New Treatment Options for Chronic Lyme Patients

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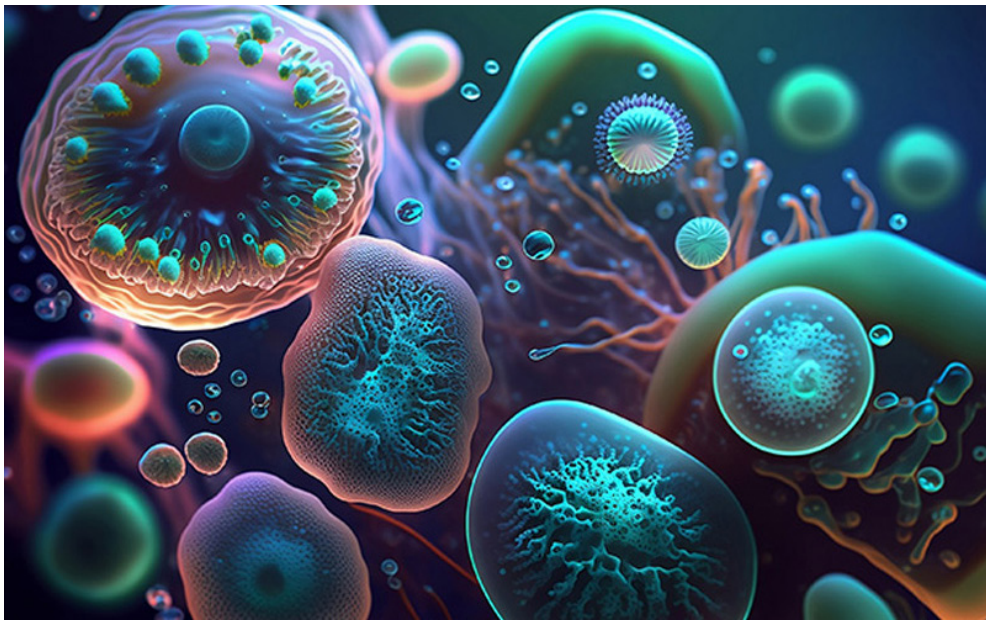


Patient Matters

Advocacy

New treatment options for chronic Lyme patients

Novel therapeutic protocols offer hope for complex cases.

By Dr. Steve Harris

Steven Harris, MD, is a board-certified family practitioner with a focus on chronic, complex illnesses including Lyme disease and associated tick-borne infections. As part of the Bay Area Lyme Foundation's Distinguished Speaker Series, he recently spoke on "Treating Complex Chronic Diseases: Novel Therapeutic Options for Lyme Patients." In his talk, he discussed wide-ranging topics including precision medicine, mitochondrial function, regenerative medicine, body alignment and toxic loads. Below is a transcript of his presentation.

What is "Precision Medicine"?

The concept of precision medicine, which is a growing area, is where we look at an individual and try to create a tailored plan for that person. I think many doctors wish that we could have a 'cookbook' approach to medicine that would work for our patients. But unfortunately, that approach doesn't work.

Dr Steven Harris speaking at the Bay Area Lyme Speaker Series in San Jose, September 29, 2022

Luckily, here in the San Francisco Bay Area, there are doctors offering precision medicine including Dr. Sunjya Schweig in Berkeley, Dr. Christine Green, with us at Pacific Frontier Medical, and Dr. Eric Gordon, at Gordon Medical Associates in Marin and others. And thankfully, we have Stanford and UCSF (our local medical centers) that we work peripherally with. In addition, the Open Medicine Foundation is making great strides in understanding illness and Dr. Mike Snyder's group at Stanford who are working on multiomics for chronic fatigue that track an individual patient's data.

These doctors are working in their own fields, not necessarily just tick-borne diseases, but our work overlaps. For example, the Snyder Lab multiomic study involves genomics, epigenomics, metabolomics, where they are looking at tons of data and assimilating a lot of this different data to try to create treatment plans that work for the individual, because of the fact that a 'cookbook' approach doesn't work for this group of chronic complex patients.

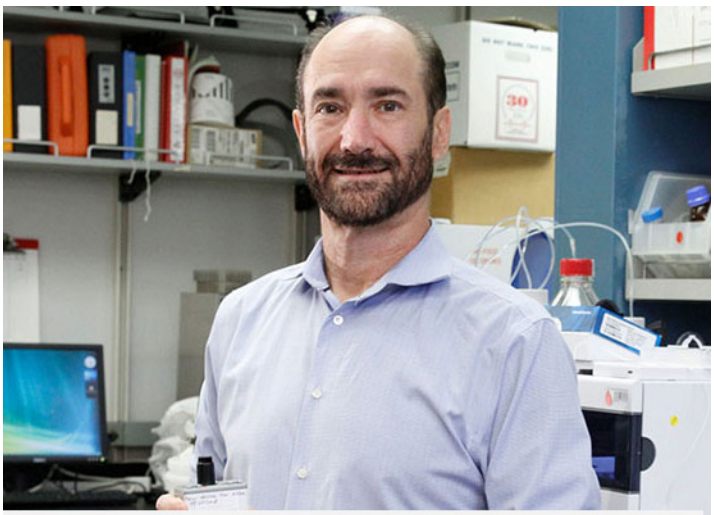
For example, we look at someone's multiome and the parts that make them up, including their microbiome, epigenome among many others, which is becoming a bigger and more exciting field. One of the practical aspects we try to determine is how to address an individual's level of inflammation, the diversity of their personal bacterial flora, and how to help compensate for any deficiencies — or over abundances — that help contribute to disease.

Precision medicine doctors are looking at as much data as we can, but we are also learning to incorporate treatments that illustrate how our bodies interact with an ever more toxic world, such as with glyphosate and organophosphates, toxic metals, among hundreds of others harmful agents. Some may argue that electromagnetic sensitivity or electromagnetic stressors are also affecting people. This needs more research and is still a very young field, but what providers report is that electromagnetic sensitivity does affect many patients. In addition, if we look at some of the old stalwarts, such as mold, actinomyces, and other biotoxins, these can contribute significantly to a patient's burden of illness. So, taking a very detailed approach to looking at what external stressors someone has is really important.

Human Energy and Mitochondrial Function

Another nascent area that is probably going to become bigger is mitochondrial work, i.e., mitochondrial function — at least in the ME/CFS world — which translates too many other areas, including the Lyme and co-infection world, because illness and wellness is fundamentally all about energy.

The concept is that if we have enough energy to mobilize our immune systems and get ourselves to detoxify, and to absorb nutrients, the body will be able to



Mike Snyder, PhD, Stanford University

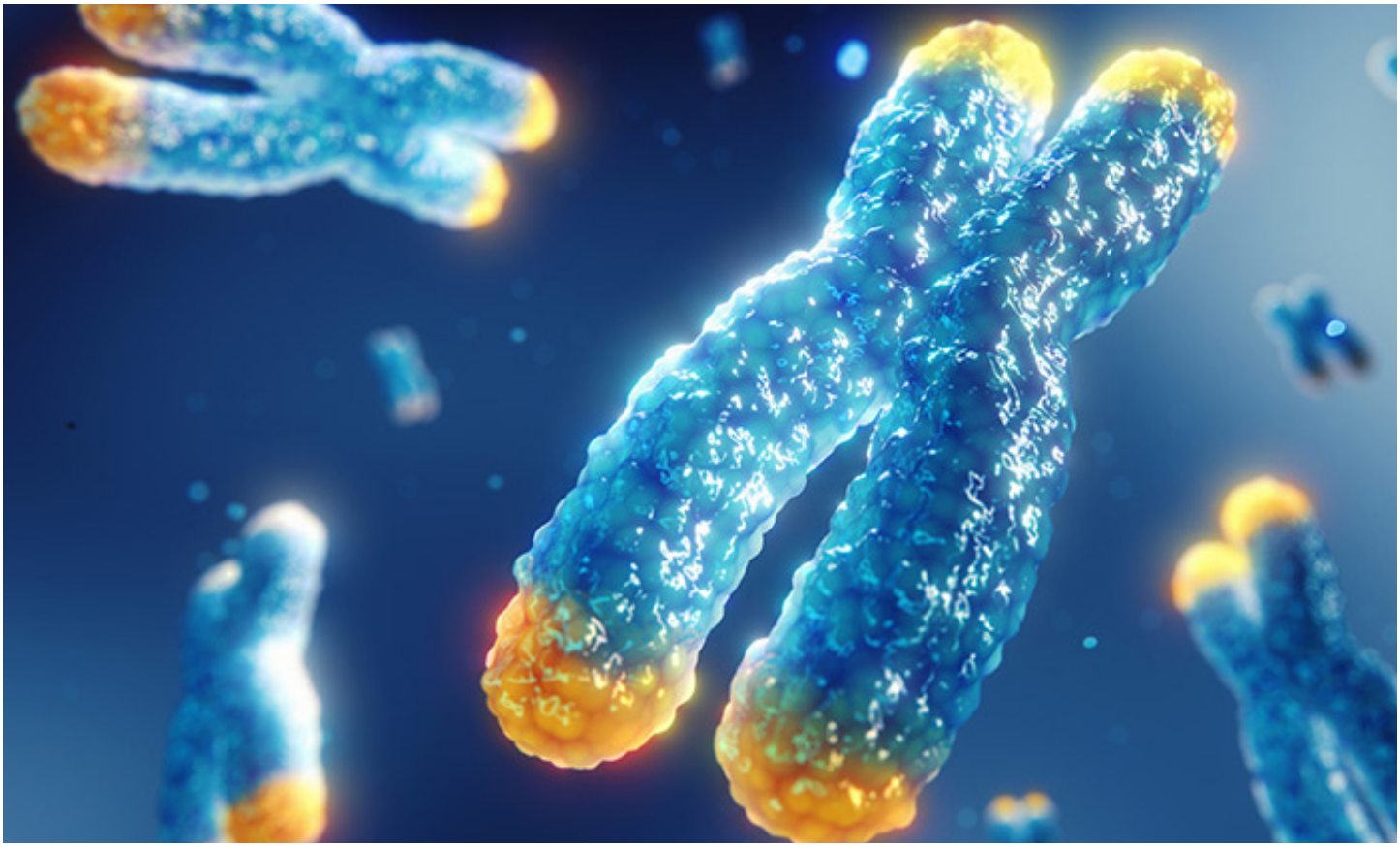
function effectively on its own. The goal of treatment is to ease the body to do what it needs to do by itself without so much external intervention. That is one of the subtle things that we're learning as we do this. The approach in the past has been, 'there's an infection and we want to knock the infection out,' but many times we have discovered that healing doesn't work that way.

Dr. Eric Gordon describes the healing exchange as being like a dance that the provider helps the patient do with various treatments. You try to tease out the way forward to get on the right path, like finding that yellow brick road. And if we are able to do that leg work early on to eliminate the stressors, evaluate and optimize the mitochondrial dysfunction, etc., then we can often take a much more direct path to wellness.

What is exciting is that there are new tests in the research world that assess mitochondrial function. Seahorse testing, for example, currently in the research phase, looks at ATP production and free phosphate production. We've been using mitochondrial muscle biopsies primarily to evaluate mitochondria in the past, but there's more to investigate regarding the way energy is made at a cellular level. In the near future more research is going to be examining the inner mitochondrial membrane to watch how the very basic pieces of electron chemistry are translating to a cell and then translating to the organism as a whole.

Telomeres and Cellular Aging

Dr. Horvath and a group at Stanford recently wrote a paper focused on decreasing cellular aging using things like growth hormone and DHEA, and met-



> *"It's like a dance that the provider helps the patient do with various treatments. You try to tease out the way forward to get on the right path, like finding that yellow brick road."*

formin (a diabetes drug), to try to decrease the age of cells. There's also a lot of talk in medical fields about telomeres and their relationship with cellular senescence. The hard part is, how do we translate this when a patient comes into the office and put burgeoning research into actual practice? Much of this is not going to be FDA approved as treatments for perhaps the next 10 or 15 years. So, part of the approach to addressing some of these very complicated patients is working in a partnership with them, because we don't have the answers. We can work towards the likely answers, but sometimes we have to do it with very short steps, and with a patient who is deeply engaged in the treatment process.

This is a very different model than we're used to. When I grew up, the doctor told you what treatments to take. You took the treatment. Then, you went back and reported your symptoms. This doesn't seem to work for this very complicated group of patients. These patients also happen to be some of the most savvy, educated, well-researched, intelligent people, mostly because they've been through so much and have seen so many doctors. By the time they come to one of us, they may have seen 20 or 30 doctors. So, we have to offer them something fresh and new that also has a high likelihood of actually working.

On top of the physical issues, we must also consider the psychological burden that chronic illness has had on people. This may seem simple and obvious, but it is such an important piece: We have to address the trauma. And sometimes we can't address trauma head on. We have to address it in a very circuitous but meaningful way.

There are a lot of non-pharmacological, non-ingestible ways to do this: Through the Dynamic Neural Retraining System (DNRS), through vagus nerve training, through neurofeedback, neuro stimulation, and through various other methods.stimulation, and through various other methods.

There is a new device called the PoNS device, which will hopefully become widely available very soon, which is a tongue neurostimulation device. It is FDA approved for head trauma, but it also works for post-traumatic stress disorder. It's an amazing way to use electricity with neuro signaling to the amygdala and help to retrain the brain to get out of that stress response. A scientist in Wisconsin, Yuri Danilov, developed it and the company that owns it is called Helius Medical technologies. They're trying to get FDA approval for it, and they are making it available to physical therapists. It's mentioned in Dr. Norman Doidge's book The Brain's Way of Healing. I've seen it used with some patients, and it's phenomenal.

Regenerative Therapies and Exosomes

In addition to the cell aging and telomere lengthening concept, one area that does seem to be slightly farther ahead is the field of regenerative therapies. Regenerative therapies include exosomes, PRP, and alpha 2-macroglobulin, among others. Some of these chemicals are injected. Oftentimes, we use it mostly for tendon issues and for osteoarthritis and for different orthopedic situations. But exosomes, especially, have other uses. There are many doctors who are using exosomes in parallel to stem cell therapies and there are many types of stem cells from autologous cells that come from your own body—to umbilical, to fetal, all the way to human embryonic.

There is a book by Amy Scher titled, This is How I Save My Life. She has become a notable author who wrote about her journey through India, where she received human embryonic stem cells, and went from a very severe neurologic case of Lyme to being quite well now.

These various therapies can be amazing if used properly, but we need more studies. Much of this is outside of the purview of many mainstream practitioners and health plans and the medical establishment at large. But many of these treatment approaches can

be done safely and effectively, and definitely have their place for decreasing that overall illness burden.

One of the thoughts about stem cells used to be that 'Oh, the stem cells can change into whatever cell, and then the cells can regenerate this way or that way.' But what we now think is that it's probably more to do with the cell signaling chemicals, and the growth factors, that are really at play here. Exosomes don't have any nucleic acid in them, it's just those chemicals themselves. Many people are using those very successfully and it's still early, obviously, but there are some very neat ways to do it, especially with some of the structural conditions such as CCI.

The Body's Structure and Craniocervical Instability

CCI is Craniocervical Instability, which is a fairly new conceptual understanding, but as a condition it's been with us for a long time. It is where micro shear forces are happening in the neurovascularly structurally dense area where the skull meets the cervical spine, which can lead to lots of inflammatory responses. Mast

cells, which are some of the allergy producing cells, are involved, among many other immune cells.

A very big inflammatory response occurs when there is a combination of an infection, such as Borrelia, Babesia or Bartonella, mycoplasma, viruses, et cetera, usually plus head trauma, or a hypermobility syndrome such as Ehlers-Danlos; it's one of the part of a triad for these people who are a setup for CCI. Dr. David Kaufman is an expert in the area who helped popularize the idea of CCI, and it's been absolutely amazing for some of these patients who have especially severe chronic fatigue. The ME/CFS world are early adopters in considering it, but for many Lyme patients and practitioners, it is not yet on their radar.

Jaw Misalignment, CCI and Spinal Issues

Another important structural approach is to investigate jaw misalignment. We can see when people have a bite that's 'off.' There's been quite a bit of work on this, mostly with the craniosacral folks, but there's some very good science that shows that every time we speak, and every time we bite that we're moving our cerebral spinal fluid, and if it moves and flows in an aberrant way, then the whole nervous system becomes 'off' as it were.

Sometimes just by repositioning the jaw we can make an incredible impact on patients. I've seen absolute magic. It's not usually something we do first, but it is something that we now think about, especially with the chronic complex illness. We look at things like root canals, and of course, that's old news, but it's still important looking at some areas of surgery and surgical scars and things like titanium rods, etc.

> *"Much of this is outside of the purview of many mainstream practitioners and health plans and the medical establishment at large. But many of these treatment approaches can be done safely and effectively, and definitely have their place for decreasing that overall illness burden."*

It should be because fatigue is one of the very significant presentations of chronic Lyme patients. I've seen four or five patients who have had this surgery with pretty astounding results. But what we're trying to do is get away from a fusion surgery if at all possible. That's where the exosomes can theoretically come in, especially properly placed injections of exosomes and PRP and these other regenerative therapies to stabilize an area in the cervical spine. The inflammation goes down with many of these injections but getting the benefits to continue when people move their heads frequently is another matter.

Obviously, this is a complicated and very new field, and the challenge is that the neurosurgery boards in America don't allow surgery for fatigue. You need something like a chiari malformation or an instance where a vital system is being compromised before the neurosurgeon can actually do surgery for this. So, sometimes by the time they do surgery, the patient can be significantly decompensated. The results aren't quite as good as they would have been if we could have done it earlier. But in addition to the environment, genomics, and metabolomics, and microbiome, a way to approach some of these pathogens is by looking at a patient's body structure — CCI being one of those aspects.

Therefore, jaw misalignment along with CCI and other spinal issues, such as scoliosis and different ways the spine presents in space can have very profound implications for a chronic illness. Let's not forget, these patients are coming to me, and they typically also have infections. So, the infections are probably one of those rate-limiting steps. There are a lot of people who have scoliosis and who have jaw misalignment and CCI, who aren't actually sick. But when you throw in what these infections are doing to people, and you combine that with the structural issues, then you start seeing the picture come together about the infections.

And it's not just about Lyme and babesia species and Bartonella and ehrlichia and anaplasma, relapsing fever, borrelia, etc. There are a lot of other organisms that come into play: there are a lot of GI parasites, brain parasites, worms, and amoebas of all kinds that compromise the human system. Not that they're necessarily making people sick by themselves, but they

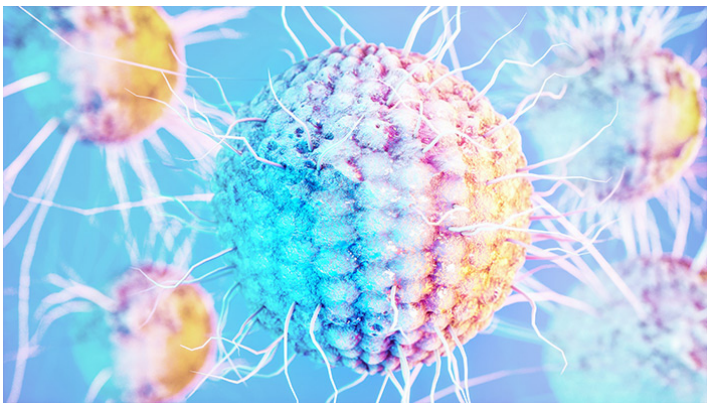
change the conditions in the body. One insult by itself isn't probably going to do anything. Throw that insult in with the Lyme, with the environment, with the structural issues, and you start seeing how complicated some of these patients are.

