New Treatment Options for Chronic Lyme Patients

THE LYME TIMES

The Journal of LymeDisease.org

SUMMER 2023

WHAT DOES IT TAKE TO GET BETTER?

An Overview of Lyme Disease Testing

Features

News

Health & Science

Patient Matters

Advocacy

Sex-based Differences In Lyme Disease

Women with Lyme disease take longer to get diagnosed and face higher risk of severe and prolonged disease

By Dorothy Kupcha Leland

Women with Lyme disease take longer to get diagnosed, have more severe symptoms and experience higher rates of disability when compared to men. They may also be more likely to develop persistent Lyme disease.

> *According to LymeDisease.org CEO Lorraine Johnson, lead author of the study, "We need to find out why more women than men develop persistent Lyme disease. Our study shows that women are diagnosed later—which increases their risk of chronic illness.*

Those are among the findings of a recent study that analyzed information from the MyLymeData patient registry. The results have been published in the International Journal of General Medicine.

The present study, which was conducted by Lyme Disease.org, assessed sex-based differences in Lyme patients who remained ill for six months or more after antibiotic treatment. In addition to responses from 2,170 patients enrolled in MyLymeData, the researchers reviewed other Lyme disease studies to evaluate the distribution of patients by sex, stage of illness, data source, and enrollment criteria.

Analysis of the study data revealed several important insights. Women reported a higher prevalence of tick-borne co-infections, more severe symp-

toms, longer diagnostic delays, increased misdiagnoses, and greater functional impairment compared to men. However, no significant differences were observed in antibiotic treatment response or side effects. The majority of both men and women who were treated with antibiotics reported improvement.

Lyme disease is a tick-borne infection caused by Borrelia burgdorferi, a corkscrew-shaped bacteria known as a spirochete. The Centers for Disease Control and Prevention (CDC) estimates that over 476,000 people are diagnosed with the illness each year in the United States. That makes new cases of Lyme disease more common than breast cancer, HIV/AIDS and tuberculosis combined in this country.

Biological variables?

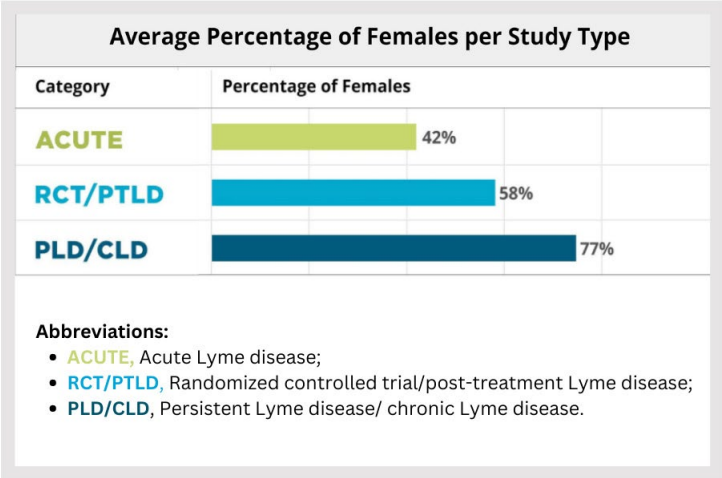
According to LymeDisease.org CEO Lorraine Johnson, lead author of the study, "We need to find out why more women than men develop persistent Lyme disease. Our study shows that women are diagnosed later—which increases their risk of chronic illness. But we must also determine whether biological variables play a role as they do in other infectious diseases."

"Science has ignored gender-based differences in research for far too long," said Dr. Raphael Stricker, the study's senior author. "Our findings underscore the need for greater consideration of gender-specific factors in Lyme disease research in order to improve outcomes for all patients."

For more information about findings from the registry, visit the MyLymeData Viz Blog.

