

Biotoxin Pathway Holds Key Pieces of Puzzle in Solving Chronic Illness

by Scott Forsgren

Chronic illnesses often seem like complex puzzles where it quickly becomes evident that many of the pieces are missing. No matter how hard we try to understand exactly what is causing us to be ill, a full understanding seems to often be evasive. The work of Ritchie C. Shoemaker, MD provides us many more pieces of that puzzle and sheds brighter light on understanding the complex nature of chronic illness.

For those struggling with Lyme disease or other chronic illnesses, understanding the numerous impacts of biotoxins, toxic substances produced by living organisms, may be the key to an improved state of health and well-being. I recently had the opportunity to sit down and discuss this exciting area of research with Dr. Shoemaker. I truly believe that the impact of his work in the field of biotoxin-associated illness is only just beginning to be realized. Fortunately, we can benefit from understanding it today.

Symptoms of biotoxin-associated illnesses may include fatigue, cognitive issues including memory loss, muscle aches and pains, joint pain, headaches, blurred vision, light sensitivity, shortness of breath and other respiratory problems, excessive thirst, sleep disorders, weight gain, and more. Often times, people with chronic illnesses have symptoms involving multiple body systems.

There is frequently a leap to a diagnosis and with that leap, the mechanism that underlies the core problem is often overlooked. It is important that we look deeper in terms of recognizing that there may be more than just an infection with Lyme disease or an exposure to mold at the core of one's ongoing symptom picture. Biotoxins, and the inflammatory responses which they initiate, may be at the center of the illness.

If a person is genetically susceptible to a biotoxin-associated illness, it is likely the case that the biotoxins themselves, rather than Lyme infection or mold exposure, are causing many of the symptoms being experienced. Even further, it is plausible to suggest that infection could be cleared, or the exposure entirely removed, and yet the remaining symptoms may be almost entirely due to circulating biotoxins. It comes down to a genetic predisposition which results in the body's inability to remove these biotoxins. Long after the initial exposure or infection is gone, the toxins may live on. Understanding that core idea alone is profound!

There are many sources of biotoxins that may be encountered including *Borrelia* spirochetes and *Babesia* infections found in Lyme disease, fungi and mold (*Aspergillus*, *Penicillium*, *Stachybotrys*, and others), ciguatera toxins from seafood, dinoflagellates such as *Pfiesteria*, some algae, various types of bacteria, and recluse spiders. With each of these sources of biotoxins, there is one thing in common. People that are impacted by these toxins, regardless of their origin, have the same or very similar symptom presentations. The similarities, which are confirmed by sophisticated statistical analysis, are compelling.

A very simple and easy to perform screening test for determining the presence of biotoxins is the Visual Contrast Sensitivity (VCS) test. It can be performed online or at your doctor's office. The test was described in detail in the November 2006 edition of the Public Health Alert. It evaluates two sets of nerves in the eye that allow one to differentiate between white, black, and gray on a gray background. It has been found that a subject with biotoxin-associated illness will demonstrate a deficit on this non-invasive neurological evaluation in that they will not be able to identify the direction of various patterns presented. Failure to successfully complete this test is a strong indicator of a biotoxin illness. Though it is possible for a person impacted by biotoxins to pass the test (a false negative result), this occurs only in about 8% of test subjects. Thus, the VCS test supports diagnosis in about 92% of affected people. False positives are quite rare.

Once a biotoxin enters the body, the resulting downstream effects can be largely predicted regardless of the origin of the biotoxin. Understanding one's genetic predisposition to a biotoxin-illness is a critical part of the journey back to health in many cases. For those with a diagnosis of Lyme disease, it is important to understand other potential sources of biotoxins that may be contributing to the overall state of illness. In many cases, ubiquitous mold biotoxins may be an additional source of exposure that should be investigated and a well-planned treatment strategy defined.

There are specific genotypes associated with specific susceptibility to biotoxins. For patients with Lyme disease or mold exposure, approximately 25% of the population has a genetic predisposition which results in an inability to clear biotoxins naturally. Understanding whether or not one is in this population can provide key insight into the cause of illness. Though the result may suggest a genetic make-up which cannot itself be corrected, once known, specific interventions can be put into play that may significantly improve the outcome.

The test is called HLA DR and it is commonly known as a test which provides insight into possible organ rejection after a transplant operation. Human Leukocyte Antigen (HLA) is a grouping of genes that lie on chromosome 6. In the case of biotoxins, HLA codes for whether or not a person is capable of clearing biotoxic substances following an exposure. For these people that are genetically incapable of clearing these toxic substances, biotoxins will continue to circulate within the body indefinitely and may reduce one's chances of recovery. There is generally no "selfhealing" in these cases without appropriate interventions.