And so, then it becomes a question of, 'Okay, let's evaluate all these different things that could be happening.' I look at it as being like an onion. What's the top layer of the onion? How do you pull that top layer off and then go to the next one and then finally get to the core? It's a model that often works. It's just sometimes slow, but it's better to be slow and complete than trying to race to the finish and then having to do it over again.

Viruses and Body Decompensation

And then of course viruses are another piece of the puzzle, that are becoming bigger and bigger. We just happen to be right in the midst of a very large viral thing right now. Viruses have their own problems, and they can cause the body to decompensate on its own. But in the case of things like Epstein Barr and human herpesvirus 6, enteroviruses and varicella, they can be very opportunistic. We know about opportunistic viruses through the HIV world.

The immune system is typically able to surveil these opportunistic infections really well. However, if the body becomes weakened, whether through the immune system already being weak or there're being too many stressors on it, those viruses can take on a life of their own.



Dr. Jose Montoya earlier and now the current folks at Stanford in the chronic fatigue center are looking closely at human herpesvirus 6. The late, great Paul Cheney, who was so important in putting chronic fatigue on the map, was looking at human herpesvirus 6 primarily, while John Chia has been very involved with enteroviruses. These different viruses definitely can contribute to fatigue and contribute to various related symptoms. But, in my view, they are often purely opportunistic and come up because the body is decompensated. So just treating those, in my experience, hasn't been fully effective, but it is very important to look at them in the overall scheme of what we're doing for patients.

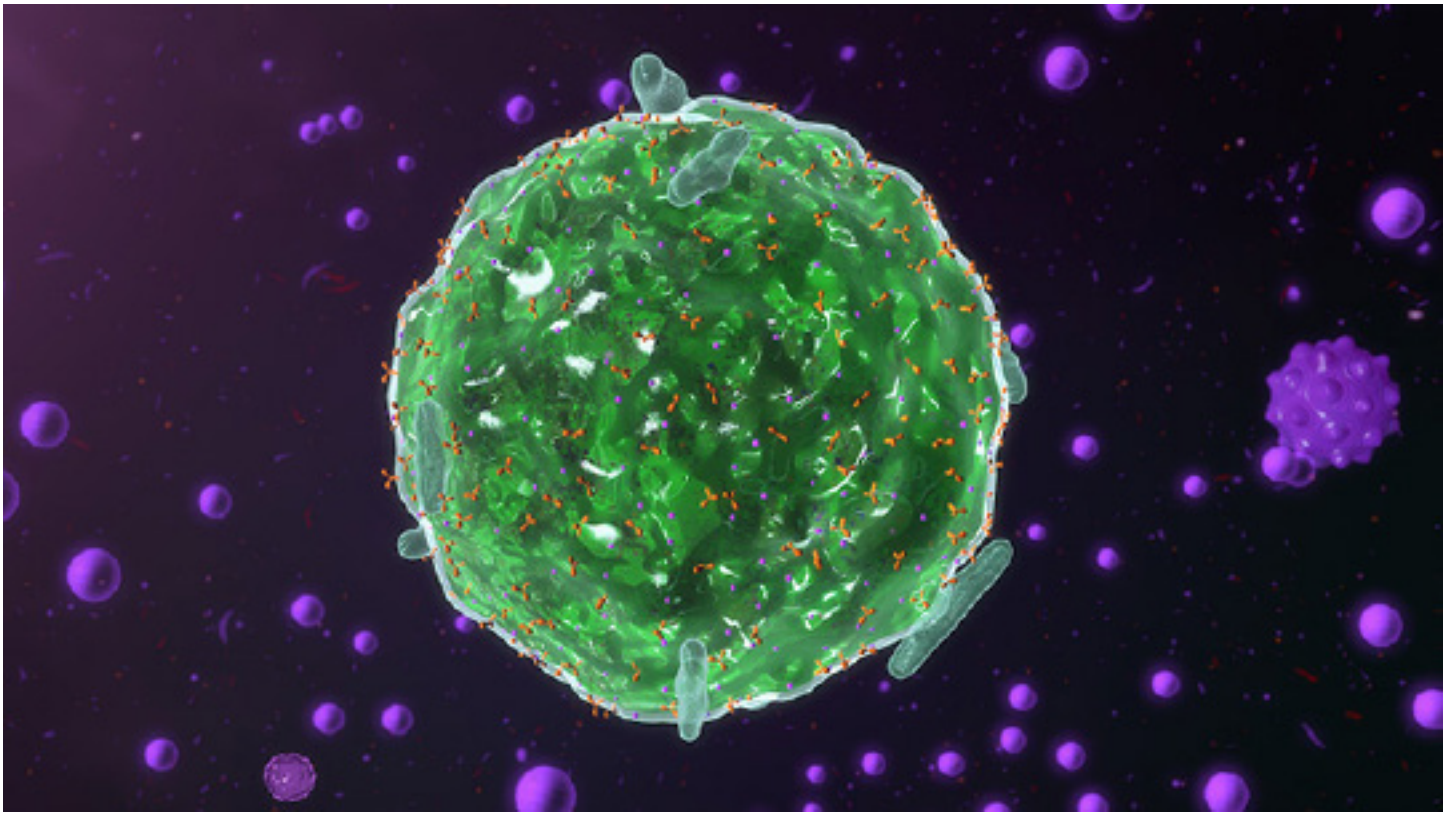
mTOR Agents and Autophagy

At an ILADS conference a few years back, Dr. Steven Phillips did an amazing talk on the use of mTOR agents, (mammalian target of Rapamycin). This process has to do with how our cells can clean the body by degrading older and dead cells. People who can clean their body of debris have a much higher chance to heal and recover. People who have high levels of autophagy can heal, because there's cellular turnover and new healthy cells taking the place of old or unruly cells.

There are many agents that we're starting to look at for people who have been sluggish, who have been sick for many years, and have been through many different treatments and have been stagnant. Trying to increase one's autophagy through the use of things like Rapamycin is starting to get attention nationwide. At the 2022 ILADS conference in Orlando, I met with many people who are starting to use this cancer drug in low doses to try to increase the body's ability to rid itself of debris. Other things include Honokiol, which is a magnolia leaf, and doxycycline, and many other agents increase autophagy including methylene blue. This is one of those areas that we're exploring as a group, and one of the ways that we approach these complicated patients. Vitamin D is another example of an mTOR agent.

Toxic Load, Nutrient Status and Environmental Stressors

One way to approach patients is to look at what's happening with their ability to absorb nutrients and then get rid of waste i.e., absorption and detox. And it always comes back to that for many of us in the day-to-day working with these patients: how do we increase their absorption and nutrients? Their ability to tolerate nutrients? Their ability to get rid of the stuff that they don't need? One way to do that is through membrane



chemistry and using different kinds of fats to flush out some of the debris, on the so-called classic lipid bilayer on the surface of cells.

There were common, simple methods used in the past to just detox patients and assist them in draining and elimination that we used to employ, but simple strategies no longer work in the most complex subset of patients. Oftentimes there is too much happening in their metabolism. There's too much junk that is causing their bodies to react. Sometimes the reactivity is so profound that nothing happens if we can't fix that reactivity.

Sometimes, this over reactivity is related to infection. Sometimes it's because there's too many bad chemicals in the body. With all of these environmental exposures that people have, a way for the body to respond to these stressors is by overreacting. While it could be driven by just the infections, it's usually a complicated causation as to why people have 'mast cell activation.'

We learned about it through a tumor of mast cells called mastocytosis. This is a little bit different because people don't have these tumors, but they elicit an infection-related, allergy-producing response. It's the body trying to help itself, but it does so ineffectively and in a way that increases a person's suffering.

David Kaufman and some other folks have found a triad of Ehlers-Danlos or hypermobility syndrome with what's called POTS or orthostatic tachycardia with mast cell activation. We're finding groups of these people where this hypersensitivity syndrome is actually the first thing that we have to assess. Unless that is successful the rest of the treatment process can't really ensue.

Again, we used to just do some detox, get patients prepared, and then work from the top down, working on the biggest thing like worms, then go to parasites, then go to metals, then go to babesia, then go to Lyme, etc. Now that initial dance to diminish the reactivity can become the bulk of the treatment regime. On the positive side, once we get past that part, the rest of the treatments can often be done faster, with very positive results, where patients develop momentum in approaching wellness.

"In conclusion, these are a few different ways to address this most complicated, most difficult group of patients. I truly believe that everybody can get better, and I think that sharing that hope with the patient is a way for them to be able to hold on during what is a marathon for many of them. Not everybody needs to take every step, but the steps are there, and it can be done." **— Dr. Steven Harris**

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In Lyme carditis, spirochetes disrupt the heart's electrical system

Proper treatment of Lyme carditis can often avoid the need for a permanent pacemaker.

By Sunjya Schweig, MD

With nearly half a million people diagnosed annually, Lyme disease is the fastest-growing vector-borne disease in the United States and is becoming increasingly widespread. Lyme is a tick-borne infectious disease caused by the spirochete bacteria, Borrelia burgdorferi.

Although Lyme disease is prevalent, research is underfunded, and many healthcare providers aren't trained to properly diagnose and treat Lyme and other complex tick-borne infections. This leaves many infected patients untreated and at risk for acute or chronic diseases, such as Lyme carditis, Lyme arthritis, neurologic Lyme, nervous system dysfunction, gastrointestinal issues, and a host of other multi-systemic conditions.

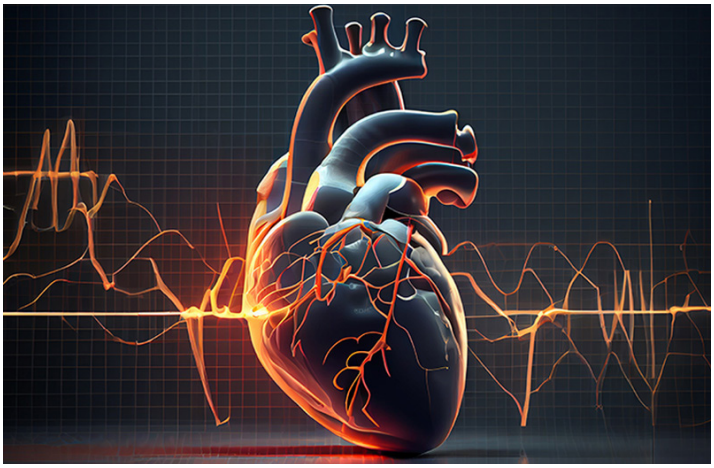
What is Lyme Carditis?

Lyme carditis occurs when the Borrelia bacteria enter and infect cardiac tissue, causing inflammation (myocarditis, pericarditis, or endocarditis), and disrupting the electrical conduction system of the heart. Ninety percent of Lyme carditis cases may present with a heart block, specifically an atrioventricular block, which causes abnormal heart function.

In addition, the bacterium may directly damage the heart tissue by invading the heart muscle or the heart's

conduction (electrical) system, leading to conduction abnormalities and heart block. Electrical signals from the heart's upper chambers are not properly relayed to the lower chambers, dramatically slowing the heart rate.

The severity of the heart block can fluctuate rapidly and the progression to a complete heart block can be fatal. Additionally, Lyme carditis can affect other parts of the heart's conduction system, as well as the heart's muscles, valves, and outer layer of the heart wall.



Furthermore, Lyme carditis may sometimes be part of an autoimmune inflammatory process. The immune system sees the bacteria as a threat and sends antibodies to attack it. However, because the heart tissue has already been infected by the bacteria, the antibodies also attack the heart tissue, causing even more damage.

Epidemiology of Lyme Carditis

The Centers for Disease Control and Prevention (CDC) estimates that there are approximately 476,000 new cases of Lyme disease each year in the United States. Studies have shown that Lyme carditis can occur in as many as 4-10% of Lyme cases, which means there are likely between 19,040 and 47,600 new cases of Lyme carditis annually. In Lyme endemic areas of the United States, where Lyme disease is more common, the incidence of Lyme carditis may be higher.

However, some Lyme experts like Adrian Baranchuk, MD, from the Department of Medicine at Queens University in Canada, believe that the number of Lyme carditis cases might be much higher because only symptomatic individuals treated by Lyme-educated medical practitioners receive proper testing like serological tests and electrocardiograms. Dr. Baranchuk feels that many more people who contract Lyme have some level of cardiac inflammation and conduction abnormalities at a subclinical level on initial presentation. Still, these are missed if no electrocardiogram (ECG) is performed.

Symptoms of Lyme Carditis

Lyme carditis can cause a range of symptoms. These symptoms can vary from person to person and can be mild or severe. While some patients experience severe symptoms, others may experience none at all, which contributes to the elusive nature of the diagnosis. Common symptoms of Lyme carditis include:

- **Palpitations:** rapid or irregular heartbeat that can be felt as a fluttering or pounding sensation in the chest.
- **Chest pain:** sharp, stabbing pain or discomfort in the chest, which can be mistaken for a heart attack.
- **Fatigue:** feeling extremely tired and having a lack of energy.
- **Shortness of breath:** difficulty breathing, especially during physical activity or exertion.
- **Dizziness or lightheadedness:** patients may feel faint or dizzy, which can be a sign of decreased blood flow to the brain.
- **Syncope:** fainting or passing out.
- **Flu-like symptoms:** fever, chills, body aches, and other symptoms that are similar to the flu.

Management of Lyme Carditis

The management of Lyme carditis usually involves a combination of supportive care to manage symptoms and prevent complications:

- **ANTIBIOTICS:** oral or intravenous antibiotics, depending on the severity of carditis.
- **HOSPITALIZATION:** in some cases, patients with Lyme carditis may require hospitalization for monitoring, temporary cardiac pacing, intravenous antibiotics, and supportive care. The management of Lyme carditis usually involves a combination of supportive care to manage symptoms and prevent complications:
- **SYMPTOMATIC TREATMENT:** may involve

medications to manage symptoms such as palpitations, chest pain, and shortness of breath. These may include beta-blockers, antiarrhythmics, and other medications to support heart function.

- **MONITORING:** close monitoring for any changes in condition, including the progression of symptoms or the development of complications. This may include an MRI, X-ray, ECG, Holter monitor, and/or blood tests.
- **ELECTROCARDIOGRAM (ECG):** to evaluate the electrical activity of the heart and detect any abnormalities that may require treatment. Top researchers like Dr. Baranchuk propose that everyone with confirmed Lyme should receive a proper cardiac physical exam and an ECG as the standard of care.
- **PACEMAKER (TEMPORARY OR PERMANENT):** a pacemaker implantation can be an effective treatment for those with a high-degree atrioventricular block from Lyme carditis.
- **PREVENTION:** patients with Lyme carditis should take steps to prevent future tick bites and reduce their risk of Lyme disease, including wearing protective clothing, using tick repellents, and checking for ticks after spending time outdoors.

Identification and Diagnosis

If you present with a heart block, we recommend using Dr. Baranchuk's evaluation methods to identify if Lyme disease is the underlying cause of cardiological issues. The first method is the Suspicion Index of Lyme Carditis (SILC). The SILC score evaluates the likelihood that a patient's high-degree AV block is caused by Lyme carditis.

Below are the variables and their point value:

- **Age less than 50 with cardiac manifestations: 1 point**
- **Male gender (5:1 higher cardiac risk): 1 point**
- **Outdoor activity/endemic area: 1 point**
- **Constitutional symptoms (fever, malaise, arthralgia, dyspnea): 2 points**
- **Tick bite: 3 points**
- **Erythema migrans rash (can be bull's-eye but not always): 4 points**

Your total score indicates your risk for Lyme carditis:

- **0-2: low risk**
- **3-6: intermediate risk**
- **7-12: high risk**

Dr. Baranchuk also notes that one can use the acronym COSTAR to remember these factors:

- **C**onstitutional symptoms of Lyme, such as fever, malaise, joint pain, and lack of energy.
- **O**utdoor activity in an endemic region.
- **S**ex: males have a higher inclination toward cardiological manifestations (5 to 1).
- **T**ick bite: not every patient has a known tick bite but if so, it highly increases the possibility of diagnosis.
- **A**ge: you are under 50 and present with cardiological manifestations.
- **R**ash: you have a shutdown of the electrical system plus rash, it is Lyme carditis until proven otherwise.

Based on your scores, your provider will need to order serological tests and you may need to begin intravenous antibiotics. You may also receive a temporary pacemaker for additional support with regular ECG monitoring. For more information, we recommend reviewing Dr. Baranchuk's methods published in the Journal of the American College of Cardiology.

> *"If you suspect you have been suffering from untreated Lyme disease or have Lyme with any of the symptoms mentioned, please contact your healthcare provider as soon as possible"*

Dr. Sunjya Schweig is founder of the California Center for Functional Medicine and serves on the Bay Area Lyme Foundation's Scientific Advisory Board.

Importance of Prompt Recognition and Treatment of Lyme Carditis

Prompt recognition and treatment of Lyme disease are of critical importance to prevent the development of Lyme carditis and other complications of the disease. If a patient with Lyme disease (or in a Lyme-endemic area) develops symptoms of Lyme carditis, such as chest pain, palpitations, shortness of breath, dizziness, or lightheadedness, they should seek medical attention immediately.

The standard protocol for high-degree (third-degree) heart block calls for implanting a permanent pacemaker. However, the heart block in Lyme carditis will most likely resolve with antibiotic therapy. Thus, identifying Lyme carditis as the underlying cause of the heart block can prevent the unnecessary implantation of permanent pacemakers.

The battery of a pacemaker lasts 7-10 years and a missed diagnosis could subject an otherwise young, healthy patient to 5-7 battery replacements over a lifetime—with each procedure bringing potential adverse events. These risks associated with the initial pacemaker implantation can be mitigated by intravenous and oral antibiotic treatment for heart block caused by Lyme carditis.

If you suspect you have been suffering from untreated Lyme disease or have Lyme with any of the symptoms mentioned, please contact your healthcare provider as soon as possible.

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An Overview of Lyme Disease Testing

There are many nuances associated with Lyme disease testing, especially in late-stage illness.

By Dr. Todd Maderis

Diagnosing acute Lyme disease is often straightforward. If someone develops flu-like symptoms following a tick bite or spending time in nature, the diagnosis of Lyme disease is often considered. However, when someone is sick with multiple symptoms for an extended period of time, it can take years to get a correct diagnosis. There are many nuances associated with Lyme disease testing. Read below to learn about accurate testing for chronic or late-stage Lyme disease.

How was Lyme Disease Testing Criteria Developed?

There may not be a more complex infection to diagnose than chronic Lyme disease. When Lyme disease was first discovered in the 1970s, the Center for Disease Control (CDC) wanted to track the number of cases in the US, so they developed diagnostic criteria for surveillance reporting to local public health departments. The criteria needed to be narrow to increase the sensitivity of cases reported. Unfortunately, the surveillance criterion made its way into doctor's offices, and physicians began using the narrow criteria as diagnostic parameters for Lyme disease.

CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

If someone had symptoms following a tick bite – or even years after a tick bite – but did not have a large bull's-eye rash, meningitis, facial paralysis, or encephalomyelitis, they were told they did not have Lyme disease.

Another limitation of the Lyme disease surveillance criteria is it only includes symptoms often seen in acute cases of Lyme disease and excludes many symptoms consistent with late-stage Lyme disease. Throw in the misconception that people can only contract Lyme disease in the northeastern U.S., and Lyme disease is not typically considered as a possible cause of symptoms in the rest of the country.

