antibody band is not measured on standard Western blots done at most laboratories. It was thrown out as a parameter on the Western blot test after a vaccine for Lyme disease, which contained that protein *because it was so specific for Bb,* was taken off the market because, you guessed it, it caused some patients to develop reactive arthritis [83]! This represents an autoimmune process.
- Already, in 1999, a T-cell lymphocyte antigen was found to be an epitope (a molecular mimic) to OspA of Lyme[84]. So now there was evidence of both cellular and antibody-generated immunity being present and what that group of researchers called "Treatment-resistant Lyme arthritis." The others even suggested that this cross-reactive autoantigen initiated by the Lyme bacterial antigen "may provide a model for development of autoimmune disease."
- Remember the study presented earlier with a patient with chronic fatigue, cognitive defects and generalized pain? This patient was making antibodies against an enzyme in their basal ganglia, an area of the brain that controls everything from movement and memory to judgment and has diverse connections to all areas of the brain. This enzyme, gamma-enolase, is specific for neurons in this brain area and is one of the enzymes in the energy-producing pathway known as glycolysis. Glycolysis is the principal system with which the brain makes energy unless the patient's metabolism is switched over to energy production by the ketogenic diet! Is it any wonder that most "chronic Lyme" patients suffer from fatigue and brain fog? These deep brain structures are known collectively as the basal ganglia, which regulate a myriad of functions including memory, learning, movement, emotion, executive function (decision-making) and routine behaviors. This gives understanding to the fact that some Lyme patients present with such a diversity of strange complaints that don't fit into a neurologist's working diagnostic pigeon holes, and thus are diagnosed as neurotic and sent to a psychiatrist to be medicated!
- A study on an autoimmune-prone mouse model (New Zealand Black) showed that, after a Lyme infection, the autoimmune-prone mice showed more "anti-myosis reactivity" than normal mice [24]. Myosin is a principal muscle protein in mammals, including humans. There was a cross-reactivity of the OspA antigen of *Bb* with an antigen from a streptococcal germ with the myosin protein. It is interesting that streptococcal infections have been implicated in causing various autoimmune diseases for more than 60 years. And by the way, carditis (inflammation of the heart) can also occur with Lyme disease. This makes sense since the protein is a principal component of heart muscle as well. It is thought that cross-reactivity to host tissue occurs normally after various infections, but the body eliminates the reactive cells after the infection is under control. In people with certain genetic variants, this process may be aborted, allowing the reactivity to continue and become a chronic illness.

- Besides cross-reactivity between Lyme antigens and human proteins, there are other mechanisms whereby a chronic inflammatory process may occur after a Lyme infection. Because there is damage to various tissues during the cytokine storm coming from the immune system, proteins that aren't normally visible to the immune system may be exposed and become targets of the system. Antibodies producing ongoing destruction can be a result. One of these mechanisms is known as the "bystander effect [85].” Also, native proteins can be altered during the highly inflammatory state connected to the immune process, and then are seen as foreign and thus attacked. This can then create an army of angry T- and B-lymphocytes that produce an ongoing barrage of inflammatory compounds. It is known that the blood of patients with autoimmune diseases contains inappropriate elevations of inflammatory cytokines such as TNFα, IL-1 etc. [86].

It is because of the possibility of an ongoing immune/inflammatory response after a Lyme infection that it is vital to treat an exposure to *Bb* promptly. All too often, a person with a tick bite or an acute illness that has the symptoms of Lyme disease goes to the emergency room, but their Lyme screening test comes back negative. They are sent home without treatment, and if the disease is present, it proliferates. Some people are fortunate and their immune response controls the disease. They may even develop permanent immunity via the memory cells of their immune system. But up to 10% of people exposed to *Bb* become chronically ill, even if they were treated early. These are the patients who present to our medical center. We will now explain our approach to treatment of these patients from an immunological standpoint.

