

# An Overview of Lyme Disease and Hyperbaric Oxygen (HBO) Therapy

## Lyme Disease

Lyme disease is a bacterial infection caused by a spirochete (spiral-shaped bacteria) called *Borrelia burgdorferi* (Bb). The *bacterium* is named after the person who discovered it, Dr. Willy Burgdorfer. *Lyme disease* is named after the Connecticut town of Lyme where it was first recognized in the United States in 1977. The first record of a condition associated with Lyme disease dates back to the 1880's.

Both humans and animals can be infected with the Bb organism through the bite of an infected tick. Over 100 strains of the bacterium that cause Lyme disease have been identified in the United States. Lyme infection is usually transmitted by, though not limited to, three species of tick:

- The black-legged tick (*Ixodes scapularis*) on the East Coast and in the Midwest (commonly known as the deer tick).
- The western black-legged tick (*Ixodes pacificus*) in the Western U.S. (also commonly known as the deer tick).
- The lone star tick (*Amblyomma americanum*), located within a rectangle encompassing Texas, Florida, Rhode Island, and Iowa.

Lyme disease is also a global problem. There are reports that 300 bacterial strains of the Bb organism have been identified throughout the world. Cases of Lyme disease have been reported in North and South America, Europe, Asia, Africa and Australia.

## Symptoms

Early signs of Lyme disease include flu-like symptoms (headache, fever, muscle aches, joint pain and fatigue) and a Lyme rash. Most symptoms show up days or weeks and occasionally months following infection.

The Lyme rash is referred to as *erythema migrans* or *EM*. It is important to remember that the rash may not show up at all, or it may appear too light in color to be noticed. The rash can be shaped like a bulls-eye, it can be smooth or bumpy, it may or may not feel warm, and there can be multiple rashes that can appear at the site of the tick bite or elsewhere on the body.

Once the infection becomes established, symptoms of Lyme disease vary but may include pain in muscles and joints, fatigue, swollen glands, fever, upset stomach, headache, forgetfulness, sleep disorders, depression, and sensitivity to light and sound, to name a few.

### **Lyme Confusion**

The medical community is often perplexed by the highly individual and complex nature of Lyme disease. Some people experience Lyme disease as a minor illness that appears to be easily treated with antibiotic therapy without any long-lasting complications. Others are not as fortunate.

When Lyme disease goes undetected, undiagnosed and untreated for months or years following infection, the bacteria can spread to the nervous system, the heart and other organs, tendons and joints. This late-stage infection can result in a wide variety of physical, emotional, and mental or cognitive symptoms. The late-stage list of symptoms is long and can include arthritis, heart abnormalities, Bell's palsy (paralysis of one or both sides of the face) and severe cognitive or mental dysfunction including memory loss, confusion, psychiatric problems, etc.

Lyme disease is often referred to as the *Great Pretender* because the symptoms of Lyme disease can so closely mimic the symptoms of other diseases. Although no official numbers exist on this subject, Lyme patients have been misdiagnosed with chronic fatigue syndrome, fibromyalgia, multiple sclerosis, menopause, depression, Alzheimer's disease, and Lou Gehrig's disease. Other patients have failed to receive any kind of definitive diagnosis long after the presentation of symptoms.

### **Early Detection Is Paramount**

Nearly all Lyme medical specialists agree that early detection and treatment of Lyme disease significantly improves the chance of a full recovery. Although not proven, some experts believe that there is up to a six to eight week window of opportunity following infection when treating the disease with antibiotic therapy can result in a high cure rate and lessen the chance of chronic, long-term problems.

It has been reported that it takes an average of 22 months and seven doctors for the average Lyme patient to be diagnosed with a Bb infection. This follows the fact that many people infected with Lyme disease do not remember being bitten by a tick, which can further delay treatment. The inability to diagnose and treat Lyme disease in a timely fashion may be adding to the number of patients who suffer from chronic symptoms.

It is estimated by some that as many as 20 percent of Lyme patients suffer from persistent and chronic symptoms. This figure may be too low. Obviously, more research would be helpful. However, what is clear is that the importance of early diagnosis and treatment cannot be over-emphasized.

## Treatment

Lyme disease is a bacterial infection and like other bacterial infections it is treated with antibiotics. Antibiotics are administered orally, with intramuscular (IM) injections, or intravenously (IV) through the veins. Physicians often prescribe combinations of antibiotics to take advantage of the diverse ways that individual antibiotics affect the Bb organism.