Poor Sensitivity of Traditional Lyme Disease Testing

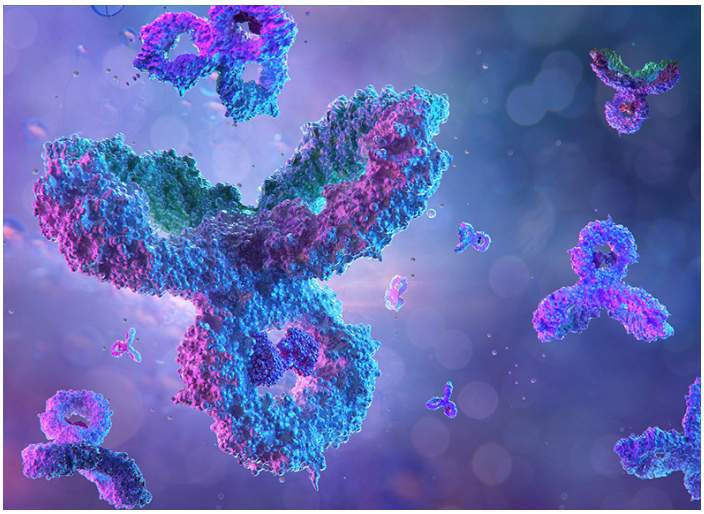
If a physician is familiar with the many presentations of Lyme disease and considers Lyme disease as a possible diagnosis, standard laboratory testing has poor sensitivity so many cases are missed. The traditional laboratory test used to diagnose Lyme disease is a "two-tiered" test. This means an ELISA test is run first, and if it is positive, a second test called a western blot is performed to confirm the accuracy. If the ELISA test is negative, the western blot is not performed. The sensitivity of the ELISA test is so poor that it reports a false negative about half of the time. This means the more sensitive western blot never gets tested.

Physicians that specialize in treating tick-borne infections have historically considered the diagnosis of late-stage Lyme disease a clinical diagnosis. A clinical diagnosis is made if the patient has signs and symptoms consistent with a tick-borne infection and other diagnoses that could explain the signs and symptoms have been excluded. However, in recent years specialized laboratory testing has advanced and should be used to confirm a suspected diagnosis.

In many scenarios, other possible diagnoses have been ruled out, there has been a possible exposure to ticks (including the distant past with chronic Lyme disease), and the pattern of symptoms is consistent with Lyme disease. Specialized laboratory testing is more sensitive than general reference laboratory testing (LabCorp, Quest, etc.) and should be used to confirm the diagnosis.

Additional Challenges with Lyme Disease Testing

Another obstacle with many Lyme disease tests is that they rely on detecting antibodies produced by the immune system against the bacteria that causes Lyme disease. In some circumstances, the level of antibodies may be low due to immune suppression which compromises the accuracy of the test. In addition, if a test is performed too soon after a tick bite, antibodies may have not yet formed. If antibiotics are taken early in an infection, the medication can prevent antibody formation resulting in future negative tests.



In late-stage Lyme disease, the Lyme spirochete has burrowed into tissues like muscles, joints, and organs. The bacteria can also form a protective structure around itself called a biofilm. These "immune-privileged" locations prevent the immune system from detecting the bacteria, so antibodies are not formed for the test to detect.

ELISA (Enzyme-Linked Immunosorbent Assay)

ELISA methodology of testing works by attaching Lyme antigens to a surface in a laboratory. If a blood sample has Lyme antibodies, the antibodies will bind to the antigen. This creates an antigen/antibody complex that is linked to an enzyme (which is another antibody). In the last step, a substrate is added that allows the result to be measured.

The limitation of the ELISA test is that the cut-off for a positive result is set extremely high to make the test highly specific. However, the high specificity comes at the cost of the sensitivity of the test. A review of research studies looking at the sensitivity of ELISA testing for Lyme disease revealed it is accurate less than half the time. Because of this, the standard two-tiered test for Lyme disease should not be relied upon to diagnose Lyme disease.

Immunofluorescence Assay (IFA)

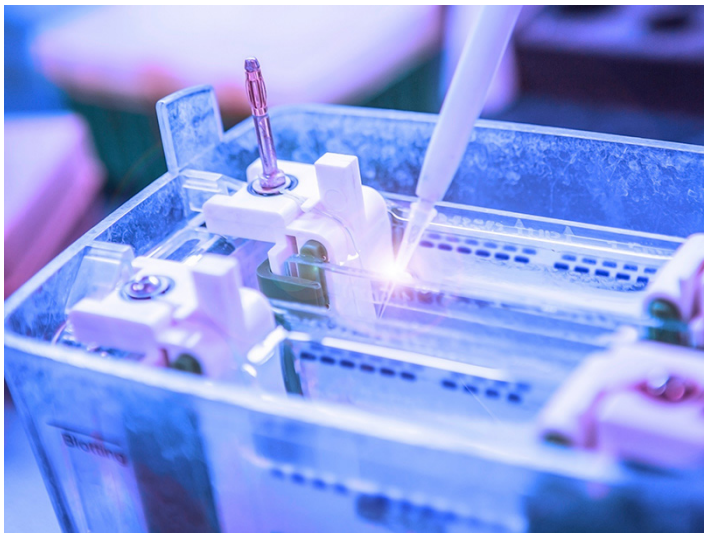
Like the ELISA, the IFA methodology for Lyme disease testing is an indirect test that looks for antibodies formed against the bacteria that causes Lyme disease – Borrelia burgdorferi.

In the laboratory, blood is added to a slide that contains the Borrelia antigens. If the blood contains antibodies to Borrelia, the antibodies will bind to the antigens on the slide. The final step is to view the slide under a fluorescent microscope (hence the name). Antibodies bound to the antigens will light up if they are present.

The IFA lacks specificity and sensitivity, so it is not a preferred method for diagnosing Lyme disease. Antibodies from other infections can bind to the antigens on the test strip (called cross-reactivity) leading to a false-positive result.

The Western Blot for Lyme Disease

The western blot is also an antibody-based test but is more sensitive and specific than the ELISA and IFA tests. Specific proteins that are on the outer surface of Lyme bacteria are produced on strips for this test. If there are Lyme antibodies in a blood sample, they will bind to the surface protein antigens. The pattern of binding indicates whether or not the result is positive. In Lyme disease, there are specific outer surface proteins (called bands), and the specific pattern formed on the blot increases the specificity of the test.



The outer surface proteins are numbered by weight in kilodaltons. Specific bands for Lyme disease include 23-25 kDa, 31 kDa, 34 kDa, 39 kDa, 41 kDa, and 83-93 kDa. The CDC criteria require at least two of three positive IgM bands and five out of ten positive IgG bands for a western blot result to be positive. The CDC criterion is stringent, so some Lyme specialty laboratories have established more inclusive criteria based on thousands of tests performed.

If someone had a possible exposure to ticks, had clinical signs and symptoms of Lyme disease, but did not have the exact pattern considered to be positive by the CDC, they were told by their doctor they do not have Lyme disease.

A limitation of the CDC criteria is bands 31 and 34 are not included in the diagnosis. The CDC excludes these two bands because a person might be positive if they received a Lyme vaccine. Ironically, very few people received the Lyme vaccine when it was available for only a couple of years before it was removed from the market due to adverse reactions (and lawsuits). Based on over 25 years of experience and validation studies, the Lyme specialty laboratory IGeneX requires two out of six bands to be positive for an IgM positive result.

Western blot tests offered by commercial laboratories such as Quest and LabCorp develop their testing strip using a synthetic laboratory strain of Borrelia called B31. IGeneX uses the synthetic B31 strain as well as the wild (occurs in nature) 297 strains to increase the sensitivity of their western blot.

Because IGeneX uses more inclusive criteria than the CDC and two strains of Borrelia for testing, their western blot may diagnose Lyme disease that is missed by less sensitive commercial laboratories.

ImmunoBlot for Lyme Disease

The Lyme immunoblot uses recombinant proteins on the blot so it is more sensitive than the western blot. This test can detect Lyme disease as early as one week after exposure to the Borrelia bacteria and detect late-stage Lyme when antibodies are typically low. Like the western blot, an immunoblot result has to meet certain criteria for a positive result.

Additional species of Borrelia bacteria fall into the Tick-Borne Relapsing Fever Group (TBRF). The TBRF group causes symptoms similar to Lyme disease, and some species may be more common in certain parts of the United States, like California. This may be why some Californians test negative on a traditional Lyme test.

Immunoblot testing is also available for multiple Babesia and Bartonella species. The panel of tests I most commonly use in my practice includes Lyme, TBRF, Babesia, and Bartonella immunoblots.

T-Cell Testing

In recent years, the sensitivity of T-cell testing for Lyme disease has improved. This methodology detects an immune cell (called a T-lymphocyte) that has formed in response to the Borrelia bacteria. T-cells are part of the innate immune response, unlike antibodies that are created as part of the adaptive immune response.

Early in infection, T-cells develop before antibodies are formed, so a T-cell test may help detect early Lyme disease. As the disease progresses, some people's immune systems do not convert from an innate to an adaptive response. This inhibits antibody formation, so a T-cell test would be helpful in this scenario.

Lyme Disease Culture

All of the above tests are considered indirect because the laboratory test is looking for an immune response to the bacteria. There are limitations to indirect testing, making it difficult to get an accurate diagnosis. For example, an elevated IgG antibody may reflect a past infection and does not confer an active infection. One of the great debates in chronic Lyme disease is whether the infection is active or if symptoms are caused by something else, like immune-mediated inflammation.

Direct-testing methodology is the gold standard for determining if an infection is active. There are a few direct tests for Lyme bacteria, but the sensitivity of these tests has historically been poor because the bacteria rarely circulates in the bloodstream. In February 2023, IGeneX Laboratory introduced a new direct test called culture-enhanced PCR. Blood is stored in a unique culture medium for two weeks and then analyzed by PCR. Validation studies for the specificity of the cePCR test were high. Direct testing may be more accurate when bacteria levels are highest, including early in infection or during a symptom flare. The cePCR is also available for TBRF, Bartonella, and Babesia.

Putting Lyme Disease Testing Together

Late-stage Lyme disease can be difficult to diagnose. The CDC criterion was established for surveillance only, so should not be used for diagnostic purposes. Lyme disease tests from commercial and hospital laboratories have poor sensitivity and specificity.

Laboratories that specialize in Lyme disease testing provide more accurate results and should be used when attempting to determine if Lyme disease is the cause of symptoms. Specialty laboratories should also test all co-infections since they can cause similar symptoms and may interfere with Lyme treatment. No one testing method is perfect, so laboratory results need to be taken into consideration by a Lyme-literate physician. Any treatment plan is only as effective as the accuracy of the lab results.

Dr. Todd Maderis is Founder and Medical Director of Marin Natural Medicine Clinic in Larkspur, CA. He blogs at DrToddMaderis.com.

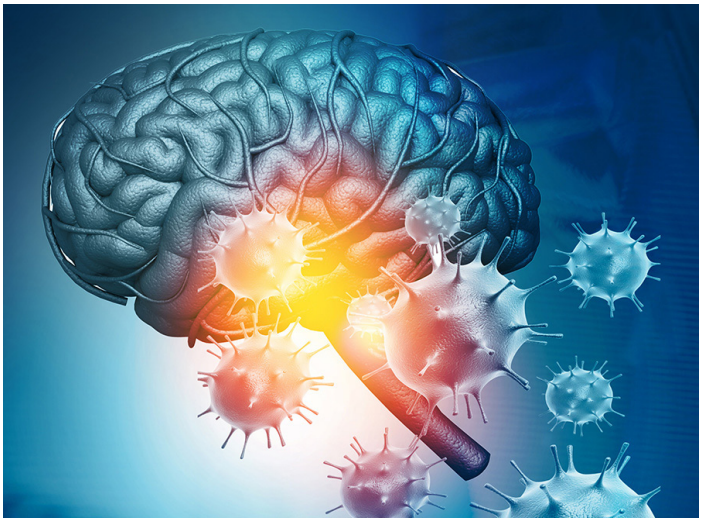
When specific foods trigger brain inflammation in children

Immune dysregulation in people with tick-borne infections often results in food sensitivities, with far-reaching effects.

By Daniel A. Kinderlehrer, MD

In previous articles posted on Lymedisease.org, I described PANS — Pediatric Acute-onset Neuropsychiatric Syndrome, and the severe mental health issues associated with it. PANS can result in everything from OCD and anorexia nervosa to anxiety/panic attacks, depression, anger/oppositional/rage issues, impaired cognition, tics and involuntary movements. PANS is "Brain on fire."

Here is what is happening in kids with PANS: the immune system's response to a microbial infection results in the formation of anti-neuronal antibodies that attack the brain. This is referred to as immune cross-reactivity or molecular mimicry. The resulting brain inflammation is known technically as autoimmune encephalitis.



The Cunningham Panel, developed by Madeleine Cunningham and colleagues, measures specific anti-neuronal antibodies as well as the activity of an enzyme that modulates dopamine activity. Several studies have confirmed the utility of the Cunningham Panel in the diagnosis of PANS.

A child's "Chernobyl meltdown"

Chuck, one of my patients, is seven years old and is typical of a child with PANS. He had a normal birth and developmental milestones. At age two, he began to have tantrums. That in itself is not unusual, but these screaming bouts were over the top — more like a Chernobyl meltdown. They escalated as he got older. He became oppositional and developed some OCD behavior in his play activities.

By six years old, he couldn't make friends and routinely got into fights at school. He was anxious and irritable.

I asked his mom about physical symptoms. She described random fevers, night sweats, light and sound sensitivity, balance issues and clumsiness, and chronic congestion as well as bedwetting and sleep issues. He was also extremely forgetful. Chuck's mom described him as having no short-term memory; he was having increasing difficulty with schoolwork.

He had several bouts of ear infections every year which were treated with antibiotics. His mom also reported that he craved cheese and sweets.

When I first evaluated Chuck, I had one lab test: a positive Lyme immunoblot from IGeneX laboratory. It turns out that his mom suffered from chronic tick-borne infections, and they can be transferred to the fetus during gestation.

From his history, I suspected Chuck suffered not only from Lyme disease but also was chronically infected with Babesia and Bartonella. Although the primary treatment of PANS is antibiotics, I often start with diet. In Chuck's case, I suspected that he had a sensitivity to dairy that was causing congestion and setting him up for his ear infections. Then the frequent antibiotics resulted in yeast overgrowth and subsequent sensitization to yeast.

Allergy-addiction syndrome

An interesting phenomenon that we see in children as well as adults is the allergy-addiction syndrome, in which people crave the food to which that they are sensitive.7 Chuck craved dairy and sweets (sugar stimulates yeast growth), and I suggested to his mom that he go off dairy, sugar and yeast. I also prescribed probiotics and the anti-yeast agent Nystatin.

On diet alone, Chuck's mood did a 180-turn. He rarely had a tantrum, and when he did, they were much less severe. He was making friends at school, doing his schoolwork and retaining lessons.

I have other PANS patients in whom specific foods are a major trigger. Dairy, eggs, gluten, sugar and yeast are major offenders, and corn is a big issue in some people.

The immune dysregulation in people with tick-borne infections often results in food sensitivities or worsens them in folks already prone to food reactions. Removing food triggers in the diet is a first step in decreasing inflammation.

Because Chuck was doing so well on diet alone, we chose to treat his infections with herbal antibiotics. We started with Nutramedix Samento and progressed the dose slowly to 10 drops twice daily, which was well tolerated. When we added Nutramedix Banderol he had a Herxheimer reaction at three drops — he became defiant and had a tantrum. Once he settled down, however, he was up to five drops twice daily and doing great. At that point, the only fights he got into were with his brothers, which seemed normal. He was happy and no longer anxious.

Samento primarily hits Lyme, but Banderol mainly hits Bartonella. I am always suspicious of Bartonella in kids and adults who have significant neuropsychiatric symptoms. Chuck's night sweats and fevers suggest he also has Babesia. I will also get him tested for Mycoplasma, as this microbe can be a major cause of neuroinflammation.

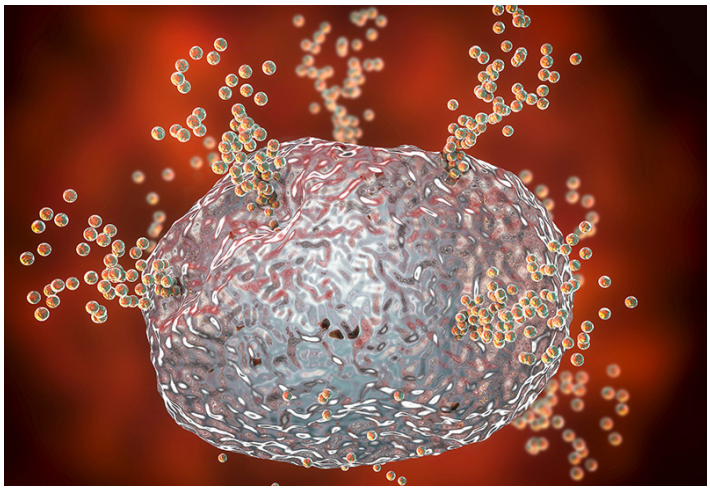
Mast Cell Activation Syndrome

The increase in inflammation and sensitivities in PANS patients can devolve into Mast Cell Activation Syndrome (MCAS), 9 in which there is an excessive release of histamine and other inflammatory mediators contributing to inflammation. Kids with PANS often benefit from treating MCAS with agents like Gastrocrom, ketotifen or quercetin, which stabilize mast cells, as well as antihistamines. And there should always be a search for possible mold exposure. 10 Other anti-inflammatory agents that sometimes help include curcumin, Boswellia, CBD and low-dose naltrexone. Nonsteroidal anti-inflammatory agents like ibuprofen are occasionally beneficial.

The next step is antibiotics. This needs to be done carefully because of potential Herxheimer reactions. When tick-borne infections are the trigger, I suggest treating Lyme first — in most patients it is less inflammatory than the co-infections. Most of my patients with PANS have not had as quick a turn-around as Chuck. But most get better when a regimen is instituted that includes dealing with food sensitivities, mold exposure and mold toxins, MCAS and appropriate antibiotics.

IVIG — Intravenous Immunoglobulins

Some patients, however, require immune modulation with interventions such as IVIG — intravenous immunoglobulins.11 IVIG is a big deal. It consists of the intravenous administration of antibodies, usually given every three weeks. It has the paradoxical effect of boosting immune function while decreasing inflammation and can be quite effective in the treatment of PANS. However, there is a significant relapse rate when the IVIG is discontinued.



A major hurdle with IVIG is the cost — up to $10,000 per injection. It's no surprise that insurance carriers make it challenging to get approval for this intervention. The exception is Illinois, where the legislature mandated that insurance companies cover treatment for PANS. I wonder if families are moving to Illinois to get this treatment covered, just like they moved to Colorado several years ago to get their kids with seizure disorders treated with cannabis. [*Editor's note: Similar measures are under consideration in various other states as well.*]

There is also a role for psychotropic medication in some kids, since the mood disturbances can be severe, and the inflammation can even result in psychosis.

PANS–or MANS?

I think the nomenclature of PANS is unfortunate. Adults with tick-borne infections (as well as viruses such as SARS-CoV-2) can also suffer from autoimmune encephalitis with severe neuropsychiatric symptoms. I have suggested the name be changed to Microbe-induced Autoimmune Neuropsychiatric Syndrome (MANS).

Dr. Daniel Kinderlehrer is an internal medicine physician in Denver, Colorado, with a practice devoted to treating patients with tick-borne illness. He is the author of Recovery From Lyme Disease: The Integrative Medicine Guide to the Diagnosis and Treatment of Tick-Borne Illness.

What patients most frequently ask their Lyme doctors

After testing and treatment discussions, physician says most common question is "Can chronic Lyme be cured?"

By Dr. Christine Greene

Christine Green, MD, is a Stanford-trained, board-certified family medicine physician with 30 years of experience treating patients with tick-borne illness.

On the board of LymeDisease.org, Dr. Green is also Co-director of Education for Invisible, is on Bay Area Lyme Foundation's Scientific Advisory Board and has served on the Education Committee for ILADS.