To reiterate, after an infection, the immune system may continue to produce various substances that create inflammation and more tissue damage. This becomes a vicious cycle. Normally the immune system restrains itself. There are a number of T-cell types which communicate with each other and cells of the innate immune system via proteins called regulatory cytokines. One of the subtypes are known as T-regs, as mentioned above. When an infection is under control, these cells send signals to the other members of the team to restrain themselves. The production of inflammatory signals is reduced. Autoreactive cells destroy themselves in a process called apoptosis. Some of the cells retain memory of the offending germs and become inactive but ready to respond if they are called on in the event of another invasion.

Imagine that because of all the confusing stimuli new to the world in the past century, as well as the nutritional state and condition of the microbiome, some genetically susceptible people have an immune system that won't settle down.

We have described a number of interventions that will help the Lyme patient, but we haven't addressed the autoimmune process itself. One can think of autoimmunity as a specific form of allergy. Treatment for allergy involves the administration of tiny doses of the allergens to gradually reduce the immune system’s inappropriate hyperactivity. In the case of allergy, such as to pollen, the hyperreactivity is manifested by the release of histamine and other irritating substances by immune cells such as basophils and mastocytes. Those chemicals cause the sneezing, itching and runny nose seen in allergies. In the case of autoimmune disease, the hyperreactivity is more complex. It involves both the cell-mediated and antibody-producing machinery of the immune system, and the substances that cause the inflammation and tissue damage are cytokines and antibodies directed against the patient's own proteins. This results in

the damage to joints, skin, intestinal lining, brain structures, thyroid gland etc. As taught by Yehuda Shoenfeld, M.D. and other researchers worldwide [22], various microorganisms are the ultimate etiologic agent of autoimmune processes. The invading microbes contain a protein which has a molecular similarity to a protein in the human body. In the process of the immune defense against the germs, antibodies form against the native human proteins, and inflammatory cytokines accelerate the immune response, which creates the damage and thus the symptoms.

In Dr. Shoenfeld's book, he presents a study discussing the use of worms, whipworm, etc., to treat autoimmune disease. Because people are hesitant to ingest worms, researchers ground up the annelids and extracted various proteins. They found one that, when administered to patients with autoimmune disease, resulted in the improvement seen with the whole worm!

This brings us to the immunological treatment for Lyme and associated diseases. Drawing from the results in the medical literature that *Streptococci*, Epstein-Barr virus, *Mycoplasmae*, *Klebsiella* and other germs drove autoimmune processes, Butch Shrader, M.D. and Ty Vincent, M.D. began to administer highly dilute extracts of *Bb* and other microbes to people suffering from various autoimmune diseases. This therapy is known as Low-Dose Immunotherapy (LDI). People got better, sometimes dramatically, i.e., cured of their symptoms.

Now some of you will be concerned about "giving" someone a germ – could it cause Lyme disease, for example? I will explain how these extracts are made. A company that manufactures these preparations uses an electron beam to destroy the germ in question. This breaks all the components (proteins, DNA/RNA, phospholipids etc.) into tiny molecular fragments. The genetic material is rendered inactive – you cannot get an infection from the altered preparation. The proteins and other fragments, however, retain some immunogenicity. While we don't know all the mechanistic details of how the treatment helps, it does appear that, like the worm extract described above, the diluted molecular fragments cause an upregulation of the T-cell population called T-regs. These cells, as described above, then signal via a set of anti-inflammatory cytokines, the inflammation-inducing T-cell types, to reduce their production of inflammatory ammunition, and also signal cells called B-regs to restrain the plasma cells which are manufacturing anti-self antibodies in order to cease production of these antibodies. This treatment differs from vaccination in that the doses of the antigens is vastly lower and there are no additives like mercury, aluminum or other chemicals.