Physicians not only prescribe more than one oral antibiotic at a time, but they combine oral antibiotics with IM or IV antibiotics. This *shotgun* (or multiple) approach to antibiotic therapy is used in hopes of affecting the Bb organism in as many ways as possible.

Just as no two Lyme patients appear to be affected by Lyme bacteria in the same way, a patient's response to antibiotic therapy is highly individual, too. The individual nature of an antibiotic's effect on a patient is believed to be due in part to the theory that different strains of the bacteria react differently to each antibiotic. Other factors may include the duration of infection, the amount of time between the onset of symptoms and treatment, and the location of the Bb organism in the body. Also, co-infections or the transmittal of more than one infectious disease can occur from a single tick bite. This can make diagnosis and treatment more difficult still.

## Jarisch-Herxheimer Reaction

A proper understanding of the Jarisch-Herxheimer reaction has helped Lyme specialists better manage the diagnosis and treatment of Lyme disease. This is especially true in light of inadequate testing. A Herxheimer reaction occurs in Lyme patients after they begin antibiotic therapy. It is important to note that a Herxheimer reaction is not a common reaction that is associated with most other diseases or with other viral, bacterial or fungal infections. A Jarisch-Herxheimer reaction is limited to a few specific bacterial infections such as syphilis and Lyme disease. It is interesting that syphilis and Lyme disease stem from spirochetal or spiral-shaped bacteria.

A Herxheimer reaction occurs when symptoms recur, flare up or become exaggerated. Some call it a *healing crisis*, while others describe it as *getting worse before you get better*. Lyme patients refer to this reaction as a *herx*, or say that they are *herxing*.

A Herxheimer reaction usually occurs within days to weeks of starting antibiotic therapy. When antibiotics directly kill Lyme bacteria or work with the body's immune system to kill the organism, toxins are released that cause either "direct reactions or indirect actions through stimulation of the immune system."<sup>5</sup> In simpler terms, a Herxheimer reaction occurs when Lyme bacteria are killed off more quickly than the body's organs (kidneys and liver) are able to process them. This increases the number of toxins in the blood stream. The higher the toxin count, the more severe the symptoms the patient experiences.

Without accurate testing, the Herxheimer reaction is often used as a clinical diagnostic tool to help determine the presence of the Bb organism. It can also be used to confirm the effectiveness of specific antibiotics or combinations of antibiotics. Specifically, some health care professionals believe that a Herxheimer reaction can confirm that the Bb organism is present in the body by the fact that a bacteria die-off is causing the herx. Thus, for the frontline physician, the Herxheimer reaction can assist in the clinical diagnosis by *unofficially* confirming the presence of the Bb organism.

### **The Politics of Lyme Disease**

This leads us to a pivotal and controversial issue that divides the medical community concerning the diagnosis and treatment of Lyme disease.

Some health care professionals are more tradition-bound and conservative in their approach to Lyme disease. They have adopted protocols for treating Lyme that don't go much beyond relatively short-term antibiotic therapy. This group believes that in almost all cases, one or two courses of oral antibiotics are all that are required to eradicate the bacteria. They believe that persistent, chronic Lyme symptoms are not the result of an ongoing infection—of active Lyme bacteria in the body—but rather, are probably the result of a dysfunctional auto-immune system response or some other process occurring in the body.

Others—especially those physicians who remain on the frontline of the long-term treatment of Lyme patients—believe that Lyme bacteria are not always eliminated by short-term courses of antibiotics. They believe that this is especially true if the disease went undiagnosed and untreated for months or years following infection.

Further, this latter group believes that the Bb organism can persist through months and even years of antibiotic therapy, depending upon a wide range of individual factors relating to the patient and to the strain(s) of bacteria. The survival characteristics of the bacteria themselves also play a crucial role in Lyme bacteria's persistent longevity.

### **Survival Tactics?**

Research has shown that the Bb organism can use the body's own protein to encapsulate itself.<sup>6</sup> This is also described as the Lyme bacterium shifting to a *dormant* or *sleeping* state. The reason that the organism undergoes this change is not fully understood. Some believe that this is a survival tactic because it may not be possible for our immune system to destroy the bacterium when it is in this state. Also, antibiotics may have little or no effect on the Bb organism when it is encapsulated and dormant.

Research also shows that the Lyme bacterium appears to be able to enter certain types of human cells. This ability may also be considered a survival tactic because it results in the bacterium evading some or all antibiotics as well as the body's immune system.