In this Q&A, she discusses common questions asked by patients about diagnosing and treating Lyme and other tick-borne disease

Q I'm achy and tired all the time. Could I have Lyme disease?

A Dr. Greene: The answer is yes. When a patient comes into my clinic for the first time, I take down their clinical history. If I suspect tick-borne disease, I ask if they've been exposed to ticks or tick habitats. Have they observed any rashes?

The typical Lyme rash expands and is ring-like, usually not itchy or painful. If it's under a person's hairline, between the toes, or on the back of the body, it may not be noticed. However, at least 21% of Lyme patients, and probably more than 50%, never see a tick or a rash.

Early Lyme patients present with flu-like symptoms. Tick bites and resulting symptoms often occur in the summer, but in my California practice, Lyme season may overlap with the fall/winter flu season, confusing the diagnostic picture.

Next, I do a complete physical exam, with an emphasis on neurological deficits, such as loss of balance, tremors, facial asymmetry (Bell's Palsy), and asymmetric reflexes. Then, I ask about the progression of their symptoms over time.

In the first few months of Lyme disease, patients often experience malaise, fatigue, mild-to-severe headaches, nerve pain or tingling in the hands or feet, all in a relapsing-remitting course. In other words, the symptoms wax and wane.

If Lyme is diagnosed four or more months after symptom onset, the picture of the disease is different and variable. The longer between infection and diagnosis, the higher likelihood that more bodily systems have been invaded.

Late-stage patients tend to have peripheral nerve symptoms that come and go, and symptoms that migrate to joints, muscles and/or nerves. Most patients with late Lyme have encephalopathy, inflammation of the brain that reduces blood supply in some areas.

This can manifest as sleep problems, memory issues, word-recall problems, or difficulty reading or carrying out executive functions–the mental processes that enable us to plan, focus, remember instructions, and juggle multiple activities. For instance, a person who organizes large events might find that they have trouble completing and sequencing tasks. Things that used to take minutes, take hours.

Patients can also experience cardiac symptoms, including irregular heartbeats, chest pain, or dizziness. These patients often come in misdiagnosed with old age, depression, anxiety, or hypochondriasis (preoccupation with an imagined illness).

Another presentation of this disease is chronic pain. The pain can be widespread and migrate around the body. These patients often come in with a diagnosis of fibromyalgia or new onset migraine headache.

Q What's the best test for diagnosing Lyme disease?

A Dr. Greene: First and foremost, Lyme disease, as with any disease, should be diagnosed based on a clinical history and physical exam, not by test results alone.

It's important to note that the complex, conservative two-tiered testing criteria for "CDC positive cases" was developed for disease-tracking only. It shouldn't be used by physicians as the sole criteria for diagnosis or denying treatment to patients.

What's more, not all Lyme tests are created equal. The major labs typically look for only one strain of Lyme bacteria, the B31 strain of Borrelia burgdorferi. I prefer using specialized labs that test for multiple Lyme strains. Three of the labs I use are MDL, Galaxy, and IGeneX.

One tick can inject multiple species of disease-causing microbes in a single blood meal, so, based on symptoms, I sometimes test for other tick-borne infections.

If a patient has night sweats, shortness of breath, stabbing chest pains, or autonomic symptoms (dizziness, nausea, vertigo, flushing), I'll test for Babesia, a malaria-like red blood cell infection.

For a pinprick rash on the extremities and/or severe illness, I'll test for spotted fever. Bartonellosis can present in many ways, including neuropathy, or neuropsychiatric symptoms, such as panic attacks, rages, psychosis, and obsessive-compulsive disorders.

Q Once diagnosed, how should you treat Lyme disease?

A Dr. Greene: Research over the last three decades suggests that Lyme bacteria have multiple ways of evading the human immune system and that treating acute Lyme with 21 days of antibiotics fails approximately a third of patients.

For that reason, I treat in two phases. For early Lyme, I treat with four weeks of doxycycline, amoxicillin, or cefuroxime antibiotics.

I follow this up with four more weeks of drugs that prevent and eradicate "persister" forms of the bacteria. The persisters are drug-tolerant and can revert to an active infection once the antibiotics are stopped.

I aggressively treat late-Lyme patients who have severe degenerative neurologic or rheumatologic cases. As noted above, the very sick patients frequently have a mixture of tick-borne infections.

For these patients, I choose a combination of oral or, when needed, intravenous antibiotics that target the pathogens known to be present.

Q Can you cure chronic Lyme disease?

A Dr. Greene: In my practice, I've helped many of my tick-borne disease patients return to full health. Every patient is unique, with different genetics, co-morbidities, and co-infections. To me, the important thing is to evaluate clinical response and not to cut off treatment at some arbitrary end point.

I assess symptoms at the beginning of each visit, then treat until symptoms improve or resolve. For any patient who is ill for an extended time, after the illness is controlled, I initiate rehabilitation protocols to help the person feel normal again. A patient must become fit to fully recover from a protracted state of ill health.

"Research over the last three decades suggests that Lyme bacteria have multiple ways of evading the human immune system and that treating acute Lyme with 21 days of antibiotics fails approximately a third of patients"

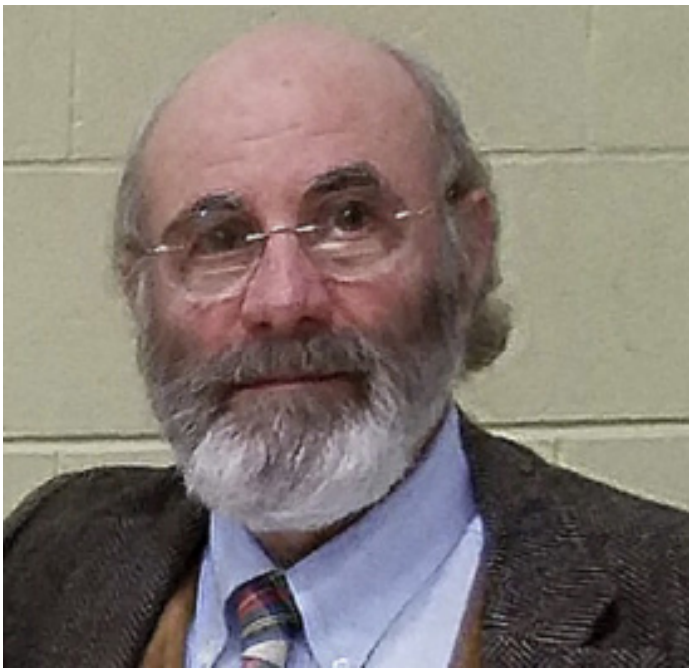
How a pioneering doctor uses disulfiram to treat persistent Lyme disease

Some chronic Lyme patients--though not all--get substantially better on this drug.

By Ken Liegner, MD

Kenneth Liegner, MD, has been on the frontlines of treating Lyme and other tick-borne diseases for more than thirty years. Recently, author Dana Parish interviewed him on the Bay Area Lyme Foundation's Ticktective™ podcast.

Their conversation addressed many topics, including the history of Lyme disease in the US and the lack of recognition of the illness among clinicians, the government, and insurance companies. They talked about the treatment challenges of co-infections like babesiosis, and touched on how a COVID infection may impact Lyme patients, causing a recurrence of latent symptoms. And they discuss Dr. Liegner 's



pioneering use of disulfiram—a drug initially used to treat alcoholism—as an off-label therapeutic for his Lyme patients.

The following is a transcript of an excerpt of the podcast interview.

Q **Dana Parish:** You were a pioneer in discovering disulfiram for the treatment of Lyme disease. How did you come upon that, and how did it go? It's been a couple years now, so what do you think now?

A **Kenneth Liegner:** Well, I can't take credit for discovering it for its utility in Lyme. It was the work of Jayakumar Rajadas. I was the first clinician to apply it in patients. Jayakumar Rajadas and his coworkers at Stanford did some high throughput testing of thousands of compounds and just tested them to see which had activity against the Lyme spirochete. And it turned out that disulfiram was way up there at the top, or near the top, if not at the top, having activity way more than doxycycline/Rocephin. So, that was published in an article in a little bit of an obscure journal, and nobody really paid all that much attention to it. Then at the first Lyme Mind Conference that was held at Mount Sinai sponsored by The Steven & Alexandra Cohen Foundation, they really got some great people together. The keynote speaker for that conference was Kim Lewis, who's from Northeastern (University).

Towards the end of his talk, he mentioned Rajadas' work, and that disulfiram had this huge activity. One of my patients had been following Kim Lewis's work and it (the keynote speech) was later posted on YouTube. This is a patient I'd worked with for quite a few years, very trustworthy. He was kept pretty well on a regimen of amoxicillin, minocycline, and malarone. But if he went off treatment, he would deteriorate. He saw this presentation, and he told me about it.

So, I viewed it, and I was already familiar with the paper. I reread it. I'd never used disulfiram because I just had no occasion to use it. It is a drug that has been used mainly for treating alcoholism, which is not my field. I knew that it existed, but I had never used it. I looked it up at the patient's request. I never would've suggested it to the patient. The patient asked if I would let him try it. Now, it's a drug that's been used for decades and is generally safe. And although it does have some potential toxicities, I allowed him to try it. And it's a long, long story. It's outlined in the articles that were published. There was the first article about the first three patients published in MDPI antibiotics. Then we published another paper a little bit later reporting on our experience with another 60 or 70 patients.

The first 30 patients that we used it on, bing! bing! bing! It was a dramatic improvement. And these are tough cases. These are not easy cases. That influenced me to publish on it. And of course, with that, it has gotten a lot of attention. It is a drug that has to be used with care. And it's not something I just throw at people willy-nilly. It's got to be the right person in the right way. And if you're going to use it, you have to be really familiar with the drug, and you have to follow the patients carefully. Even today, we're still trying to figure out different ways in which it can be used.

Q **Dana Parish:** It occurs to me it should not be the first line of defense against Lyme.

A **Kenneth Liegner:** I'm not using it that way. I'm not using it as a first line. First of all, it's still relatively new. I would not say it's, quote, 'the standard of care,' you know?

Q **Dana Parish:** Is it getting people durably better? Now that you've had a couple years with it, are there patients that have gotten well with it, that were intractable before and now don't need to come see you every three or six months anymore?

A **Kenneth Liegner:** Yes. But I don't ever tell them to expect it. Nor do I declare that they are, quote, 'cured.' Because I don't know. All I know is that there's a subset of those who are treated, but not everybody who seems to get substantially better or well, and where they don't need to see me for years at a time. So, I think it's very potent. But again, it has certain toxicities that can be quite serious, even fatal, or resulting in irreversible neurologic injury. So, you have to be judicious with who you use it with. People need to be fully informed. As a clinician, you are obliged to follow them carefully and be vigilant. Usually with some of these complications if you recognize it, you need to stop the drug. And usually, those adverse reactions will reverse. But even then, you can't say that. You don't always know that they're going to reverse. So, it's tricky. It's potent, but it has to be used with care, judiciously.

Q **Dana Parish:** I've heard some really remarkable stories for sure, some remarkable recovery stories. Early on, when you were first using it, people that were languishing for years, trying different things, were finally improving.

A **Kenneth Liegner:** The thing about it is, it's as cheap as borscht! I mean, relatively speaking, compared to intravenous Rocephin, which is expensive and inconvenient. It also has risks. To me, it's just another tool in the toolbox. And you can't have too many tools. We need more tools in the toolbox.

Q **Dana Parish:** But it's great that you found that, and it's helped a subset of your patients and other people have gone on and adopted it and have helped some of their patients. We need more innovation of course. But thank you for that. What my hope is now is that all this Long Covid research will inform chronic Lyme. Do you think that might happen? Is there hope on the horizon for chronic Lyme patients? In light of all the awareness now of what a chronic common infection can do?

A **Kenneth Liegner:** I think there's going to be some synergy there. But I think really in order to solve the problem, you need to acknowledge it for what it is. And that's why I reiterate it's important to acknowledge chronic Lyme, the infection. There can be other elements, like neuro autoimmune components for sure. Or maybe even post-infections in some people. But for many people it's the infection. And if you don't acknowledge that, then your research for treatment is going to be misaligned. You need to find a way to definitively deal with the infection. And of course, the hope and the goal would be to find something that's absolutely curative, that eliminates the infection completely—unless you get reinfected—that should be the goal. That should be where the effort should be directed. Also, the other thing that's important is to have a definitive direct detection test that's qualitative, as well as semi-quantitative, that can help us to know the status of the infection and also the response to treatment in an objective way. That's been lacking.

Q **Dana Parish:** Absolutely. I love this quote. It's your quote. I remember the first time I read it, I almost fell off my chair because it just says it all. So, I'm going to read it. You said, "In the fullness of time, the mainstream handling of chronic Lyme disease will be viewed as one of the most shameful episodes in the history of medicine. Because elements of academic medicine, elements of government, and virtually the entire insurance industry have colluded to deny a disease." If that just doesn't say it all. Nobody could say it better than that. That's just the truth.

> *"In the fullness of time, the mainstream handling of chronic Lyme disease will be viewed as one of the most shameful episodes in the history of medicine. Because elements of academic medicine, elements of government, and virtually the entire insurance industry have colluded to deny a disease."*

CLICK TO LISTEN TO THE ENTIRE INTERVIEW

Dr. Kenneth Liegner is the author of In the Crucible of Chronic Lyme Disease, Collected Writings and Associated Materials. Dana Parish is co-author of Chronic: The Hidden Cause of the Autoimmune Pandemic and How to Get Healthy Again.

Hi-Dose Dapsone Combination Therapy

Two-thirds of chronic Lyme patients receiving this protocol went into remission

By Dr. Richard Horowitz

Dr. Richard Horowitz recently sent out the following public message regarding his latest journal publication.

Good news. Our paper on high dose dapsone combination therapy (HDDCT) for the treatment of chronic Lyme disease/Post-Treatment Lyme Disease Syndrome (PTLDS) was accepted for publication. Please see the link below and share broadly with the chronic disease community.

Horowitz RI, Freeman PR. Efficacy of Short-Term High Dose Pulsed Dapsone Combination Therapy in the Treatment of Chronic Lyme Disease/Post-Treatment Lyme Disease Syndrome (PTLDS) and Associated Co-Infections: A Report of Three Cases and Literature Review. Antibiotics. 2022; 11(7):912. https://doi.org/10.3390/antibiotics11070912

I want to explain why I think this paper from Phyllis and myself may be one of the most important ones we have done.

Dapsone Combination Therapy

As you know, double dose dapsone combination therapy has approximately a 50% remission rate in those with chronic Lyme disease and PTLDS for one year or longer, if all abnormal MSIDS variables were addressed, and if they didn't have persistent Babesia or Bartonella

This paper addresses the 50% that failed double dose dapsone. The most important take-home point is that it was not just the time on the antibiotics that determined success and remission, it's the dose of the persister drug.

In the case of dapsone, 200 mg per day worked much better than 100 mg per day. And a 4-day high dose pulse of 400 mg per day of dapsone, with higher doses of methylene blue, which hits both Lyme and Bartonella persisters, ended up giving us roughly another 33% of patients that went into long-term remission (and some of these had active Bartonella!)

2/3 of participants went into remission

This means that this protocol provides the first short-term antibiotic protocol, i.e., 8 weeks of double dose dapsone and one 4-day pulse (or more) i.e., 9-10 weeks total of oral, generic antibiotics, that results in roughly a 66% long term remission rate.

This is the study and eventually, the randomized trial I have been waiting to do for years. It should prove to the world once and for all the role of persister/biofilm forms of Borrelia and Bartonella, the role of co-infections like persistent Babesia, and how MSIDS variables like low adrenal function, POTS, mitochondrial dysfunction, mold and heavy metals, mast cell activation, etc., are what we are finding in the thousands of patients we have been helping.

It's a paradigm shift from a one disease–one cause model to a multifactorial model with several underlying forms of inflammation and downstream effects of that inflammation causing symptoms in chronic Lyme and PTLDS.

The paradigm will most likely have some positive applications to other chronic fatigue, musculoskeletal illnesses with neuropsychiatric symptoms like CFS/ME, fibromyalgia, long COVID, ASD, etc.

For the Lyme community, this is big news and is the culmination of over 30 years of my research trying to find a cure. We now have the first short term antibiotic protocol for chronic Lyme with a reasonably good long term remission rate with some efficacy against resistant co-infections.

Figuring out the details

We still have to figure out details on how to improve efficacy against chronic Bartonella infections as well as Babesia. (Tafenoquine is not enough in all patients who have failed Mepron and Zithromax and Clindamycin and Quinine, Coartem, Malarone, cryptolepis, etc. Please read the article.)

However, the randomized control trial I would like to do next year should be the bridge to allow other researchers and clinicians to take what we have found and improve upon the efficacy, looking at higher dosing of new and novel persister drugs.

Consider that 14.5% of the global population has now been exposed to Borrelia sensu lato species, and at least 20% go on to chronic Lyme disease. That implies that 3% of the 8 billion people worldwide now have chronic Lyme (240 million). A 2/3 success rate with a short term, oral, generic protocol using HDDCT would help 160 million chronic disease sufferers.

If that turns out to be true, my life's work will have been a blessing in disguise. Thanks to the MSIDS Research Foundation for their support in helping to get the article published. Please share this article widely with the broad Lyme community!

READ THE STUDY

Dr. Richard Horowitz is a board-certified internist and medical director of the Hudson Valley Healing Arts Center, specializing in the treatment of tick-borne disorders. He has treated over 13,000 chronic Lyme disease patients in the past 30 years and was a member of the U.S. Department of Health and Human Services Tick-borne Disease Working Group and other governmental panels. He has authored two books.

Is there a connection between autistic spectrum disorders and tick-borne illnesses?

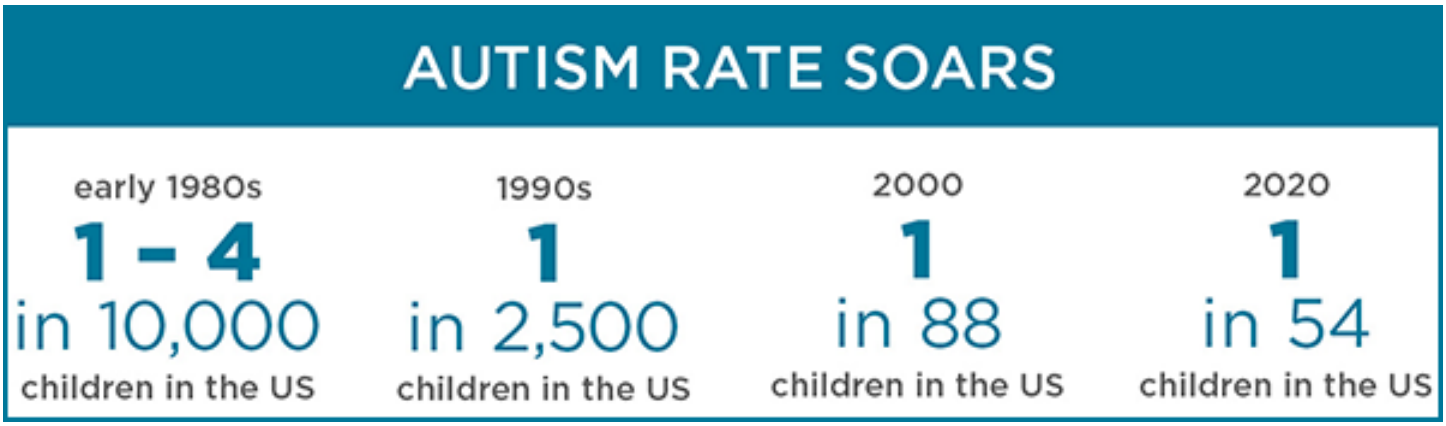
Studies indicate that approximately 25% of those with ASD show evidence of infection with Lyme disease.