What surprised me when I saw the positive results of this treatment was that very high dilutions of the materials, even to the point of being homeopathic, reversed the disease activity. Homeopathy is a medical systems in which highly dilute substances – diluted so many times that no actual molecules are present in the preparation and thus works on an energetic level. In fact, the strongest solution used is called 4C, and that means it is a 10^8 or 100-million-fold dilution! In some cases, we start with a 15C ($10^{30)}$ dilution. This is truly homeopathic. Homeopathic-level dilutions start at 12C or 10^{24}. For people wanting a rationale or proof of the efficacy of homeopathic dilutions, I refer you to the eminent French scientist Dr. J. Benveniste, as well as Dr. Luc Montagnier [87]. Benveniste has shown categorically that even greater dilutions than we use in LDI have biological effects in a standard immune cell degranulation assay [88] that is widely accepted by the medical establishment.

In our use of LDI in treating patients, we take a careful history to determine what infections a patient may have experienced from their birth forward. Also remember that along with *Bb*, ticks may carry *Babesia*, *Bartonella* and a number of viruses. Fortunately, our Lyme disease LDI contains a variety of strains of *Borellia* and a number of species and strains of *Babesia*, *Bartonella* and *Erlichia*. We also have dilutions of Epstein-Barr virus and a number of other viruses, other bacteria such as *Mycoplasma*, *Streptococcus* and a skin bacterial mix, as well as mixtures of parasites and fungi, including *Candida* species. A judgment is made as to where to start in reference to the dilution of the microbial extracts. In frail, very ill patients we need to start low and work the dose up gradually. At some point, the patient notices a definite change for the better. We stay at that dose until progress stops, and then increase it. If the patient experiences a serious exacerbation of their symptoms, we go even more dilute.

And, as indicated above, besides "molecular mimicry" between proteins of the germ and host, altered human proteins or proteins that are not generally exposed to the immune system become "visible" as a result of free radical damage to such proteins, and cytokine action. In these cases, it may be necessary to use dilutions of collagen, myelin sheath protein or even autologous antigens. The latter represent dilutions of the patient's own microorganisms taken from samples of the mouth, skin scrapings or stool. Since the immune system gets out of balance, or "confused," people can start to overreact to new and heretofore tolerated molecules – foods, molds, chemicals and any number of substances. We must work to reduce the "total load" of forces that are making the patient ill.

It is the total load that determines health or illness.

We must remove as many factors contributing to the patient's problems as possible. Improving their diet, reducing exposures in their home, etc., correcting endocrine imbalances, restoring their gut microbiota, and detoxification therapies such as sauna for organic compounds and chelation therapy for heavy metal toxicity, are all methods to reduce total load and bring the patient back from "Cave In."

The predecessor to LDI therapy was Low-Dose Allergy (LDA) therapy. It was developed by an allergist in the United Kingdom, Leonard McEwen, M.D., in the 1960s. He discovered serendipitously that tiny doses of the enzyme beta-glucuronidase, when administered with extracts of reactive foods, increased his patients' tolerance to those foods. Dr. Schrader brought this treatment to the USA in 1991, partly because he himself suffered from food allergies and environmental illness.

LDA, like LDI, uses tiny dilutions of antigens – foods, molds, pollens, animal dander, etc., to treat (in this case) allergy problems. Dr. McEwen chose a variety of foods with cross-reactive antigens. As a result, no testing is required to determine which antigens to use. The antigens are administered either by a subcutaneous injection into the forearm or by being placed under the tongue. Likewise, the environmental mix consisting of molds, pollens, animal dander, etc., are given every two months. The mold mixes within the environmental preparation have been combined from many sources since the pioneers of environmental medicine put them together in the 1930s to 1940s. This makes the treatment more broad-based than the standard allergists'

technique, in which skin testing determines the exact molds to be used. How can we be certain that the molds to which the patient may react were actually used in the skin testing?

Another difference between standard allergy treatment and our immunotherapy is the dose of the antigens. In LDA and LDI the doses are much lower, and therefore, much safer. There has never been a case of anaphylaxis caused by these treatments. This isn't the case for standard allergy treatment.