Once the results of the HLA DR test are obtained, Dr. Shoemaker provides an interpretation guide which maps the HLA DR combination to specific conditions which may be associated. For example, some combinations are susceptible to mold biotoxins while others are susceptible to Lyme biotoxins while still others are susceptible to both mold and Lyme biotoxins in what is termed a "multi-susceptible" genotype. If the HLA DR test results in a combination that suggests any of these, it is time to better understand the "Biotoxin Pathway" and possible treatment options. These options may result in significant relief.

The "Biotoxin Pathway" illustrates an ongoing, amplifying cascade of events that starts with exposure to a biotoxin in those individuals who are genetically susceptible. The biotoxin then binds to Toll receptors, primarily in fat-cells and cells that line blood vessels, resulting in the production of proteins called cytokines which are involved in immune response and inflammatory processes. Cytokines recognize invaders and recruit additional cytokines in response. In the world of biotoxins, it is the biotoxin itself that continuously signals the body to produce more cytokines. It is this excess cytokine production that makes us feel unwell. Excess cytokines result in flu-like symptoms, body aches, temperature fluctuations, cognitive difficulties and other symptoms. This increase in cytokines has further downstream effects.

VEGF (vascular endothelial growth factor) is often reduced which leads to fatigue and reduced blood flow. Hypoperfusion, this resulting reduction in blood flow, results in a starving of cells for nutrients and oxygen. There is also an increase in MMP9 (matrix metalloproteinase) as the cytokine itself causes the white blood cells to release MMP9. MMP9 is a superb marker for the presence of excess cytokines.

MMP9 may be responsible for delivering inflammatory compounds out of the blood and into the brain which causes plaque formations similar to those seen in MS. In Lyme disease, MMP9 levels may skyrocket as the result of treatment with antibiotics and the resulting bacterial die-off in what is commonly referred to as a Herxheimer reaction. Taking this even further, if you give a Lyme-infected person antibiotics and they are not HLA-susceptible, they generally have an uneventful recovery.

An increase in cytokines may also trigger auto-immunity. There are three key types of antibodies observed in those with biotoxin-associated illnesses. These are myelin (the protective sheath around nerve cells) antibodies, gliadin (a protein found in gluten) antibodies, and cardiolipin antibodies which impact circulation in the small blood vessels.

There may be notable increases in markers which reflect activation of the complement system, namely in C3a and C4a. There is a significant difference in C3a and C4a levels between controls and the Lyme or mold population. In fact, C4a levels invariably become elevated, often as early as twelve hours after a tick bite. In the case of those with a mold-susceptible HLA type, C4a significantly increases within four hours after re-exposure to a moldy environment. C4a can be a helpful marker in determining whether or not a remediated home is still a danger for someone with mold biotoxin susceptibility. If C4a levels have been reduced via appropriate interventions and C4a levels rise upon reintroduction to the suspect environment, it is a sure sign that the environment is not safe for the patient.

We have seen some of the downstream effects that result from elevated cytokine levels resulting from biotoxin exposure in susceptible individuals. This is only the beginning. Beyond an increase in cytokines, there is an observed increase in leptin. Leptin is a hormone made by fat cells which helps to regulate the storage of fat. When leptin increases as the result of a biotoxin exposure and MSH (alpha melanocyte stimulating hormone) is reduced, people become obese and weight loss becomes difficult. Wait a minute! Who ever imagined that weight gain could be related to exposure to Lyme disease, to mold, or to any number of biotoxins?

MSH, which is made in the hypothalamus, is the most potent anti-inflammatory compound we have. It is responsible for regulating innate immune response and is involved in numerous hormone pathways. Reduced MSH is at the heart of the "Biotoxin Pathway" in that many negative downstream effects result when MSH is low. Of interest here is that in Lyme disease, chronic fatigue syndrome, mold illness and any other biotoxin illness regardless of the source of the biotoxin, MSH is low in about 95-98% of patients.

When MSH levels are low, people become sleep disturbed; they have chronic pain; they experience leaky gut syndrome; their recovery from illness is delayed; they develop multiple antibiotic resistant coagulase negative staph colonization (MARCoNS); they have frequent thirst as a result of lowered anti-diuretic hormone (ADH); they have a loss of libido due to a lowering of sex hormones and more.

MSH is involved in the production of melatonin and endorphins. This resulting lack of endorphins increases our perception of pain. MSH regulates the protective cytokine responses in the blood, skin, digestive tract, and respiratory membranes. Lowered MSH results in abnormalities in production of cortisol and fluctuations in ACTH (adrenocorticotrophic hormone) which regulates adrenal function. It is when the biotoxin illness disrupts the production of MSH that so many of the symptoms begin to appear. When looking at the results of lab tests for reduced MSH and increased C4a, the difference between patients and controls is clear. Using these markers, the diagnostic accuracy of the Shoemaker model is compelling.

Now that the importance of the "Biotoxin Pathway" is understood, we shift focus to the interventions that can be put in place to improve one's state of wellness.