By Dr. Rosalie Greenberg

Dr. Rosalie Greenberg

I live and work in New Jersey, a Lyme-endemic area. It also has the distinction of having a high rate of youth diagnosed with Autistic Spectrum Disorders (ASD). The most recent statistics indicate that as many as 1 out of 32 children may be affected by some form of the disorder.

Included under the heading of ASD are: autism, Asperger's syndrome and pervasive developmental disorder not otherwise specified (PDD-NOS.) In general, these terms are used to describe and differentiate a group of individuals who share difficulties with social, emotional and communication skills which can



potentially have a profound effect on their ability to function. The past few decades have seen a dramatic worldwide rise in the cases of ASD. The natural question is "Why?"

As in many neurobiological disorders, complex genetic and environmental factors need to be considered. With the rise in ASD, the escalation in the number of cases can't be simply attributed to genetics, however, as changes in genes don't occur so rapidly as to have such a broad and dramatic impact.

This means we must look to the environment for at least some answers. And as we are looking, is it possible that infections play an important role?

Tick-borne infections

When I first heard that Lyme disease and other tick-borne illnesses (TBIs) can play a role in the development of ASD, I thought that it was the reaction of people who were perhaps a bit overzealous in their desire to attribute almost every medical problem to TBIs. Over time I learned that this was a connection with real merit and more investigation was needed.

Autism is a disorder that in some, can be detected shortly after birth. Regressive autism is the diagnostic name given when sometime before age three, typically between the ages of 15 and 30 months, the child shows a regression in already acquired basic skills. He/she may lose speech, social skills and/or exhibit regression in developmental milestones. The onset can be unexpectedly sudden.

Manifestations of ASD

The following is a list of potential ASD symptoms according to the National Institute of Mental Health. Although not every child will show every symptom, typically many are present.

Problems in social communication and interaction as evidenced by:

- Making little or inconsistent eye contact
- Tending not to look at, or listen to people
- Rarely sharing enjoyment of objects or activities by pointing or showing things to others
- Failing to, or being slow to, respond to someone calling her/his name or to other verbal attempts to gain attention
- Having difficulties with the back and forth of conversation
- Often talking at length about a favorite subject without noticing that others are not interested or without giving others a chance to respond
- Having facial expressions, movements and gestures that do not match what is being said
- Having an unusual tone of voice that may sound sing-song, or flat and robot-like
- Having trouble understanding another person's point of view or being unable to predict or understand other people's actions

Demonstrating restrictive/repetitive behaviors which may include:

- Repeating certain behaviors or having unusual behaviors. For example, repeating words or phrases, a behavior called echolalia
- Having a lasting intense interest in certain topics, such as numbers, details or facts

- Having overly focused interests, such as with moving objects or parts of objects
- Getting upset by slight changes in a routine
- Being more or less sensitive than other people to sensory input, such as light, noise, clothing or temperature.

Autism rates are soaring

When I finished my training in the early 1980s the autism rate was 1 – 4 in 10,000 children in the United States. In the 1990s, prevalence rose to 1 in 2,500. By the year 2000, the number soared to an estimated 1 in 88 children.

This trajectory sadly continues. The most recent (2020) Centers for Disease Control report indicates that 1 in 54 children in the U.S. has a diagnosis of an autistic spectrum disorder by age 8.

Boys are four times as likely as girls to get the diagnosis, which cuts across all races and economic groups. It is interesting to note that the rates of ASD also vary by geographic region, from a low of 1 in 76 in Colorado to a high of 1 in 32 in New Jersey.

In part, different degrees of awareness as well as dissimilar approaches to diagnostic assessments may contribute to this disparity. Nonetheless, the overriding observation is that the rate has dramatically increased and not just because we're better at recognizing it.

From a geographic perspective, there is a shared commonality between places with high rates of ASD and those with increased rates of diagnoses of TBIs. Similarly, there are areas in which TBIs are very uncommon and the rates of ASD are quite low.

A few studies have looked specifically at the overlap of ASD and TBIs and the rate of positive tick-borne testing in ASD youth. (These used different labs and sometimes dissimilar criteria.) In general, it appears that the few existing studies indicate that approximately 25% of those with ASD show evidence of infection with Borrelia burgdorferi (Bb), the bacteria responsible for Lyme disease.

In addition, studies found that in those individuals with ASD, who were Bb positive, at least 68% had evidence of co-infections including Mycoplasma, Bartonella, Ehrlichia and Babesia. All of these infections are generally considered TBIs (although there is still some controversy about Bartonella being carried by ticks).

Symptoms in common

A variety of symptoms are common to those affected by TBIs and ASD.

These may include:

- Increased sadness
- Emotional lability (emotions easily changeable)
- Increased irritability and/or oppositional behavior
- Heightened anxiety, presence of obsessive-compulsive symptoms
- Behavioral rigidity
- Being somewhat emotionally detached
- Problems with transitions
- Insomnia
- Gastrointestinal problems – diarrhea and/or constipation

> *"Studies indicate that approximately 25% of those with ASD show evidence of infection with Borrelia burgdorferi (Bb), the bacteria responsible for Lyme disease."*

The role of infections

The idea of infections contributing to the development of ASD is not new. Syphilis, congenital rubella and toxoplasmosis are associated with causing ASD. In a 2018 paper, Dr. Robert Bransfield, a neuropsychiatrist who specializes in TBIs, notes that at least 23 different kinds of infections have been associated with ASD.

- Food sensitivity or intolerance – modifying the individual's diet can be beneficial
- Sensory hypersensitivity – extra sensitivity in any one or more of the five senses: sound, vision, touch, taste and/or smell
- Decreased muscle tone

- Attention Deficit Hyperactivity Disorder (ADHD) symptoms
- Cognitive problems including issues with memory, learning and processing information
- Experiencing a variety of co-existing psychiatric disorders
- Difficulty dealing with stress
- Problems with speech (e.g. word-finding issues)

Individuals with both ASD and TBIs experience immunosuppression, immune dysregulation and autoimmunity. In addition, they share biochemical similarities such as changes in antioxidant enzymes, decreased glutathione levels and changes in homocysteine/methionine metabolism.

Similarities also exist in brain imaging of young people with ASD and TBIs.

These can include evidence of:

1. Significant temporal lobe dysfunction (the part of the brain involved in emotion, comprehension, memory, language, sensory input and vision) and
2. A predominance of findings in the white matter of the brain (which is important for learning and coordinates communication between different parts of the brain and spinal cord).

Two categories

There are probably two groups of individuals with ASD and TBIs. Some investigators feel that one group can be attributed to having experienced the congenital transmission of Lyme disease – from mother to child. The other group is made up of those who have experienced TBIs during the crucial early developmental years. These youth can demonstrate the new onset of, or a heightened intensity of, previously present ASD symptoms.

Why is recognizing these associations important? Evidence in the literature indicates treating Lyme disease in the mother who has the infection during the pregnancy can help prevent the development of ASD in the child.

If you have a child with what is considered somewhat "atypical ASD" you might consider TBIs as a possible contributing or exacerbating factor. Finding that a child with ASD has one or more underlying TBIs has the potential to make a difference in that individual's life.

Early detection and proper treatment are often key components to the positive changes that can be seen. How large an impact treatment can have is hard to know at the outset.

The following are two case examples from my practice:

CASE #1

John is a 6-year-old who was born two months early at 32 weeks and weighed 3 lbs. 1 oz. He spent the first few weeks after birth in the hospital until doctors felt his lungs were mature enough and he no longer needed close observation.

Soon after being home, he began exhibiting a variety of issues including feeding problems with gastroesophageal reflux (GERD), poor eye contact, difficulty soothing, very sensitive to touch, and he didn't like being held.

He exhibited a particular interest in staring at rotating objects, especially ceiling fans. His language development was delayed and his motor milestones were achieved a bit late.

As he grew, it became clear that he was highly impulsive. Once he could walk well, he would gladly dash off from his parents' side if he saw something that captured his interest whether there was heavy traffic or a crowd of unfamiliar people in front of him. It's as if no obstacle, no matter how dangerous, was significant enough to stop him when he was in pursuit of seeing or doing something.

By age 3, he was given an autism spectrum disorder diagnosis. John seemed close to his mother and father. He would allow them to show him affection, but he displayed little reciprocity or enjoyment of these actions. Because of his various difficulties, John qualified for and received early intervention services in his educational district from a young age.

While taking his medical history, I began to suspect congenital Lyme disease. John's mother described having had neurologic Lyme disease (neuroborreliosis) at one point in her life, a few years after John was born.

In retrospect, she had probably had TBIs prior to conception, but proper diagnosis and treatment did not occur until John was close to 3 years old. John had no known history of a tick bite. On blood testing, he showed evidence of exposure to Borrelia burgdorferi, Bartonella, Babesia and Anaplasma.

Given the test results, I referred John to one of my medical colleagues who specializes in the diagnosis and treatment of TBIs. The doctor confirmed the diagnoses of multiple TBIs and recommended antibiotic treatment.

Medication was started slowly and after a few weeks John's mother noticed some changes. She said that he was no longer trying to escape from his parent and run out of his room when told to brush his teeth. He was definitely more cooperative with his morning routine which went from taking 45 to 15 minutes because he was a more active and compliant participant. One day, he spontaneously walked over to his mother, took her arm, placed it around his head and snuggled. His communicative skills and desire for social interaction showed some improvement.

Although many would consider the changes subtle, he was slowly but clearly becoming less self-involved and much more available and involved in the world around him. Thus, change was being made in some of his core ASD behaviors. It is still very early in John's treatment and much time and work are needed to see how much progress he is capable of making and sustaining.

CASE #2

Then there is Andres. Andres wanted me to use his real name because he believes strongly in self-advocacy and is proud of the progress he has made, although he recognizes how much further he would like to be able to go.

Andres is a wonderful 26-year-old young man who is the sole survivor of an identical twin birth complicated by significant cerebral bleeds in both boys. Due to abnormalities in social and communication skills he was diagnosed at an early age as having an autistic spectrum disorder.

Within a few years he was additionally diagnosed as having an attention-deficit hyperactivity disorder. By age nine, when I first saw him, he also appeared to have a bipolar or manic-depressive disorder, with intense, angry, aggressive mood shifts intermixed with periods of self-loathing.

Psychological testing at age 12 revealed an intelligence quotient in the low 70s which is considered a borderline level. His mother felt he had stopped learning, hit a plateau and actually showed some cognitive decline when he was in 4th or 5th grade. Teachers felt this was probably due to him reaching his cognitive ceiling and weren't overly concerned.

Neurologic consultation and workups in a variety of academic hospitals were unrevealing. Given his difficulties, and a new onset of a seizure disorder at age 15, Andres was hospitalized for a more intensive neurologic evaluation and to change his high dose psychiatric medication safely.

He was on 600 mg of quetiapine (Seroquel) and it was unclear if the medication was contributing to his newly observed seizure disorder. While in the hospital, he was transitioned to ziprasidone (Geodon), a different psychiatric medication. Andres was also given one treatment of intravenous immunoglobulin G (IVIG) due to evidence of immunodeficiencies and autoimmune thyroiditis. It was hoped that it would also help with his cognitive struggles.

Short-lived gains

Following discharge, Andres started showing cognitive gains and continued to do well for at least six months. A year after his previous testing, the same examiner retested Andres intelligence quotient (IQ) using the Wechsler intelligence scale for children, 4th edition-revised (WISC-IV-R). The results showed an elevation of 10 points in total IQ – an unusual gain and also a significant life-affecting change. His short-term memory had improved; he was better at focusing and was more aware of social cues.

Unfortunately, the gains were short-lived. This was near the point in my practice when I decided to check all my previously diagnosed pediatric bipolar patients for any evidence of TBIs. I tested Andres for evidence of exposure to an infected tick. To my surprise he was found to be positive for Lyme, Babesia and Bartonella without any known history of a tick bite.

This was the start of consultations with many specialists and multiple interventions that have varied and still continue. Presently, Andres has been able to take some community college level courses and do quite well. For the last four years, he has enjoyed a nice relationship with a young woman who also has an autistic spectrum disorder.

Special talents

Like many people with ASD, Andres has some special talents. Most striking among them, is that he is an amazingly gifted drummer.

Dr. Rosalie Greenberg is a Board-Certified Adult, Child and Adolescent Psychiatrist, known for her expertise in the diagnosis and management of complex psychiatric problems in children, and pediatric psychopharmacology. For the past few years, she has focused on the psychiatric manifestations of infectious diseases, especially, tick-borne illnesses in children and adolescents. Her website is rosaliegreenbergmd.com

Below is an excerpt of a piece he wrote on his own for his photojournalism course:

02/2021

Am I A Drummer With Autism Or Am I A Person With Autism Who Plays Drums?

AUTHOR: ANDRES ORTIZ

My name is Andres and I have high functioning autism. I've been playing drums for about 16 years. Playing drums makes me feel energetic, happy and special both inside and out. Learning to play the drums has helped me in lots of ways. Not only do I have a better appreciation of lots of kinds of music, but my social skills have gotten a lot better because being in a band means that you have to understand other people. Music has been my link to the neurotypical community. When I'm behind the kit, no one knows that I am different.

Music has helped my behavior, social and communication skills. It doesn't matter if I am playing or listening to music. Playing the drums makes me a better musician and a better person. When I first started jamming with people, I was worried about being accepted and being a good enough drummer, but I learned how to get along with them thanks to my love of music and making friends in general.

My first teacher, Mr. M, taught me to play the basics at home. We started with two Beatles classics, "If I Fell" and "Hey Jude" because I am a huge Ringo fan. He said that to be a real drummer I had to play with other people, so I joined School of Rock. I am now in their Grad School program for people 19 and older. SB is our bassist and he's really good. He also has autism and is also my good friend. He's not my friend because he has autism but because we both love music and because we have the same sense of humor.

SB and I are not the only musicians who have autism. Did you know that many famous musicians like Mozart, Courtney Love from Hole, Marty Balin from Jefferson Airplane, Craig Nicholls from The Vines, Alan "Blind Owl" Wilson from Canned Heat, some say Keith Moon from The Who, James Durbin from American Idol in 2011 and then Quiet Riot and of course the 2019 winner of America's Got Talent, Kodi Lee also have autism? I even got to jam with the members of The Austistix when I was in London. They are a band of musicians who just happen to have autism.

Some things about having autism are actually helpful when it comes to playing music. People with autism can understand the smallest details of music very easily and even better than neurotypical people. Many have perfect pitch for singing and harmonies. Because we perseverate, we get really smart or really good at whatever we're interested in. We don't mind rehearsing the same thing over and over again. Eye contact is easier when we are concentrating on playing which is important in a band. Sometimes though loud noise can be a problem, but headphones can help...

More research needed

To say that discovering and treating Andres's TBIs made a real difference in his life is an incredible understatement! Not all kids with ASD and TBIs can achieve such accomplishments even with treatment of their infections. It's important to remember that Andres is still undergoing treatment all these years later.

There is no question that research on the link between ASD and TBIs requires much more study. It is however, tremendously encouraging to witness the potential change treatment for TBIs can make in the lives of these of young people and their families.

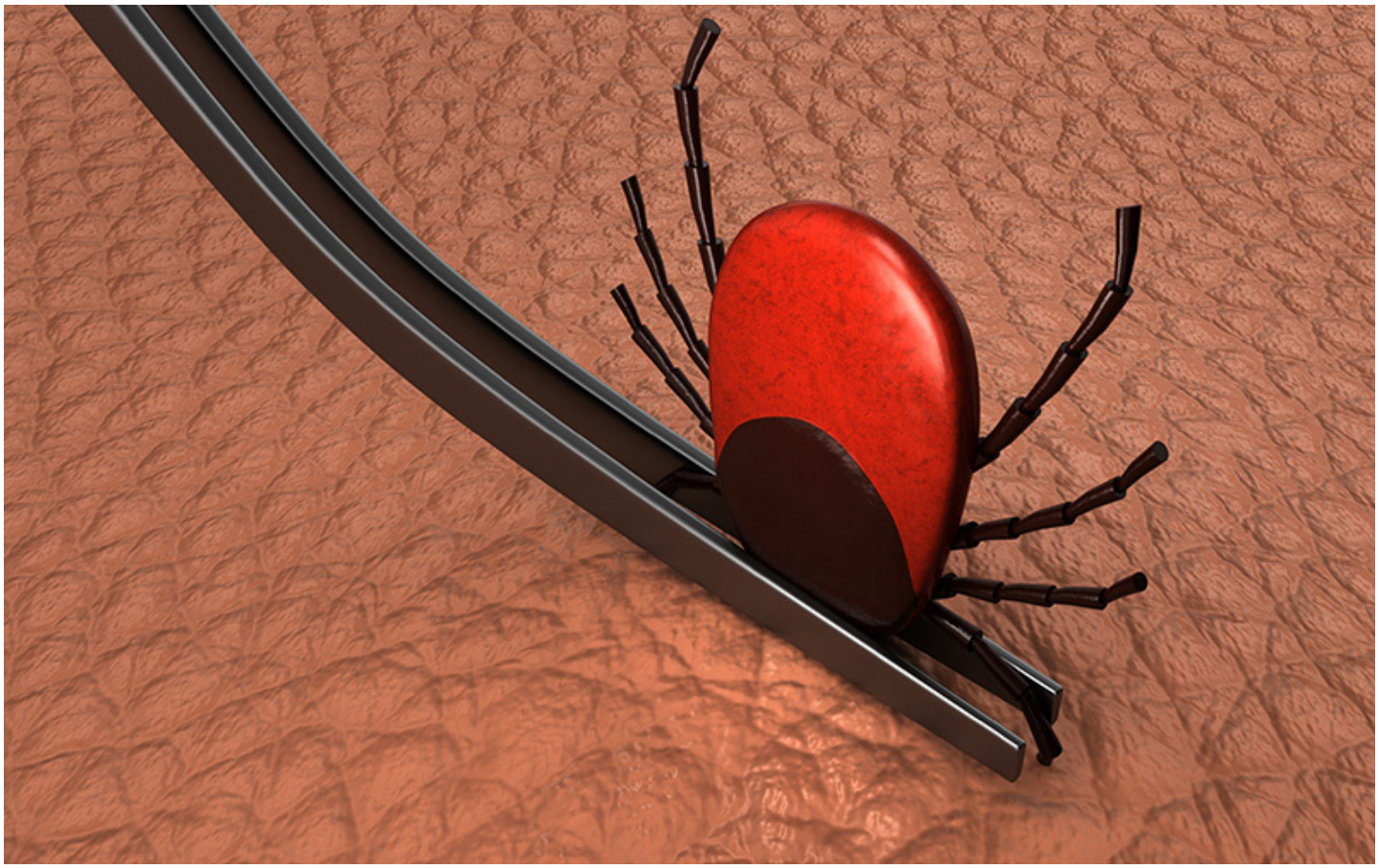
Recognizing and treating Lyme disease in young children

In addition to physical symptoms, Lyme can also cause behavioral or mood changes in children.

By Dr. Charlotte Mao

Dr. Charlotte Mao is a pediatric infectious disease physician who trained at Harvard Medical School and Boston Children's Hospital. She also practiced at The Dean Center for Tick-borne Illness, Spaulding Hospital, where she treated children with complex Lyme disease. She currently serves as the Curriculum Director for Invisible International's Medical Education Initiative.

Here are some frequently asked questions that she encounters in her practice.



Q What do I do if I find a tick on my child?

A Dr. Mao: If you see a tick embedded in your child, position a fine-tipped tweezers where the tick's head meets the skin, then swiftly pull it straight out. Do not grasp, squeeze, or twist the tick's body. Then place it in a plastic baggie with a small piece of damp paper towel. Wash the extraction area and your hands thoroughly with soap and water.