An important difference between the two systems is the ultimate mechanism by which they work at the molecular level. It is thought that the standard allergy treatment works by stimulating IgG4 antibodies against antibodies that are causing the release of substances like histamine, which ultimately cause the allergic symptoms. The problem is, years of treatment are required, often weekly, and when the treatment is stopped, the reactivity returns. In contrast, it appears that the very low dilutions of LDA and LDI antigens result in changes in the different T-helper cell populations. The T-regs are triggered to restrain the other T-cells from pouring out ammunition against “self” antigens, in the case of using the microbe extracts of LDI. Every time the antigens are administered, more of the aberrant T-cells are restrained, and they eventually die off. What remains are the B- and T-cell populations that are preprogrammed to recognize and destroy a particular microbe during a new exposure. This is a protective, immunologically stable setpoint, ready for appropriate action should a new invasion occur.

These processes take out one of the bricks that is adding to the Total Load that resulted in the "Cave In" represented by the chronic Lyme or post-Lyme syndrome patient. While this immune adjustment continues over months, the other arms of the treatment are doing their work. Bacteriostatic antibiotics and herbs are inhibiting any active germs present, balancing the pro- and anti-inflammatory cytokines, and promoting effective immune response by killer cells, phagocytes and antibody-producing plasma cells. Nutritional supplements are supplying the body with key substances needed to make the energy to repair tissue and mount effective immune responses. In addition, replacement of fatty acids and phospholipids repairs the structure of cell membranes, and thus facilitates the function of ion channels, neurotransmitter receptors, nutrient transport proteins, etc.; and of course, the dietary changes reduce the “Total Load” of inflammatory substances coming into the body.

Although a person may not be aware of adverse effects of certain foods and exposures to molds or other environmental factors, in the confused state of the Lyme patient’s immune system they may be hidden, buried in the mire of other components of the "Total Load.” If a person had been allergic to dairy products when they were a child, they are almost certainly still reactive. The symptoms may have changed from middle-ear "infections" requiring the insertion of ear tubes, to joint pain of unknown cause. I discovered this for myself, after a fast and reintroduction of dairy products 30 years ago, when I converted my practice over to biological medicine. Food and environmental components of the "Total Load" are removed over time by LDA therapy. This allows the body to spring back to a state of health more easily than if the problem was left untreated. We have seen patients who came for LDA treatment for sinus congestion, and happily find that their unexplained joint pains went away, energy came back and, in one young woman, dyslexia vanished! We never promised her that, but we are very thankful for the "side

effect." Just about everyone can benefit from LDA treatment, whether or not they suffer from Lyme or other illnesses.

We have now described the eight-pronged program we have developed for the treatment of the multi-system syndrome that is often attributed to chronic Lyme disease or post-infectious Lyme syndrome.

I would like to give my perspective on why there are so many patients suffering from this syndrome – more than ever before and accelerating in number as well. This problem was unknown when I became a physician in 1976. What happened? Is it a new disease? Has the Lyme spirochete changed to a much more virulent bacterium? Or have *we* changed?

A research group at Yale School of Public Health, led by Dr. Katherine Walter, discovered that the Lyme disease bacterium, *Bb*, has been present in the forests in North America for at least 60,000 years – long before the disease was first described in Lyme, Connecticut, 40 years ago; and 40,000 years before the arrival of human beings in North America [89]. Dr. Walter claims that the increase in Lyme disease was caused by ecological changes, namely, deforestation and subsequent suburbanization of New England and the Midwest. As I remember it, the European invaders started cutting down the forests and populating the land ever-increasingly for the past two to three centuries. Granted, the human population is at a new high, and warmer winters, lack of foxes, and huge deer populations have all contributed to the increase in *Bb*-bearing ticks.