## Antibiotics

Because antibiotics are the main tools that are used to fight Lyme disease, we can gain a better understanding of Lyme disease if we better understand how antibiotics affect the Bb organism. For a better understanding of how antibiotics work it helps to understand the mechanism of action they employ. Generally speaking, antibiotics fall into two categories:

- Bactericidal—An agent that directly destroys bacteria.
- Bacteriostatic — An agent that arrests or hinders the growth of bacteria.

Antibiotics that are bactericidal (for example, think... homicidal) can directly attack the cell wall of the bacteria. This causes a rupture and the death of the organism follows. Antibiotics from the penicillin family of antibiotics are usually bactericidal, unless concentrations fall too low.

Antibiotics that are bacteriostatic (for example, think... manipulative) do not directly attack bacteria. Instead, they interfere with the ability of the organism to reproduce. Without the ability to reproduce the bacteria can eventually die out. Bacteriostatic antibiotics include tetracyclines such as Doxycycline. It is important to remember that most antibiotics can be both bactericidal and bacteriostatic, depending upon the amount or concentration of the antibiotic in the body. More clearly still, most bacteriostatic antibiotics can become bactericidal if the concentrations are strong enough.

One of the main points to understand about bacteriostatic antibiotics is that they are usually effective in debilitating bacteria only when bacteria reproduce. This is significant for two reasons. First, it is believed that dormant Lyme bacteria don't reproduce, which diminishes bacteriostatic antibiotic's effectiveness in fighting Lyme disease. Second, Lyme bacteria have a long reproductive cycle. A mature Lyme bacterium reproduces once every 7 hours or so. This reproductive cycle may vary from species to species. In comparison, some species of the strep throat bacterium reproduce once every 20 to 30 minutes. It is not known how many reproductive cycles are needed before all Lyme bacteria are debilitated by antibiotics.

However, according to Karen Vanderhoof-Forschner in her book, *Everything You Need To Know About Lyme Disease*, the strep bacterium is normally treated with antibiotics through 480 reproductive cycles<sup>7</sup>. She says that if we were to treat Lyme disease through the same number of cycles it would take somewhere between 5 to 30 months of antibiotic therapy. If this is true, it is significant that some physicians follow a protocol for treating Lyme disease that allows just two to six weeks of antibiotic therapy. Based on the above scenario this may be inadequate.

If either of the above examples are true, this may mean that physicians who are acting in good faith by using conservative treatment protocols may actually be prolonging and thus

complicating Lyme infection in their patients. However, much of this theory is speculative. Obviously, more research is needed.

### **Devastating Survival Tactic?**

We have discussed how it is believed that Lyme bacteria primarily use two methods of invading the body's immune system and evading certain antibiotics. If the theory behind this belief is true then the two methods of evasion used by the Bb organism include:

1. The Lyme bacterium encapsulates itself in the body's protein (the cell wall membrane) and lies dormant for undetermined periods of time.
2. The Lyme bacterium hides by entering the body's cells.

In both cases the bacteria may be able to evade the body's specialized defensive mechanisms, along with evading the offensive mechanisms of antibiotics. However, the final piece of this puzzle has to be considered a genetic marvel no matter how devastating it is to Lyme patients. When Lyme bacteria shift from a dormant to an active state they can resume reproduction and effectively re-seed the body. This reestablishes the Lyme infection. If it is true that dormant bacteria can *wake up* and re-seed the body, this particularly devastating maneuver indicates that short-term courses of antibiotics may be ineffective in eradicating Lyme bacteria from the body.

### **Mechanism of Action**

Antibiotics and other anti-infective agents (anything that counteracts infection) can kill different kinds of bacteria. However, an antibiotic's mechanisms of action—or *how* they kill bacteria—varies depending upon the type of antibiotic used. Because the mechanism of action varies among antibiotics and anti-infective agents, a specific antibiotic—or specific combinations of antibiotics—may be a better choice than other combinations when attempting to eradicate the Bb organism.

For example, Zithromax (azithromycin) is known to have higher tissue concentration levels when compared to the blood concentration levels it usually attains. Zithromax is also known to have an ability to penetrate some cells in our body more effectively than other antibiotics. This may have an added benefit when treating the Bb organism because we believe that Lyme bacteria have the ability to enter certain types of our cells.

Later, we will discuss in more detail why specific combinations of antibiotics work better than other combinations when treating Lyme disease. At this point we simply want to identify how the treatment of Lyme disease becomes a complex task with a myriad of options and protocols that are dependent upon an ever-widening circle of circumstances. As we stated earlier, until research catches up, the treatment of Lyme disease cannot be anything but subjective, open to question, individualized, and often complex.