Cholestyramine (CSM) is a resin which has been historically used for lowering cholesterol. It has a positive charge that binds to a wide range of different lowmolecular- weight, negatively-charged toxins and helps to shuttle them out of the body through the digestive tract. It is not systemically absorbed. Without CSM, these toxins are largely reabsorbed and continue in circulation indefinitely. Though gastrointestinal side effects are not uncommon and include constipation and other digestive issues, less than 10% of patients stop using CSM due to the side effects experienced.

Before one can expect to see results from CSM therapy, the source of the biotoxin must be addressed. This may mean treating Lyme disease or removing yourself from an ongoing mold exposure. If CSM therapy is implemented while there is a continued ongoing exposure to biotoxins, the likelihood of any lasting improvement is reduced and the patient will generally remain ill.

The vast majority of people treated with CSM will have a notable fall in C4a if the inflammatory activation from the biotoxins has not gone on too long. A small group of patients, especially those with longer-duration illnesses, may not see this fall in C4a while on CSM. Even in this small group, effective interventions have been recently identified.

If there is an ongoing infection, as may be the case in some patients with Lyme disease, C4a will often fall but slowly rises back to pre-treatment values after the cessation of treatment. This may be an indication that living Lyme organisms are still present and may be an indication that further antibiotic therapy is justified. A rapid rise of C4a back to pre-treatment levels may also suggest that mold biotoxins are to blame.

Treatment for biotoxins will often incorporate targeted gene therapy using Actos. Actos is a drug approved for the treatment of diabetes that also has a significant number of benefits for those with biotoxin-associated illness. Beyond being anti-inflammatory, Actos lowers leptin, lowers MMP9, raises VEGF, and positively affects other markers not discussed in the scope of this article. It is one of the most important interventions known in treating biotoxin illnesses.

In fact, for people with Lyme disease, CSM alone may create a significant intensification of symptoms similar to a Herxheimer reaction. This intensification is observed in over 50% of patients and is likely the result of a cytokine storm. This storm is effectively blocked by pretreatment use of Actos. This is a very important part of treating a biotoxin illness in someone with Lyme disease. CSM alone is generally more difficult for that patient to tolerate and less successful in terms of eventual outcome. The benefits of CSM therapy are limited to the binding of toxins; it cannot do more than that.

Unfortunately, Actos confers none of these important benefits if the patient continues to consume a high-glycemic index diet. Dr. Shoemaker specifically uses a noamylose diet that restricts the intake of carbohydrates, which contain amylose. These consist of wheat, rice, oats, barley, rye, bananas, and any vegetable that grows beneath the ground. Failure to implement this restriction will result in a less than optimal outcome.

Generally, if one corrects MARCoNS colonization, VEGF deficiencies, and avoids gliadin, treatment with CSM and Actos will result in more than 92% of patients showing a 75% or greater reduction in symptoms.

To summarize, in susceptible individuals, biotoxins lead to increased leptin, increased cytokines, increased MMP9, increased C4a, reduced VEGF, reduced MSH, reduced ADH, reduced sex hormones, changes in cortisol and ACTH, prolonged illness, resistant staphylococci colonizations, gastrointestinal problems, chronic pain, and sleep disturbances. All of these are downstream effects of the "Biotoxin Pathway" in an HLA susceptible individual.

It is mind-boggling to try and comprehend the magnitude of the effect of these biotoxins on so many body systems. The beauty of understanding the "Biotoxin Pathway" however is, once understood, there are options for resolving the effects of the biotoxins and regaining health and wellness. Onward and upward!

Resources:

Dr. Shoemaker has recently released a comprehensive web site on biotoxin illness at <http://www.biotoxin.info>. This site is a must read for anyone with chronic illness.

For information on the VCS test or to take the test online, visit <http://www.ChronicNeurotoxins.com> or <http://www.biotoxin.info>.

For a full listing of tests commonly performed by Dr. Shoemaker, visit the "Testing" section at <http://www.biotoxin.info>.

To learn more about biotoxin-associated illnesses and the "Biotoxin Pathway", the book "Mold Warriors" is an impressive resource. Even if one is of the opinion that mold is not part of their issue, the book is an invaluable source of information. Remember, biotoxins are biotoxins and whether they are from mold or from Lyme disease, or any number of other sources, the concepts, symptom-presentation, and treatment options are very similar.

To hear a recent radio interview with Dr. Shoemaker on the "Biotoxin Pathway", visit <http://communityradio.coop/Audio/RIV08022006.mp3>.

Scott Forsgren has been impacted by Lyme disease for over 10 years. Through the work of Dr. Shoemaker, Scott learned that he has a multi-susceptible HLA genotype and is impacted by both Lyme disease and mold exposure. Scott shares the information he has learned on his journey on his website at <http://www.BetterHealthGuy.com> and can be contacted at Scott@BetterHealthGuy.com.

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