Consider sending the tick to a testing lab, to identify the species and what microbes are inside of it. Because the current Lyme disease screening tests are unreliable in the first few weeks after a bite (it takes this long for humans to develop antibodies that can be measured), the results might provide your physician with useful information, especially if your child later comes down with symptoms.

You can also go online to identify which tick species transmit various disease agents. Lyme disease is carried by blacklegged ticks, Ixodes scapularis in the Eastern United States and Ixodes pacificus in the West.

Some experts say that it takes at least 36 hours for an attached tick to transmit Lyme bacteria to a host because this is the minimum time it takes for these bacteria to travel from a tick's midgut to its saliva glands.

However, transmission can happen in some cases with a shorter duration of attachment, specifically when bitten by a partially fed tick that already has Lyme bacteria in its saliva from a previous attachment.

This occurs in about 5 to 10 percent of infected ticks, according to the Lyme bacteria discoverer, Willy Burgdorfer. Other tick-borne microbes, such as the potentially deadly Powassan virus, can be transmitted in as little as 15 minutes after tick attachment.

Time is of the essence in preventing serious tick-borne disease. So, in Lyme endemic areas, I personally advise parents to begin preventative antibiotic treatment before tick testing results come back, within 48 to 72 hours of attachment.

Over the following month, closely observe a child for symptoms, such as an expanding skin lesion at the bite site, fever, malaise, headache, mild neck stiffness, aches/pains in muscles, or joints aches. If these develop, visit your pediatrician.

Q How can I tell if my child has Lyme disease?

A Dr. Mao: Early signs of Lyme disease include flu-like symptoms, such as fever (often mild), chills, head and neck pain, body aches (muscle and joint), malaise, and fatigue. Unfortunately, these symptoms can be mistaken for irritability or viral infections, such as the flu or COVID.

Check your child for a Lyme disease rash and don't forget to check the scalp and skin-fold areas (groin, armpits, behind the knees, and ears). Not everyone gets the classic "bull's-eye" rash. An expanding rash without central clearing is more common. You can find some sample rash images on the Internet.

Other classic Lyme manifestations that can develop include a weakness or paralysis of facial muscles (Bell's palsy); intense headaches, numbness, tingling, or weakness in extremities (neuropathy); eye and heart issues (especially cardiac rhythm abnormalities); and joint swelling or pain. Gastrointestinal symptoms, generally underappreciated as potential Lyme manifestations, may include nausea, abdominal pain, vomiting, loss of appetite, gastroparesis (stomach paralysis), and/or constipation.

Q What are some of the late-stage Lyme symptoms?

A Dr. Mao: Physical complications can involve the joints, nervous system, and eyes. Lyme arthritis most commonly involves one or a few large joints, especially the knee. But it can also affect the jaw (temporomandibular joint or TMJ), and, occasionally, small joints of the fingers and toes. Fatigue and aches/pains are common in late and early disease.

Lyme disease can also cause behavioral or mood changes in children. Some children develop neuropsychiatric manifestations such as anxiety, depression, panic attacks, or obsessive-compulsive disorders. All these symptoms can come and go, and this can be confusing to a patient, their family, and teachers. But trust that you know your child best, and if you suspect Lyme, visit your pediatrician.

Q What are the best Lyme disease tests?

A Dr. Mao: A Lyme disease diagnosis ultimately needs to be made based on a multifaceted clinical evaluation with lab work viewed as supportive (or not), but not definitive. My diagnosis is based on a comprehensive medical history, a physical exam, and diagnostic testing for other potential explanations besides Lyme disease.

In testing, I prefer to use Lyme specialty labs that provide more diagnostic information than standard commercial labs. I particularly like Medical Diagnostics Laboratory for Lyme immunoblot testing. Immunoblots detect the presence of antibodies to specific proteins of a microorganism that develop after a person has been exposed to a target infectious organism. Once detected, these antibodies can be seen as dark bands on a blotting membrane or an imaging system.

MDLab's immunoblot reports include detection results for more than the 10 CDC-specified Lyme bands, and a photo of the patient's actual blot with an objective optical density score grading the intensity of each detected band. In some cases, fainter bands that do not meet the lab's positivity threshold still might provide useful clinical information, increasing the suspicion of a past or present Lyme infection.

Q What's your treatment approach for young children?

A Dr. Mao: As an infectious disease specialist, I typically see children who've already been treated by their pediatrician but have continuing symptoms after standard treatment courses. These more complex cases often require individualized management approaches.

If a child has not yet received an initial antibiotic course for Lyme disease, I start with recommended oral antibiotics—doxycycline, amoxicillin, or cefuroxime. While doxycycline has traditionally not been prescribed for children under 8 years of age due to concerns of dental staining, studies have shown the risk of dental staining is much less with doxycycline than older tetracyclines.

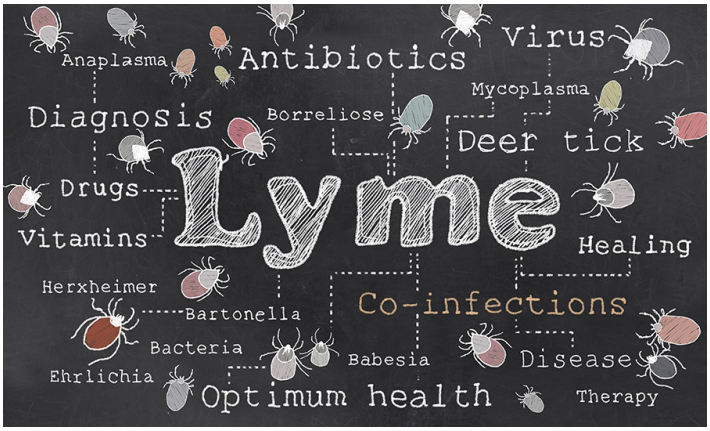
The American Academy of Pediatrics now says doxycycline can safely be used in children under 8 years for short durations, up to 21 days. Notably, doxycycline has long been the treatment of choice, regardless of age, for tick-borne rickettsial diseases such as Anaplasma, Ehrlichia, and Rocky Mountain Spotted Fever.

For acute central nervous system issues such as Lyme meningitis, I prescribe recommended intravenous antibiotics (typically ceftriaxone), which more effectively reaches therapeutic drug levels in the brain and central nervous system. I also use intravenous ceftriaxone for Lyme arthritis when symptoms haven't resolved after two courses of oral antibiotics.

To avoid gut issues, I prescribe probiotics and monitor for adverse effects such as diarrhea.

Q What if symptoms continue after treatment?

A Dr. Mao: In the U.S., ticks are known to carry 18 or more disease-causing microbes, and sometimes concurrent infections can cause lingering symptoms, even after recommended Lyme disease treatment.



A considerable degree of overlap exists among the nonspecific manifestations of Lyme disease and other tick-borne infections, but there are certain symptoms that are more prevalent for specific co-infections. I routinely test for Bartonella, Babesia, Anaplasma/Ehrlichia, and *Borrelia miyamotoi* if the child has not already had this testing done.

Bartonellosis, an under-recognized bacterial infection that can be transmitted by fleas, lice, or cat scratches/bites, can cause a multitude of symptoms, some of them overlapping with those of Lyme disease.

These might include fever; swollen lymph nodes; an enlarged liver or spleen; skin "tracks" that may resemble striae or stretch marks; "evanescent" rashes that come and go; and neuropsychiatric symptoms, especially anxiety, panic attacks, anger/aggression/rage episodes, and obsessive-compulsive disorders.

Other potential symptoms include tremors; jerky movements; sudden muscle weakness (e.g., "legs giving way"); a sensation of internal vibration; seizures; musculoskeletal pain, including in soles of the feet or shins (the latter is a reported feature of trench fever, caused by Bartonella quintana); abdominal pain; and eye issues (including uveitis and retinitis, both also seen with Lyme).

Lab findings occasionally seen with Bartonella, all typically mild, include decreases in white blood cell count; increased eosinophils or monocytes; hemolytic anemia (rarely); increased C-reactive protein levels; and liver enzyme elevations.

Common babesiosis symptoms, caused by a parasite that infects red blood cells, include night or day sweats, fevers (can be high), chills, fatigue, malaise, hemolytic anemia and low platelets.

Less common symptoms include headache, dry cough, shortness of breath (sometimes described as "air hunger"), nausea, abdominal pain, vomiting, and diarrhea.

The combination of low white blood cell and platelet counts make me suspect Anaplasma or Ehrlichia.

I always ask about factors that increase risk for repeat exposure/infection, such as outdoor hobbies (hiking, camping, gardening) and exposures to animals and blood-sucking bugs such as ticks, fleas, and lice.

For the child with persistent symptoms after recommended treatment regimen(s), I also explore the possibility of nutritional/vitamin deficiencies or environmental toxic exposures, such as water-damaged buildings with mold contamination. Mold toxins or mycotoxins, produced by certain mold species, can complicate Lyme disease or co-infections by causing overlapping symptoms or negatively impacting treatment response.

The decision to administer additional antimicrobial therapy in patients with persistent or recurrent symptoms following standard treatment for Lyme disease is a controversial issue.

According to treatment guidelines of most major medical societies, there is no good evidence that these persistent "post-treatment" symptoms are driven by an active infection that might benefit from additional antimicrobial therapy. The topic is too complex to cover here, but I'll say simply that I do not agree with this blanket statement. The question of how best to treat this subgroup of patients is an area that requires more research and funding.

Q I'm pregnant. Can I pass Lyme disease to my unborn child?

A Dr. Mao: Borrelia infections can be transmitted from a pregnant mother to her infant. How frequently this occurs and the range of potential health risks for the infant/child have not been well-established. Studies to-date indicate significantly fewer adverse outcomes in treated compared to untreated pregnant women. This is another area that has been under-studied and requires more research attention and funding.

Q I'm sending my kids to summer camp. Any advice on keeping them safe?

A Dr. Mao: I recommend pre-spraying clothing with permethrin to keep ticks away. This typically remains effective for six to eight washings. Have them pack insect repellents and don't forget to teach them how to do tick checks.

Q What resource can I give my child's pediatrician to learn more about tick-borne illness?

A Dr. Mao: Invisible International has created the first-ever continuing medical education platform that focuses on tick-borne illness. It is accredited by the American Academy of Family Physicians. Courses on this platform are available at no cost to physicians and other providers. Learn more and share this with your child's pediatrician. Invisible's Medical Education Initiative is supported by the Montecalvo Foundation.

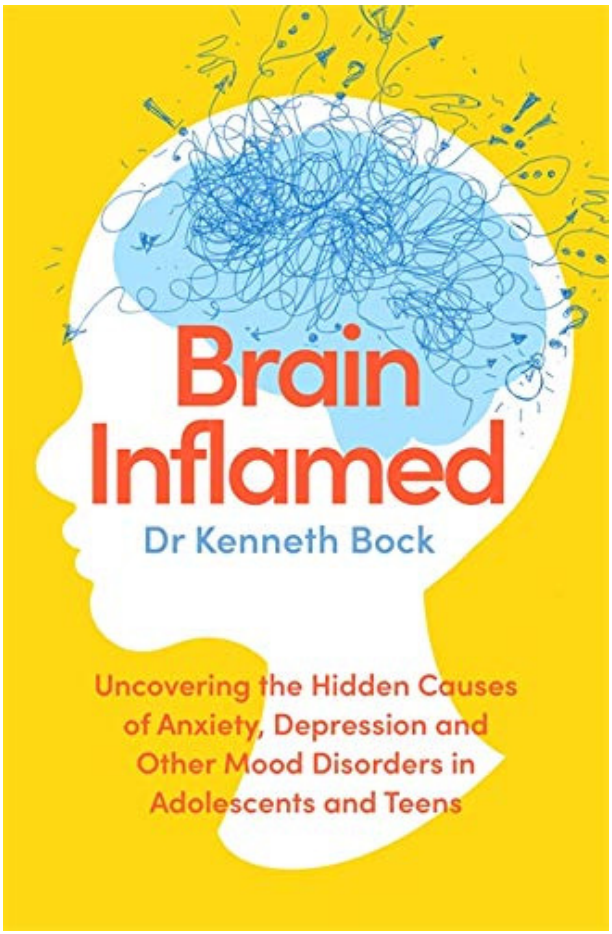
Rooting out hidden causes of anxiety, depression, mood disorders in teens

Conditions that present as psychological disorders often have physical causes

By Dr. Kenneth Bock

The following is an excerpt from Dr. Kenneth Bock's book *Brain Inflamed: Uncovering the Hidden Causes of Anxiety, Depression, and Other Mood Disorders in Adolescents and Teens.*

This passage concerns the case of Stacy, an adolescent who experienced years of psychiatric symptoms which started after she was bitten by a tick at age 4. By the time she first saw Dr. Bock at age 13, she'd already been prescribed these drugs: Ritalin, Focalin, Strattera, Lexapro, Venlafaxine, Lamictal, prednisone, Zyprexa, Zoloft, Ativan, sertraline and Seraquel. She had also had several doses of IVIG, a treatment for autoimmune conditions.



Signs of Brain Inflammation

Stacey's elementary school years were punctuated by hypervigilance, school phobia, paranoia, fear of contamination, and uncontrollable rages. Together with neurological symptoms, like the foot drag and the tics, and the OCD, all the symptoms and behaviors screamed brain inflammation to me.

Here are some of the other clues I observed:

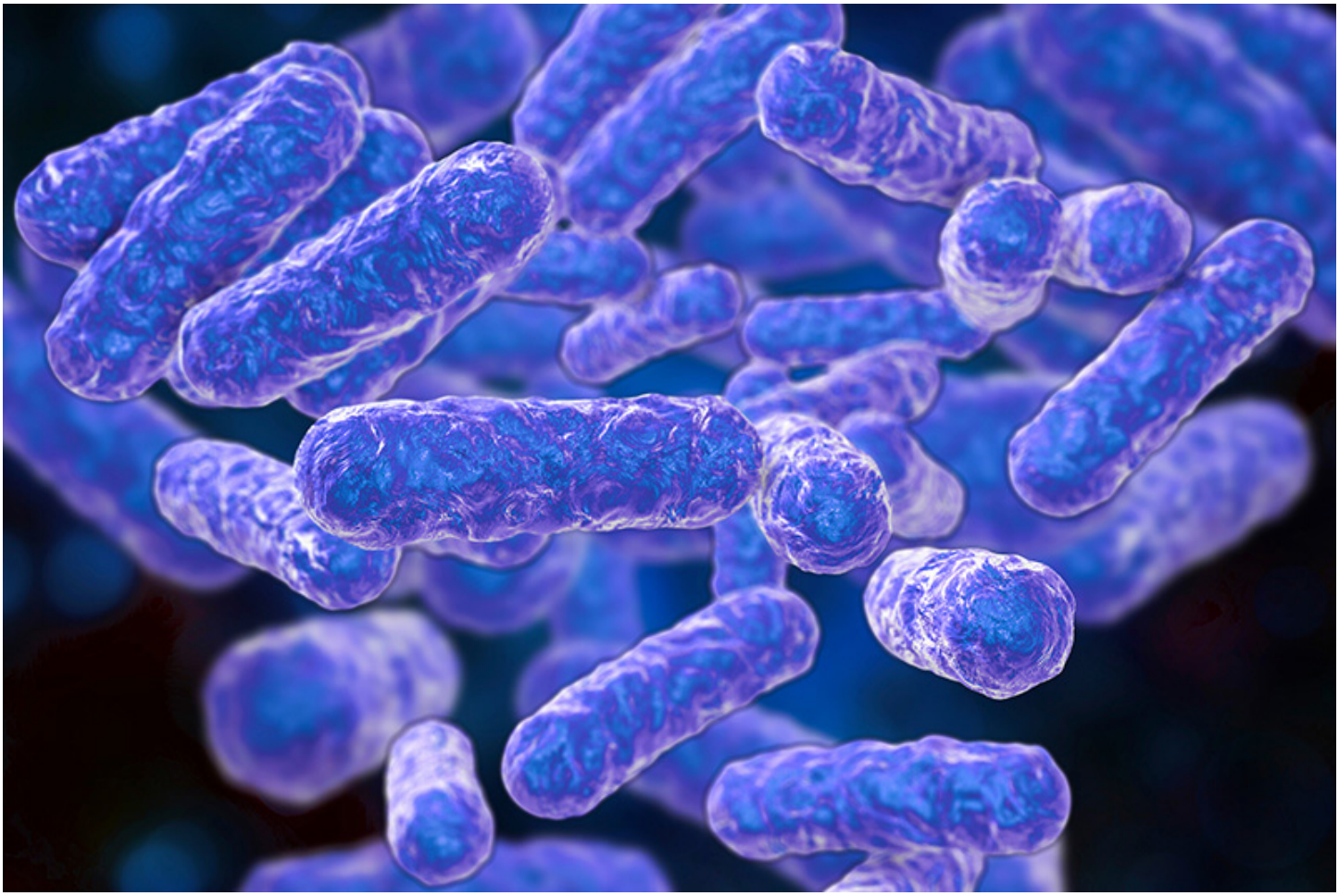
1. **CHRONIC INFECTIONS:** In addition to multiple strep infections, Stacey had battled chronic sinusitis since early childhood. So many infections suggested a compromised immune system.
2. **FOOD ALLERGIES:** At some point, a doctor suggested that Stacey had a sensitivity to dairy and possibly egg whites, and sure enough her symptoms improved when she eliminated these foods, as well as gluten, from her diet (though she strayed from this diet once she felt better). Food sensitivities would point to the possibility of a leaky gut, which can cause widespread inflammation. If her symptoms improved once her gut health improved, that would suggest the gut could be a contributing factor in her neurological and psychological symptoms. For as we've read, a leaky gut can contribute to a leaky blood-brain barrier, which would put a patient at a higher than average risk for brain inflammation. Increased permeability of the blood-brain barrier would make it easier for inflammatory elements, such as those triggered by Lyme disease, to get into the brain.
3. **STALLED PROGRESS:** The temporary nature of Stacey's improvement after IVIG told me that something was blocking the treatment's efficacy. Could it be that she wasn't getting a high enough dose? Typically, low doses of IVIG are used to treat immune deficiency conditions, whereas neurological autoimmunity and brain inflammation require higher doses. Stacey's first two IVIG treatments, the ones that had worked best, were administered at a high dosage, but perhaps to mitigate her severe headaches, her doctor had lowered the dose for the subsequent ones.
4. **DILATED EYES:** Stacey's pupils were massive the first time I saw her. Living with chronic anxiety means living in a perpetual state of fight or flight. The sympathetic nervous system is on high alert, and to me, that suggests brain inflammation, as dilated pupils are frequently seen during flares of ITABI. [Also known as PANS/PANDAS.]
5. **HOMICIDAL THOUGHTS:** Though Lyme patients typically report crushing exhaustion, there have been instances of people with Lyme committing violence against others or reporting homicidal or suicidal thoughts.

Co-infections

While ticks are the primary vector for Lyme disease, they frequently carry many other diseases as well, all of which can be transmitted at the same time. In fact, slightly over 50 percent of Lyme disease patients are also diagnosed with at least one co-infection such as Babesia, mycoplasma, or Bartonella.

Lyme disease can be bad; Bartonella can be worse. The same bacteria that causes cat-scratch fever, in which the lymph vessels become inflamed, Bartonella is treated relatively effectively with intracellular antibiotics when caught early. Unfortunately, because it can burrow into red blood cells, it doesn't always show up in bloodwork. When patients come in with symptoms like numbness or tingling feet, a doctor might test for Lyme, but if the Lyme titer is negative, they'll assume that whatever is ailing the person can't be tick-borne.

However, if they haven't checked the western blot, and they haven't tested for any of the common co-infections that travel with Lyme disease (which is especially important in patients who come from endemic areas, work with animals, or spend a lot of time outside), it's premature to rule out tick-borne diseases.