## **Hyperbaric Oxygen (HBO) Therapy**

HBO therapy is a medical treatment that uses the administration of 100 percent oxygen at controlled pressure (greater than sea level) for a prescribed amount of time—usually 60 to 90 minutes. HBO therapy is commonly used to treat conditions such as burns and difficult or stubborn healing wounds.

HBO therapy increases the amount of oxygen in the body, which in turn causes several physiological changes that can result in accelerated healing. The basis for these changes is the fact that HBO therapy increases the amount of oxygen in the blood by up to 2000 percent, depending on the treatment depth. This, in turn, dramatically increases the amount of oxygen at the cellular level and creates other physiological changes. These changes can be extremely complex. One scientific research study indicates that Lyme bacteria are microaerophilic, or debilitated in high oxygen environments.

In the case of Lyme disease, William Fife, Ph. D., a Hyperbaric Medicine specialist at Texas A & M University (now retired), established the protocols for HBO treatment in his Texas A & M research project, to be discussed later. Dr. Fife's Lyme disease protocol calls for HBO therapy to be administered at 2.36 ATA (Atmospheres absolute), or equivalent to a depth of 45 feet below sea level. Each treatment lasts one hour and two treatments are prescribed each day, five days per week.

The total number of treatments given in each case varies. It is common to administer 30 to 40 treatments in the first phase of treatment. The question of further HBO therapy is then resolved after the patient's condition is reevaluated. However, many believe that if the patient has been impacted by the first phase of HBO therapy, such as by experiencing a Herxheimer reaction (this can help to confirm Lyme bacteria die-off), then a break of three to six weeks should be taken followed by another 30 to 60 HBO treatments. A physician can prescribe more sets of HBO therapy based on the patient's individual evaluation.

### **A Promising Therapy**

Why does HBO therapy show promise in helping Lyme patients? First, we are reminded that Lyme bacteria are microaerophilic, or debilitated in high oxygen environments. Research by F. Austin demonstrated the effect of oxygen on the Lyme organism. The study suggests that the Bb organism is sensitive to high concentrations of oxygen at the cellular level, or what is termed, *elevated tissue partial pressures*. In other words, the Bb organism doesn't do well in a biological environment similar to that created in the body during HBO treatment.

Once it was clinically determined that Lyme bacteria may be adversely affected by the conditions created in the body during HBO therapy, the next step was to conduct a more in-depth study. One such subjective study was completed in 1997 by William Fife, Ph. D. at the Texas A & M Hyperbaric Laboratory and approved by the Texas A & M University Review Board.

The results of the study were significant: improvement in approximately 85 percent of the 66 patients treated. Improvement is defined as a decrease or the elimination of symptoms.

It is also notable that all of the study's participants were veterans of antibiotic therapy. These were adults and children who had tried and failed antibiotic therapy, including the big gun in the antibiotic arsenal: intravenous antibiotics. It appeared that the study had chosen the most difficult subjects to test. These were Lyme patients with chronic symptoms and most of them probably had nothing to lose. The fact that 85 percent of *these* Lyme patients showed improvement seems remarkable.

### **Other Benefits of HBO Therapy**

There are other benefits of HBO therapy that *may* play a role in treating Lyme disease, but were not mentioned in the Texas A & M study. Some of these benefits are theoretical and not proven; others are well known and considered established fact in Hyperbaric Medicine. Many of these additional benefits are based on the belief that HBO therapy and antibiotic therapy work in a synergistic manner. In this context, *synergistic* is defined as the combination of both treatments (HBO therapy and antibiotic therapy) being greater than the effect of either one alone. First, let's review.

Earlier we discussed how antibiotics and the immune system might not be able to adversely affect (or kill) Lyme bacteria for two distinct reasons. First, it is believed that the Bb organism is able to switch from an active to a dormant (or sleeping mode) by coating itself in the body's protein. It is also believed that the Bb organism can hide in the body's cells. Both tactics may result in the immune system failing to react to the Bb organism as a foreign organism that should be destroyed. Some believe that this has the effect of neutralizing the body's defensive mechanisms and the offensive mechanisms employed by antibiotics.

### **Complicated Therapy**

Lyme physicians take all of this relatively new knowledge about bacterial biology into account when deciding which antibiotic, or combination of antibiotics to prescribe. The above scenario suggests that, depending upon dosage, some classes of antibiotics such as penicillins and cephalosporins may not be able to eradicate Lyme bacteria from the body because they circulate mainly in the body's fluids and are incapable of entering cells where the Bb organism can reside. If true, this contradicts many current conservative antibiotic protocols for Lyme disease.