But by Dr. Walter's account, an epidemic of Lyme disease has emerged only over the past 40 years. Her genetic studies of the Lyme spirochete over the years 1984 to 2013, and the changes in its genome, show that "diversity is ancient and geographically widespread." She concludes that the ticks' and the spirochetes' genetic capabilities have not changed. They have not become more virulent. Instead, according to her, "land use and climate change" must explain this 40-year-old epidemic.

My question is: "Is it possible that we, the host of the deer tick and its partner *Bb*, have changed?" Certainly not genetically, but possibly epigenetically. And certainly, the change in environmental factors from GM foods, farm chemicals, electromagnetic frequencies (EMFs), and our use of vaccines in the USA (we use triple the vaccination per capita than the Japanese and they have robust health compared to Americans), as well as increased exposure to mercury from coal-fired electrical plants, especially from China and India, with their incredibly rapid infrastructural and population growth and, of course, a panoply of synthetic, pharmaceutical drugs and industrially-produced, endocrine-disrupting chemicals like plasticizers. Autoimmune disease has also increased dramatically in the past 40 years, and another epidemic, autism spectrum disorder, has arrived out of nowhere in the same 40 years. Coincidence? I doubt it.

It makes more sense that the changes in the "Total Load" that humans have experienced in the past 40 years have contributed more than any other factors to the epidemic of chronic, inflammatory diseases of "unknown etiology" that the medical establishment has been trying to pin on our genes, spending billions on the effort. So far, it appears that only a small fraction of our ills can be attributed to our collective genetic variations. The genetic variances that have been implicated as factors related to autoimmune disease, autism, etc., are only cofactors in the

pathophysiological processes of these diseases. In other words, certain variants (single nucleotide polymorphisms or SNPs) may act to make some individuals more susceptible to conditions like autism or rheumatoid arthritis, but just having the variant in and of itself does *not* give a carrier of such a gene any of these diseases. Just as obesity has been shown to have genetic associations, overwhelmingly it has increased due to changes in our environment, food and other lifestyle factors; certainly not to genetic changes. People who have "thrifty" genes, which cause them to have a tendency to gain weight (a superior adaptation in ancient times), now pile on weight when they so much as look at processed food. So, what could be the common denominator that has led to the alarming rise in chronic Lyme disease, autism, obesity, diabetes, autoimmune disease and psychiatric syndromes?

The scientific literature supports inflammation as the culprit in all these diseases. As detailed laboratory tests have been developed in the research community to measure markers of inflammation, every chronic disease has been found to be associated with this process. The molecules we have talked about above, IL-1, IL-6, TNFα, upregulated NFκB, and antibodies against "self" proteins, are elevated in every condition studied, even in osteoporosis and type II diabetes. All diseases have an autoimmune component. We are all "on fire," as our immune systems react to endocrine disruptors, toxic metals, glyphosate and other farm chemicals, EMFs, and devitalized food stripped of its essential nutrients by processing and polluted with preservatives and other chemical additives.

So, when an opportunistic bacterium like *Borrelia bergdorferi* gains access to our immunoconfused, overloaded, already-inflamed body, it becomes the "straw that breaks the camel's back" – it becomes the component of the "Total Load" that causes the "Cave-In." The inflammatory processes triggered by the bite of an *Ixodes* tick, with its potpourri of microbial felons, brings the victim to a health crisis. We are seeing young people who were academic, social and athletic stars hit a wall and have to leave college. They attend a series of medical specialists and never get a firm diagnosis, let alone effective treatment. They are usually told they are depressed, and given psychotropic drugs, which aren't much more effective than placebos, and often have unacceptable side effects.

To get well, patients with the multifactorial syndrome of chronic Lyme disease must approach treatment from the multifactorial interventions described in this writing. It is hard work for the patient and doctor. It requires experimentation and the willingness to change, including shifting gears at times during treatment.

But the payoff is getting your health and very life back. This quotation by the great German philosopher Artur Schopenhauer sums up succinctly what every chronically ill, and especially chronic Lyme patient, knows all too well:

"Health isn't everything, but without it, everything else is nothing."

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