And early detection is important; as with Lyme, the longer Bartonella is left in the bloodstream, the harder it is to eliminate.

The most distinguishing symptoms of Bartonella are soreness on the bottom of the feet, especially the heel; ice pick–like pain in and around the eyes; headaches; and violaceous striae, reddish-purplish tracks that look like stretch marks. But it can also cause intense joint pain, GERD, difficulty swallowing, and crawling, burning sensations in the skin. Another symptom of Bartonella is intense, violent anger, sometimes accompanied by homicidal thoughts.

The other co-infections that frequently travel with Lyme have overlapping symptoms. Babesia, however, is a protozoan parasite that invades the brain and nervous system and causes fever, chills, sweats, chest pain, and most notably, air hunger. Mycoplasma, a type of bacteria, can cause severe fatigue, dry cough, and generalized pain. The more co-infections you have, the more complicated it becomes to treat the Lyme disease.

Explosive reaction

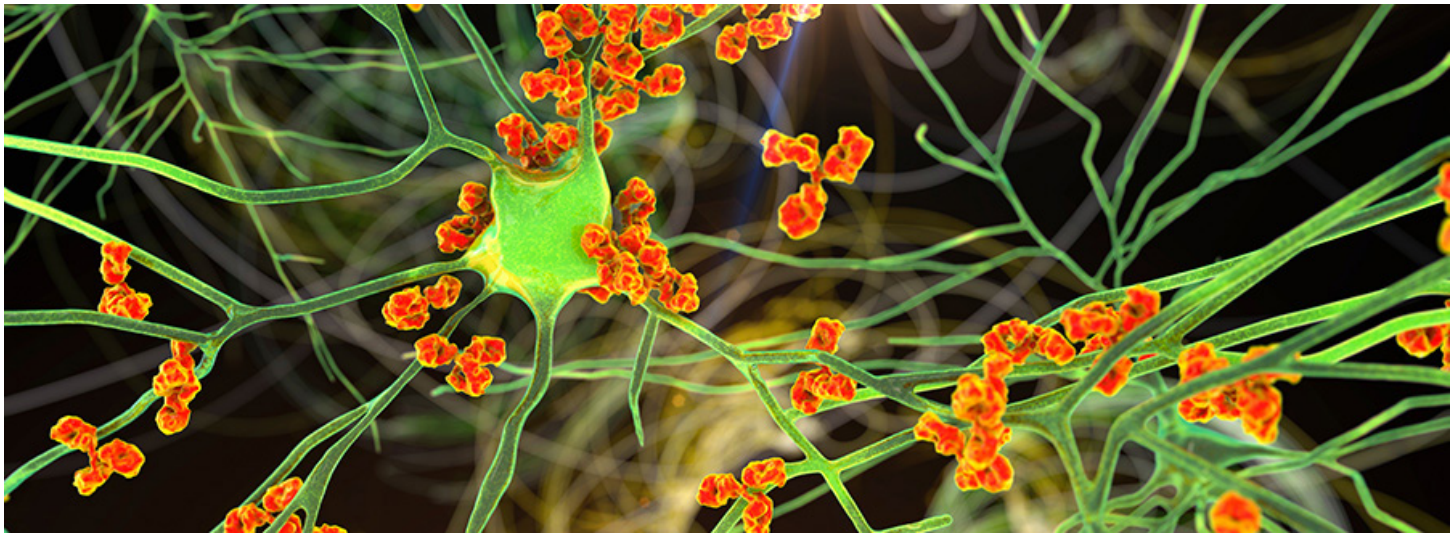
Stacey's explosive reaction to the ADHD and psych meds could have been caused by a new Bartonella infection if she'd been bitten by another tick. More likely, however, the cause was brain inflammation, which is often what I find in children who don't respond at all or have adverse reactions to psychiatric meds. ADHD medicines increase dopamine levels. For a kid with brain inflammation, that's like throwing a lighted match on a vat of gasoline.

Some psychotropic meds are actually anti-inflammatory, which may be one of the mechanisms for their effectiveness in certain patients. Considered along with all of her history, Stacey's reaction to these medications seemed extremely relevant to me.

If she did have brain inflammation, I had to consider that she could also have an autoimmune problem. Some doctors will say that the symptoms of post-Lyme are residual, that like PANDAS and strep, Lyme disease can provoke a secondary autoimmune problem that persists even when the bacterial infection is gone. That's the big controversy when discussing persistent Lyme disease: is it a chronic infection, is it an infection with autoimmunity, or is it just a case of autoimmunity?

Over several decades, researchers have found emerging links between autoimmune disorders and neuropsychiatric disorders, prompting more investigation into whether a subset of what we currently diagnose as primary psychiatric disorders are in fact autoimmune disorders with psychiatric symptoms.

If I ran a Cunningham panel—a special test that measures the concentration of antibodies present in the blood—and the results revealed elevated antineuronal antibodies, it could indicate that Stacey's neuropsychiatric symptoms were being caused by an infection-triggered autoimmune reaction, which would also explain why IVIG had helped calm her neuropsych symptoms so dramatically.



I think it's a combination. You can kill the infection and still be left with fragments of dead bacteria that can stimulate the immune system and cause an autoimmune reaction, and at the same time bacteria can instigate molecular mimicry that triggers autoimmunity in genetically susceptible individuals.

In fact, about half of patients with persistent Lyme symptoms, in particular neuropsychiatric symptoms, test positive for antineuronal antibodies — antibodies produced against nerve cells, especially when they break down and release their neural antigens. The presence of these antibodies points to evidence of autoimmune inflammation in the nervous system.

From the book BRAIN INFLAMED: Uncovering the Hidden Causes of Anxiety, Depression, and Other Mood Disorders in Adolescents and Teens by Kenneth Bock, M.D. Copyright © 2021 by Kenneth Bock M.D. Reprinted courtesy of Harper Wave, an imprint of HarperCollins Publishers.

Natural remedies for the chronic inflammation of Lyme disease

Diet, toxins, stress, and microbes can all contribute to inflammation. Herbs can help tame the fires.

By Dr. Bill Rawls

Everyone knows that inflammation isn't good, especially when it becomes chronic. But to do something about it, you need to understand what's driving the inflammation in the first place.

Though you can't actually see chronic inflammation, you can certainly feel it. It manifests as joint discomfort, stiffness, general achiness, fatigue, low stamina, brain fog, slow mental activity, depressed mood, and all the other symptoms associated with chronic Lyme disease. Simply put, you feel "inflamed."

The root of inflammation is excessive turnover of cells. We all lose cells, and up to a certain point, it's perfectly normal. Cells in the body are constantly wearing out, getting injured, or being invaded by microbes. In fact, we typically lose 50-70 billion cells every day. While much of cellular turnover is accounted for by cells that are shed from the body, such as skin and intestinal cells, tissues inside the body are losing cells, too.

When cells die, they break apart and create debris. If enough debris collects in tissues, it obstructs the flow of water, nutrients, and oxygen that cells need to stay healthy. At the same time, metabolic waste produced by cells is trapped around the cell, which, of course, isn't a good thing. If enough debris collects, cells start to choke in their own waste.

Keeping cells free of debris

You depend on your immune system to keep the spaces between cells free of debris so that they get good flow. Specialized immune cells, called macrophages, constantly patrol your tissues searching for debris — they are the garbage collectors of the immune system. Macrophages engulf debris from dead cells and then break it down with strong acid and potent free radicals.

This process is happening in the body all the time–you couldn't survive without it. As long as the collection of debris doesn't exceed the capacity of the

immune system to clean it up, you never know it's happening. It's deemed inflammation only when accumulation of debris from cell turnover is greater than the immune system can process.

Tissues congested with debris stresses cells. When cells suffer, you feel it as symptoms. The type of symptoms depend on the types and location of cells that are suffering. Symptoms associated with inflammation can be transient and localized when cell injury is finite, such as with an acute injury, or chronic and systemic when cell injury is ongoing, such as with chronic Lyme disease or really any chronic illness.

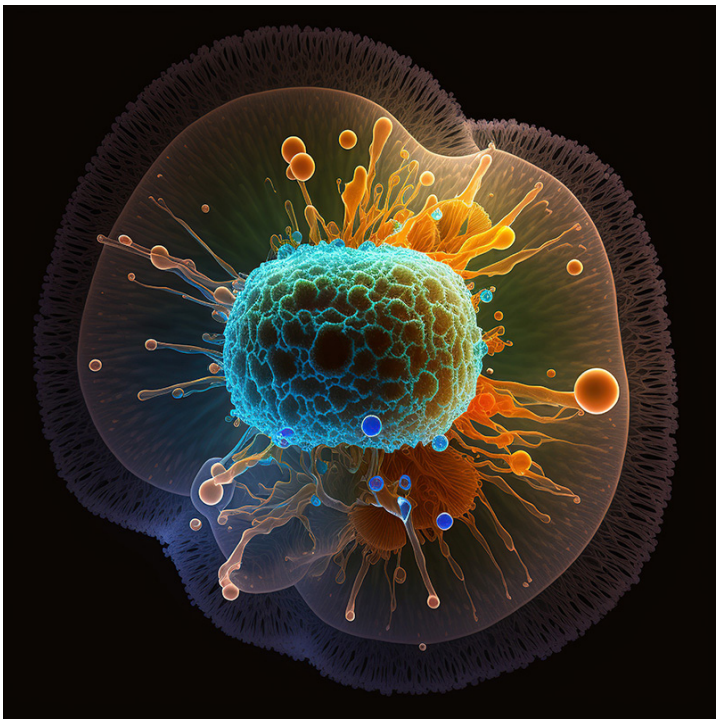
Let's take a look at inflammation in more detail, particularly chronic inflammation as it impacts people with Lyme disease, along with the best ways to quash it.

Understanding the acute inflammatory response

Suppose you're walking barefoot in the yard one summer day and accidentally step on a sharp piece of glass hidden in the grass. Pain alerts you to the injury and you stop to assess the situation. If the wound isn't deep, you're up to date on your tetanus vaccination, and a rinse in the sink reveals no foreign objects in the wound, you place a bandage over the area, and you're back on your way.

By later in the day, however, the wound is slightly swollen, red, hot, and painful. What you're feeling is your body's inflammatory response. The very second the injury occurs, your immune system goes to work. Macrophages in the area immediately begin cleaning up debris left by injured cells. If the debris is more than they can handle, the macrophages release chemical messengers, called cytokines, to call in reinforcements from other white blood cells (WBCs). Injured cells release substances that activate nerves, alerting the brain to the injury (felt as pain at the site).

Swelling occurs because blood vessels dilate to allow an influx of WBCs and flush the area with fluid. Macrophages and arriving WBCs engulf debris, foreign matter, and microbes that have entered through the open wound, and destroy the material with potent free radicals and hypochlorous acid. It's a noxious process that causes collateral damage to normal cells, but it's part of the healing process.

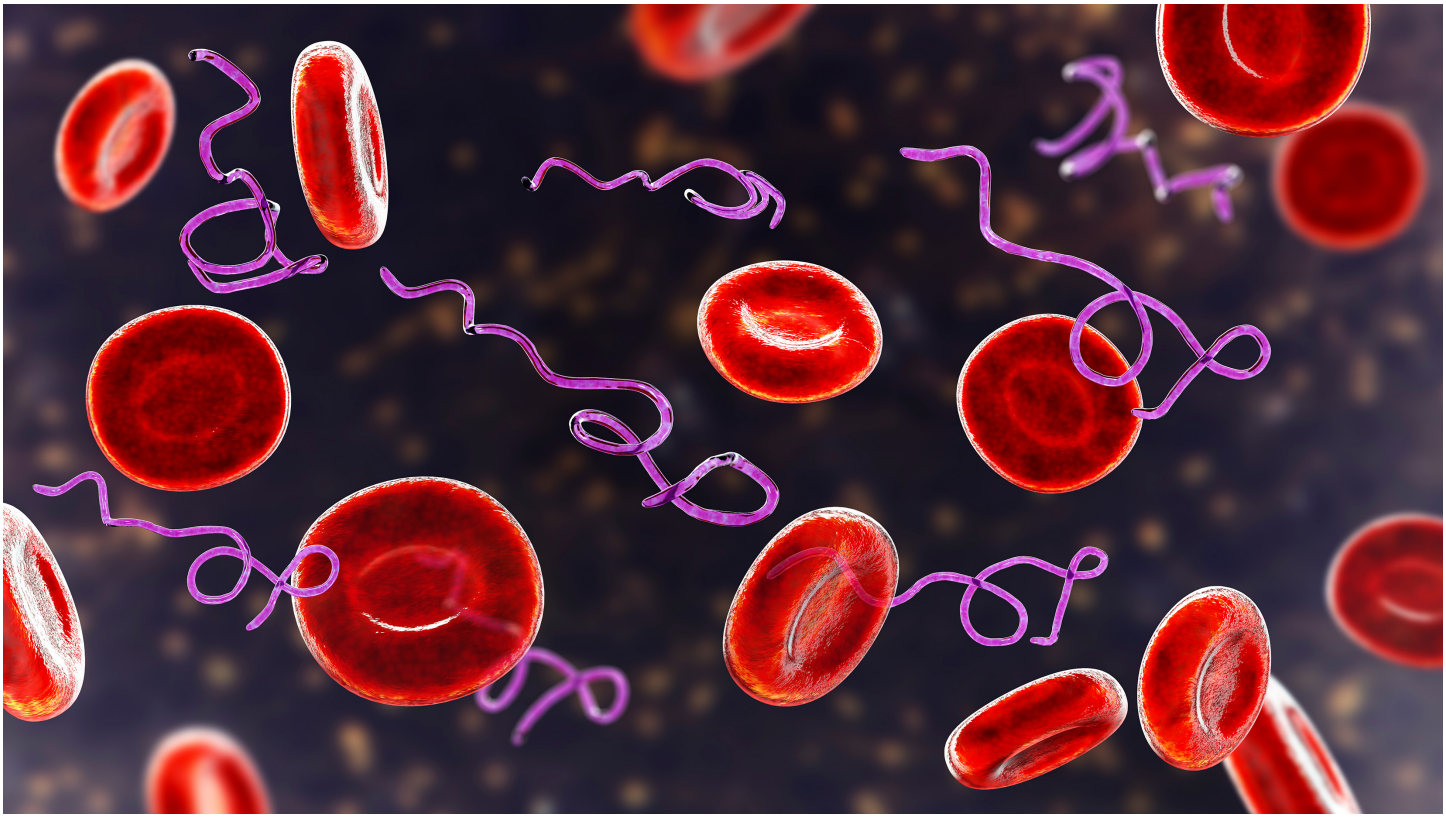


Once the injury is contained and the mess is cleaned up, WBCs migrate out of the area. Surviving cells repair damage from the injury and the inflammatory process itself. Gradually evidence of the injury disappears like nothing had ever happened.

When inflammation becomes chronic

Imagine if the acute inflammatory process was going on in tissues throughout your body and it never resolved. That's exactly what happens with the chronic inflammation associated with chronic Lyme disease. The driving force is bacteria invading cells. It's not an all-out invasion like you would find with an acute infection, such as pneumonia, however. It's an insidious migration of bacteria into tissues throughout the body — in the brain, heart, joints, muscles, kidneys, intestines, everywhere.

When Lyme bacteria enter the bloodstream from a tick bite, WBCs gobble up the bacteria in an attempt to get rid of them. The bacteria, however, have sophisticated ways of staying alive inside the WBCs. Instead of eradicating the bacteria, the WBCs unintentionally become transport vehicles to distribute bacteria to tissues throughout the body. On arrival, the bacteria surface and infect other cells. It's not as much a deluge of invasion as it is a random sprinkling. Tissues throughout the body become peppered with cells that have been infected with bacteria.



The Lyme bacteria, *Borrelia burgdorferi,* are intracellular, which means they infect and live inside cells. The cells provide nutrients to make new bacteria as well as protection from the immune system. Once the bacteria have used up the resources a cell has to offer, they surface and infect other cells.

The immune system, of course, doesn't just stand idly by. It's a delicate situation, however. With infected cells nestled amongst healthy cells, the immune system must call in its special elite tactical WBCs (which are part of the adaptive immune system) to selectively target infected cells without harming normal uninfected cells. It's a tedious process. To minimize collateral damage to normal cells, the immune system often ends up settling for leaving a few infected cells in place.

Healthy vs. weak cells

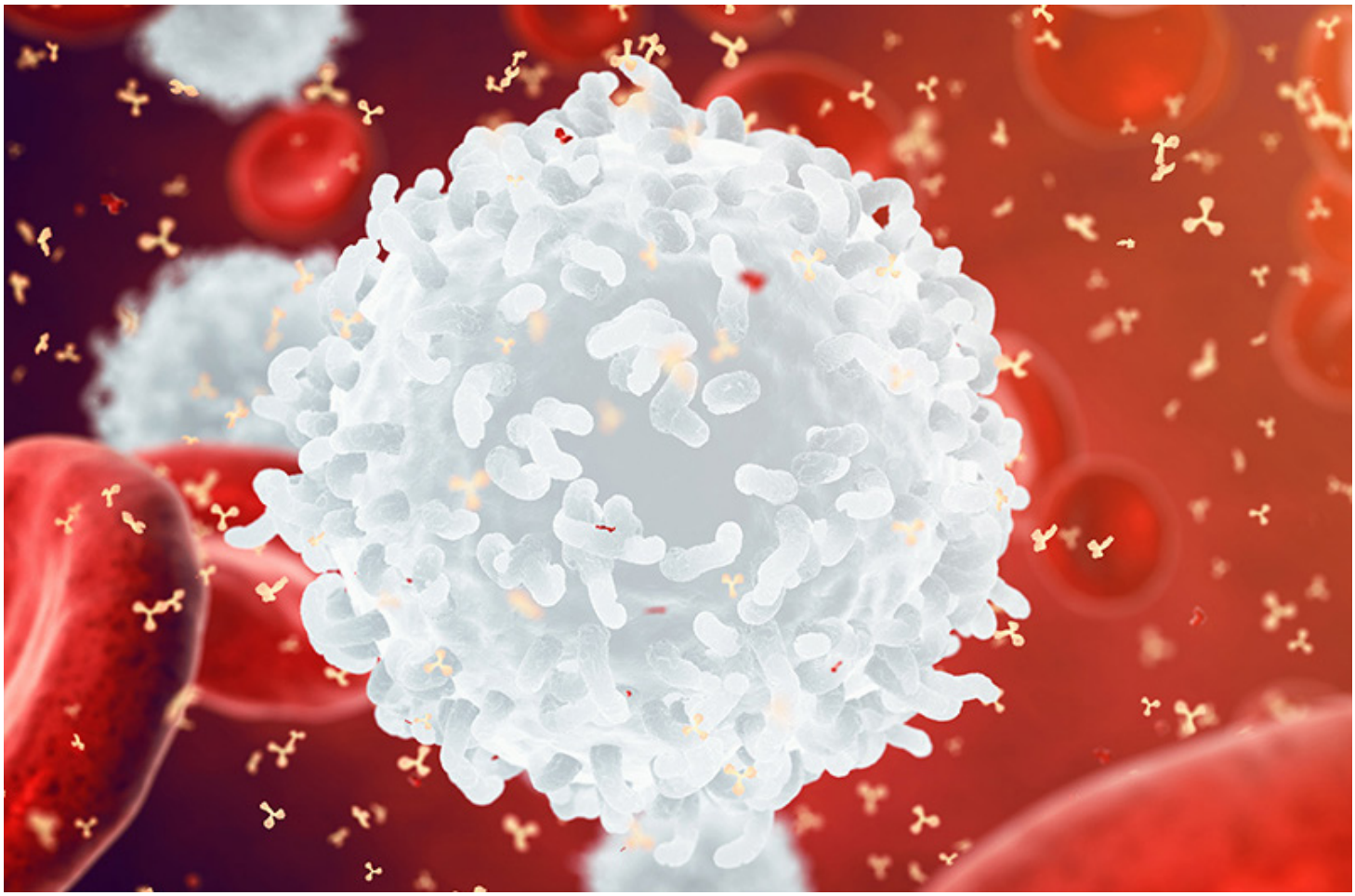
How all this plays out is a function of the health of cells as much as the aggressiveness of the bacteria: Cells that are weak from being chronically stressed are more vulnerable to invasion by bacteria. A healthy person with healthy cells who is bitten by a tick may not have much in the way of acute symptoms and may never develop chronic symptoms. It doesn't mean, however, that the bacteria have been eradicated from the body. They can stay dormant in tissues for a lifetime.