The good news is that other classes of antibiotics, such as macrolides (azithromycins such as Zithromax) are prescribed specifically to attack the Bb bacteria that may become established within the body's cells, along with killing Lyme bacteria residing outside the cells in deep tissue areas of the body.



It is important to recognize that this is a case in point where a *shotgun* approach to antibiotic therapy may be an effective tool in fighting Lyme disease. For example, a physician may prescribe a penicillin such as Amoxicillin, along with a macrolide such as Zithromax. The Amoxicillin stays mostly in the body's fluids and blood stream. Meanwhile, Zithromax not only penetrates the cell wall where the Bb organism is residing (and/or hiding), but it also penetrates deep tissue areas, which Lyme bacteria also inhabit. When Lyme bacteria move to deep tissue areas they have effectively moved away from normal blood flow and away from fluid-based antibiotics. Antibiotics such as Zithromax can help to counter this survival tactic.

Also, Amoxicillin is mainly bactericidal (remember, think... homicidal), which means that it directly kills the Bb organism. Zithromax is a macrolide, which means that it can either be bactericidal or bacteriostatic (think... manipulative) depending upon concentration levels. By prescribing these two antibiotics, physicians hope to increase the opportunities for killing as many bacteria as possible, and affecting Lyme bacteria in numerous and complex ways. Obviously, physicians prescribe many other combinations of antibiotics to combat the Bb organism.

Even though physicians can out-manuever some of the Lyme bacterium's survival tactics—such as using combinations of antibiotics—there are those who believe that antibiotics probably cannot eliminate the Bb organism if it is in a dormant state. Again, if this is true, it has serious consequences for the diagnosis and treatment of chronic, persistent symptoms. Specifically, this means that conservative treatment protocols, which call for short-term courses of antibiotics, may actually prolong some cases of Lyme infection. If chronic Lyme symptoms are the result of an active, late-stage Lyme infection, any delay in full and comprehensive antibiotic treatment may have devastating results for the Lyme patient.

### **Adding HBO Therapy**

Now we add HBO therapy to the mix. We previously stated that Dr. Fife's study suggests that the Bb organism is sensitive to elevated levels of oxygen at the cellular level. This is an environment similar to that created in the body during HBO therapy. Unfortunately, at this time we do not know much about HBO's effect on dormant Lyme bacteria. However, Fife's study conclusively showed that HBO therapy does have a significant and positive impact on a high percentage of Lyme patients who failed antibiotic therapy. The exact reasons why this is so are not clear.

It is interesting to note that some believe that HBO therapy can kill the Bb organism directly. This begs the question, "Can HBO therapy directly kill the Bb organism on its own?" It seems possible that the answer to this question may be yes. A positive response seems reasonable because Lyme patients who have undergone HBO therapy without taking antibiotics seem to have experienced a Herxheimer reaction during treatment. This suggests that HBO therapy alone was responsible for the bacteria die-off. If true, HBO therapy would indeed be capable of killing the Bb organism directly. Again, more research would be helpful.

## **Angiogenesis Plays a Role**

HBO therapy facilitates angiogenesis. Angiogenesis is defined as the development of blood vessels in the body. This may become important in the treatment of Lyme disease because it is believed that Lyme bacteria effectively evade antibiotics by moving away from normal blood flow into tissue, organs and bone. Thus, the farther that the antibiotic can move into these areas through a more dense and extensive system of blood vessels, the greater the opportunity to kill the Bb organism. HBO therapy's facilitation of angiogenesis allows the antibiotic to potentially have a greater effect on Lyme bacteria by helping to move the antibiotic closer to those parts of the body where the bacteria may be residing.

## **Bacterial Cell Wall Penetration**

There is emerging evidence that certain antibiotics may be more readily incorporated into the cell wall of the bacteria itself in the presence of *elevated oxygen tension*, which is an environment similar to that created in the body during HBO therapy. If true, this is a clear example of HBO therapy working in a synergistic manner with antibiotic therapy. In other words, the effectiveness of antibiotics to kill the Lyme organism is increased through the use of HBO therapy.

Research is currently being conducted that may indicate that the Bb organism can be killed by oxygen free radicals. Oxygen free radicals are produced during HBO therapy. The deeper the depth of treatment, the greater the number of free radicals produced. It is believed by many that oxygen free radicals have an antibiotic-like effect.

Finally, it is well understood that HBO therapy can enhance certain aspects of the body's natural immune system. This may play a significant and positive role for Lyme patients because their immune systems have probably been compromised over a long period of time as a result of persistent symptoms.