All it takes is a shift in the health of cells for dormant bacteria to surface and invade more cells. The immune system scrambles to keep a lid on things as bacteria erupt and infect other cells. Dead cells break apart and create debris. Macrophages secrete acid and free radicals to break down debris. Reinforcements are called in. More acid. More free radicals. More collateral damage. More debris. Flow of nutrients and oxygen is obstructed, and cells are weakened even further.

The invasion intensifies as more cells are infected. Along with inflicting injury to cells in tissues, bacteria infect and kill WBCs. In addition, bacteria throw the immune system off balance by disrupting the cytokines the immune system uses to coordinate the resistance. As the process spirals out of control, the immune system loses the capacity to keep microbes in check. Before long, tissues throughout the body start to look like a war zone. Cells suffer. Symptoms result. It becomes a never-ending cycle of misery.

Setting the stage for chronic inflammation

Though the immune system plays a key role in protecting cells of the body from microbe invasion, the health of cells is also a major player. When cells become chronically stressed, they are more susceptible to being invaded by intracellular bacteria and other microbes.



There are five primary categories of factors that weaken cells and set the stage for the chronic inflammation associated with Lyme disease.

1. **POOR DIET:** When cells aren't fed properly, they can't function properly. Processed foods sourced from grains, beans, and grain-fed meat are overloaded with raw carbohydrates and refined fats that disrupt cellular functions. On the other hand, they're deficient in the nutrients that cells need to function properly. Poorly nourished cells can't properly defend themselves against microbes.
2. **TOXIC ENVIRONMENT:** In the modern world, chronic exposure to low levels of toxic substances and free radicals in food, water, and air is hard to avoid. The list includes man-made toxins associated with petroleum products, free-radicals in processed food, and natural toxins such as mold. In addition, the acid and free radicals associated with inflammation are highly toxic to cells. Toxic substances disrupt cellular processes, damage internal working parts of the cells, and weaken cell membranes. Weakened cells are more vulnerable to microbe invasion.
3. **CHRONIC STRESS:** Being bombarded by the constant stimulation of the modern world is like being chased by a tiger 24/7 — you're always on high alert. Maintaining a continual fight-or-flight response prevents cells from repairing internal damage. Chronic stress also disrupts sleep, which is prime time for cells to repair internal damage created by working all day. Lack of adequate sleep stresses cells as much as any other factor and always sets the stage for chronic inflammation.
4. **PHYSICAL STRESS:** Acute trauma can tip the balance toward chronic inflammation if enough cells are injured. Head trauma seems to be especially significant. Excessive physical activity can certainly contribute to unwanted and unintended inflammation, but being sedentary can be just as bad. The body is designed to move — it stimulates immune system functions, gets blood flowing to flush accumulated debris, and generates endorphins that normalize the inflammatory response —

and so lack of movement stresses the body.

5. **MICROBES:** Borrelia isn't the only microbe you have to be concerned about if you have Lyme disease. Ticks carry a wide range of microbes, and most people who identify as having chronic Lyme disease are found to have co-infections with multiple tick-borne microbes such as mycoplasma, Bartonella, or Babesia. Beyond that, we all pick up microbes as we go through life. Sometimes all it takes is a new infection, such as flu or COVID-19, to tip the balance toward chronic inflammation. Any type of microbial infection has the potential to contribute to chronic inflammation.

Natural remedies to tame the fires

Eating a healthy diet, living in a clean environment, learning to live around stress, and staying active are all very important for keeping cells in your body healthy. However, the chemical substances in plants defined as herbs can take that protection to the next level. Taking herbs can give you the advantage that you need to overcome chronic inflammation and return to a normal life.

Plants must protect their cells from a wide range of stress factors: damaging free radicals, physical stress from harsh weather, toxic substances, harmful radiation, insects, invasive fungi, parasites, and, last but not least, every variety of microbe. Plants do this with their own natural chemistry. In fact, plants are the most sophisticated chemists on the planet. The chemical substances that plants use to solve problems and protect cells are called phytochemicals.

Mushrooms, which are technically fungi, also have to deal with similar stress factors as plant. They also produce a wide range of protective substances that mirror the protective properties of phytochemicals found in plants.

When we consume plant phytochemicals, the benefits are transferred to us.

The three primary things that phytochemicals do for us:

1. **SUPPRESS MICROBES:** All plants contain phytochemicals with antimicrobial properties, but some plants are more strongly antimicrobial than others. It all depends on the types of microbes the plant is exposed to in its natural environment. Herbs with strong antimicrobial phytochemicals directly suppress a wide range of bacteria, protozoa, viruses, and fungi. This allows the immune system to regain its footing and get the microbes under control.
2. **REDUCE INFLAMMATION:** By protecting our cells from harmful stress factors such as free radicals and toxic substances, cell turnover is reduced, along with the destructive inflammation that comes with it. This lessens the immune system's workload so it can better do its job.
3. **IMPROVE CELLULAR COMMUNICATIONS:** Phytochemicals help normalize disrupted hormones and other chemical messengers in the body. Because all cells must be in constant communication for the body to function as a unit, wellness is only possible when cellular functions are coordinated. This includes toning down inflammatory cytokines that push the immune system into overdrive.

How herbal supplements can help

The best way to gain the level of phytochemical protection you need to help your immune system win the internal battle against invasive microbes is to take herbal supplements — specifically, standardized botanical extracts.

Standardized botanical extracts take herbal supplements to the next level. They're made with wild plants or plants that have been cultivated to enhance their phytochemical content and are grown in an environment that doesn't introduce unwanted chemical toxins. The extraction process also yields the greatest concentration and the widest spectrum of phytochemicals in the plant. And the final product is standardized to a concentration of one or several key phytochemicals in the plant, so you know what you're getting.

Below are a few of my favorite herbs for mitigating the systemic chronic inflammation associated with chronic Lyme disease. Though all of the herbs have value in suppressing microbes and reducing inflammation, three of the herbs mentioned below — Japanese knotweed, cat's claw, and Chinese skullcap — were found in a 2020 study from Johns Hopkins University to have greater activity against Borrelia burgdorferi than the antibiotics, doxycycline and azithromycin.

JAPANESE KNOTWEED *(POLYGONUM CUSPIDATUM)*

Japanese knotweed with resveratrol has been used for centuries in traditional Asian medicine. It's a potent antioxidant with antimicrobial and anti-inflammatory properties. Japanese knotweed may eradicate various phases of Bartonella bacteria, according to a study in the journal bioRxiv.

Suggested dosage: 200-800 mg Japanese knotweed (standardized to 50% trans-resveratrol), two to three times daily.

Side effects: They're rare, with low potential for toxicity. Caution is advised if you're also taking anticoagulants, because resveratrol has blood-thinning properties. Avoid it during pregnancy.

CHINESE SKULLCAP *(SCUTELLARIA BAICALENSIS)*

When combined with other herbs, Chinese skullcap has potent synergist properties. Additionally, it has strong antimicrobial and immunomodulating properties that are beneficial for suppressing mycoplasma and protecting tissues and organs infected with the microbe.

Suggested dosage: 400-1,000 mg, two to three times daily. Root extract standardized to >30% baicalin is preferred. Note: American skullcap does not offer the same antimicrobial properties and should not be substituted.

Side effects: Gastrointestinal upset can occur, but side effects tend to be rare, even at high doses.

CAT'S CLAW *(UNCARIA TOMENTOSA)*

Cat's claw has been used for thousands of years by indigenous people of the Amazon for treating a variety of inflammatory conditions. Not surprisingly, the name comes from the shape of the thorns on the woody vine from which the medicine is extracted.

The medicine is derived from the inner bark of the vine. Common traditional uses include age-related cognitive issues, rheumatism, asthma, stomach problems, and tumors. It was also one of the pre-antibiotic treatments for syphilis.

Cat's claw offers immune-modulating properties, and it has been found to increase WBCs, including B and T lymphocytes, natural killer (NK) cells, and granulocytes. Cat's claw is known to enhance a specific type of natural killer cell, called CD 57, which is commonly deficient in people with Lyme disease.

Suggested dosage: 375 mg, one to two times daily. Inner bark extract standardized to 3% alkaloids is preferred.

Side effects: Occasionally, cat's claw can cause stomach upset, but it is generally very well tolerated. Cat's claw requires activation by stomach acid to be effective and should be taken with food. Acid-blocking drugs can prevent the activation of cat's claw. Taking apple cider vinegar with the herb may enhance activation.

Benefits of Cat's Claw:

- Anti-inflammatory and antimicrobial properties
- Beneficial healing properties for the intestinal tract
- Enhances DNA repair and prevents cells from mutating
- Potent antioxidant properties
- Dilates blood vessels and normalizes blood pressure
- May reduce amyloid deposition associated with cognitive decline

ANDROGRAPHIS

Native to India, andrographis has antibacterial, antiviral, and antiparasitic properties to defend against a spectrum of microbes. The herb has immune-enhancing, cardioprotective, and liver-protective qualities. Like cat's claw, andrographis is a staple among natural Lyme protocols.

Suggested dosage: 200-800 mg (extract standardized to 10-30% andrographolides), two to three times daily.

Side effects: Approximately 1% of people who take andrographis develop an allergic reaction with whole-body hives and itching skin. This is a higher percentage than most other herbs. The reaction will resolve gradually over several weeks once the herb has been discontinued.

REISHI *(GANODERMA LUCIDUM)*

Reishi is a mushroom known for exceptional immune-modulating and antiviral properties. Immune modulation means that it strongly reduces destructive inflammatory processes, but at the same time, enhances normal immune function and increases the ability of the immune system to deal with threatening microbes.

Suggested dosage: 175 mg, one to two times daily. Fruitbody standardized to 7% beta glucan is preferred.

Side effects: Reishi is extremely well tolerated, with rare side effects and no known toxicity.

Benefits of Reishi:

- Immune-modulating
- Anti-inflammatory
- Antiviral
- Adaptogenic (restores calm in the face of stress)
- Restores normal sleep
- Anti-fatigue
- Supports normal cardiovascular function
- Liver protective

TURMERIC *(CURCUMA LONGA)*

With its natural bright yellow color, turmeric is the spice that defines an Indian curry. It's perhaps in part the reason India has half the cancer rate as the United States and possibly the lowest Alzheimer's rate in the world.

Turmeric offers powerful anti-inflammatory properties and has long been used for arthritis and similar conditions. The herb is also known to inhibit cancer formation in multiple stages, in addition to decreasing the risk of dementia.

Not only does turmeric have antioxidant and anti-inflammatory properties, but it may be useful in reducing stomach ulcers, unlike anti-inflammatory drugs. It's also known to protect liver cells.

Suggested dosage: 250 mg, one to two times daily. Rhizome extract standardized to 45% curcuminoids is preferred.

Side effects: Turmeric has a very long history of use in humans, and side effects are rare.

Benefits of Turmeric:

- Useful for decreasing inflammation-related symptoms of arthritis
- Reduces the risk of dementia
- Protects liver cells
- Heals stomach ulcers

RHODIOLA *(RHODIOLA ROSEA)*

The name of this herb rolls off your tongue just like it is spelled: Row-dee-oh-la. Traditionally, rhodiola was used to improve work tolerance at high altitudes, and research suggests that it may increase oxygen delivery to tissues, especially the heart. It's a favorite adaptogen of Russian athletes and workers for decreasing fatigue, increasing alertness, and improving memory.

Rhodiola rosea is primarily sourced from Siberia (though interestingly, it can also be found in the mountains of North Carolina); other species of rhodiola grow worldwide. In addition to enhancing immune function, it has multiple benefits.

Suggested dosage: 275 mg, one to two times daily. Root extract standardized to 3% rosavins and 1% salidroside is preferred.

Side effects: For some people, rhodiola is mildly stimulating. In general, however, it's a well-tolerated, calming herb.

Benefits of Rhodiola:

- Reduces fatigue and restores energy
- Improves stress tolerance
- Enhances immune function
- Enhances cardiovascular function and is heart protective
- Protective of nerve and brain tissue
- Has antidepressant properties by increasing serotonin in the brain

ASHWAGANDHA *(WITHANIA SOMNIFERA)*

Ashwagandha is one of the best herbs for balancing hormones and reducing the detrimental effects of stress. Native to India and Africa, the herb is derived from the root of a plant distantly related to tomatoes and potatoes.

Ashwagandha is a calming adaptogen that is particularly useful in balancing the HPA axis in the brain (the control center for hormone regulation). By restoring balance in this critical pathway, ashwagandha improves stress resistance, allows for improved sleep, reduces brain fog and fatigue, eases the transition through menopause (especially hot flashes), and has anti-inflammatory, antioxidant, and immune-enhancing properties.

Suggested dosage: 225 mg, twice daily. Root and leaf extract standardized to 10% withanolides is preferred. [Editor's note: "withanolides" is a compound found in this and some other herbs.]

Side effects: Ashwagandha has been used as both food and medicine for thousands of years. Side effects of any type are unusual and mild. Ashwagandha is appropriate for men, women, and adolescents. Occasionally, ashwagandha causes mild stimulation in some individuals. Ashwagandha does contain iron and should be avoided by individuals who retain iron (hemochromatosis).

Benefits of Ashwagandha:

- Balances the HPA axis (central hormone pathways of the body)
- Improves stress tolerance
- Reduces brain fog
- Improves sleep quality
- Balances thyroid function
- Increases energy
- Reduces menopausal symptoms

CANNABIDIOL *(CBD)* OIL

Cannabis sativa was one of the earliest plants cultivated by humankind. The very first use of cannabis was documented in China around 4,000 BC. A very versatile plant, it was used for food, medicine, religious and spiritual rituals, industrial fiber, and, of course, recreation.

Cannabis sativa has several alter egos, but marijuana and hemp are the two best known. Though the two plants look the same, their chemical composition is quite different. Whereas marijuana contains both THC (the compound that gives marijuana its euphoric effects) and CBD (which causes no euphoria), hemp contains almost exclusively CBD — only cannabis with less than 0.3% THC can be legally classified as hemp.

CBD has been linked with reduction of pain, fewer seizures, improved mood and sleep, protection of the nervous system, and a range of other health benefits.

Suggested dosage: 15-30 mg, one to three times daily, as needed. (You can slowly increase the dosage to 50-100 mg, three times daily, if needed, depending on your tolerance.) A hemp aerial parts full-spectrum extract is preferred.

Side effects: Reported side effects of hemp oil with CBD are generally mild and uncommon and can include tiredness, loose stools, and slight changes in appetite and weight (either increased or decreased). Both hemp oil with CBD (hemp flower-bud extracts) and purified CBD (CBD isolate) have been shown in both animal and human clinical trials to be safe and well-tolerated.

Benefits of CBD:

- Anti-inflammatory
- Decreased pain
- Enhanced sense of well-being
- Increased calm
- Improved sleep
- Reduced stress (thanks to CBD's adaptogenic properties)

Inflammation Solutions Beyond Herbs

When inflammation occurs in excess, free radicals and acid break down normal cells and tissues as well. In chronic systemic inflammation, all tissues in the body are adversely affected. To add to the anti-inflammatory benefits of herbal therapy, the following lifestyle factors can help neutralize free radicals and excess acidity, reduce damage to tissues, and ease inflammation.

Eat an Antioxidant-Rich Diet

Antioxidants in foods help neutralize free radicals before they have an opportunity to damage tissues. Vegetables and fruits, such as berries, are loaded with free-radical neutralizing antioxidants.

For the most nutritious anti-inflammatory diet, skip the center aisles of the grocery store, which are often filled to the brim with boxed and prepackaged items that are significantly lower in antioxidants than fresh foods. Instead, head to the perimeter of the store and stock up on whole foods, including vegetables, healthy protein sources (fish, beans, eggs, or organic meats), healthy fats such as olive oil and avocados, and low-sugar fruit

Take Omega-3 Fatty Acids

Omega-3 fatty acids are important molecules that our bodies cannot make and so they must be consumed. (The number 3 refers to the position of a certain bond within the molecular chain.) "Omega 3s," as they are often called, are a particular group of unsaturated fats that are found in abundance in fish, krill, and certain nuts and vegetables.

When you consume Omega 3s regularly, they offer extraordinary health benefits. There is much evidence that they significantly reduce the risk of heart attack. Their anti-inflammatory properties also provide some relief from arthritis (and help to prevent arthritis). Notably, Omega 3s also promote brain health, protecting cognitive function. Some studies suggest that they may even help with mood stabilization. They also help optimize your blood lipids, such as by reducing LDL cholesterol.

Fish oil supplements are a popular way to enhance the benefits of dietary omega 3s, but Antarctic krill oil offers significant advantages over fish oil. The omega 3

fatty acids in krill oil are phospholipids (as opposed to triglycerides found in fish oil) which are easily absorbed by the intestinal tract and utilized by cells. Better absorption means you need less of it to achieve the same health benefits as compared to fish oil. Krill oil also has astaxanthin, a potent antioxidant with more anti-inflammatory properties.

Whether you use fish oil or krill oil supplements, be aware that they are concentrated: At high doses, Omega 3s act as a blood thinner. If you notice bruising, discontinue use. Talk with your healthcare provider about recommended doses.

Alkalize Your Water

Alkalized water helps to oppose the acidity in your body, which is brought on by stress, poor diet, chronic infections, and even Herxheimer reactions. Drinking alkalized water (which has a pH of 8-10) may help reduce inflammation in your body. It is a simple and cheap way to turn down the heat.

Spend Time Outside

Negative ions associated with being outdoors in the fresh air have been shown to neutralize free radicals, bolster the immune system, relieve stress, and calm the nervous system — all of which can help curtail inflammation. Negative ion concentrations are highest in pine forests and around open water, but any natural, vegetated area is rich in negative ions.

In contrast, cities, highways, and industrial regions are loaded with positive ions that can have unfavorable effects on inflammation. So, by just taking a walk near the ocean, through a forest, or in a park, you'll infuse your body with inflammation-calming ions.

Get Moving

Low-impact, restorative exercises will allow you to reap the benefits of an active lifestyle without pushing yourself over the edge. Regularly enjoying activities like yoga, Pilates, a slow walk, or qigong can help reduce inflammation, increase circulation, and stimulate endorphins (your body's natural painkillers).

Ultimately, exercise should be a pleasurable part of your recovery. If you're not enjoying the activity, or if the movement is causing any discomfort, change things up and take breaks as needed.

Final Thoughts

To break the cycle of pain and chronic inflammation, it's crucial to reduce the microbial load on your tissues, strengthen your immune system, and support the health of your cells. For most people, a combination of herbal therapies and lifestyle changes will do just that. Soon, you'll be an inflammation-fighting pro, with less pain and an overall better quality of life.

Dr. Rawls, a physician who overcame Lyme disease through natural herbal therapy, is the author of Unlocking Lyme. You can also learn about his personal journey in overcoming Lyme disease and fibromyalgia in his popular blog post, My Chronic Lyme Journey.

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