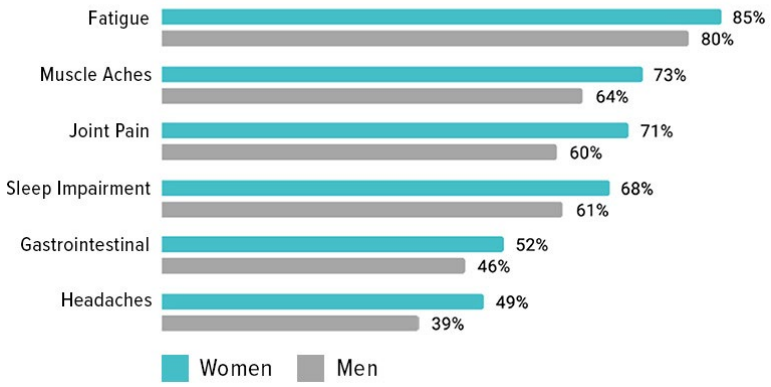
The study coauthors are Lorraine Johnson of LymeDisease.org, San Ramon, CA; Mira Shapiro of Analytic Designers LLC, Bethesda, MD; Sylvia Janicki of Georgia Institute of Technology, Atlanta, GA; Jennifer Mankoff of University of Washington, Seattle, WA; and Raphael Stricker of Union Square Medical Associates, San Francisco, CA.

Distribution of Women in Lyme Disease Research



Source: Johnson L, et. al. Does Biological Sex Matter in Lyme Disease? The Need for Sex-Disaggregated Data in Persistent Illness. Int J Gen Med. 2023;16:2557-2571 https://doi.org/10.2147/IJGM.S406466

Symptom severity in men versus women



DOWNLOAD THE STUDY

ENROLL IN MYLYMEDATA

A New Way of Thinking About Long-haul Disease May Steer Research in Promising Directions

Use of the term "infection-associated chronic illness" has become a crucial first step in changing how scientists approach persistent disease

By Dorothy Kupcha Leland

Infection-associated chronic illness" sounds like a mouthful. But using that name has turned out to be a crucial first step in getting scientists, health officials, doctors, patients, and the public at large to think differently about ailments that can keep people sick for years—with few or no options for getting better.

For decades, people who remained ill after contracting Lyme disease, multiple sclerosis, ME/CFS and other poorly understood chronic conditions typically found themselves shunted aside by the medical establishment—often told they weren't even sick. Federal support for researching better diagnostics and treat

ments for these disorders (or sometimes even acknowledging their existence) was minimal at best.

And then the COVID pandemic hit. Before long, it became clear that some people survived the disease but continued to suffer profoundly debilitating symptoms. Soon, the term "long COVID" entered the public vocabulary. Experts estimate the condition has forced 1.6 million full-time workers out of the US labor market,

with significant ripple effects throughout the economy and society at large.

Shifting the paradigm

Fast-forward to June 29-30, 2023. The National Academies of Sciences, Engineering, and Medicine held a paradigm-shifting event in Washington DC titled "Toward a Common Research Agenda in Infection-Associated Chronic Illnesses: A Workshop to Examine Common, Overlapping Clinical and Biological Factors."

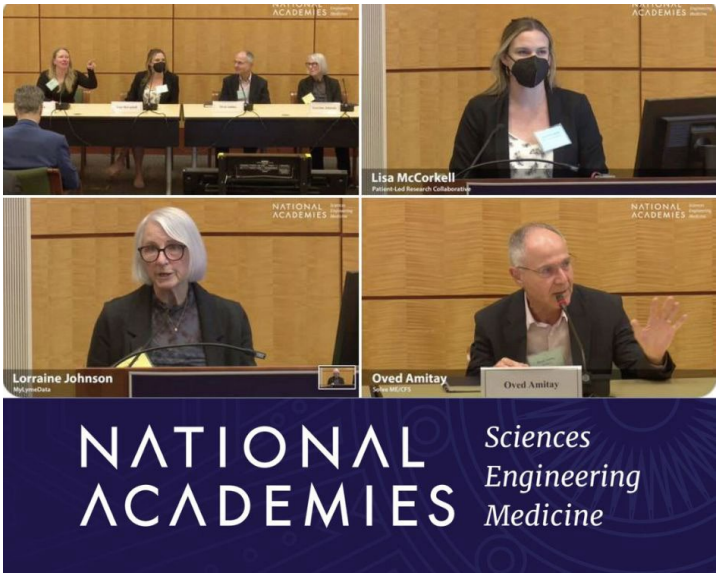
It brought together high-level health officials, prominent researchers, and knowledgeable patient advocates from around the country. Their shared goal was to find a way to work collaboratively for the benefit of all these "long haul" patients.

The presentations were enlightening, inspiring and immensely gratifying. As chronic illness author Meghan O'Rourke highlighted in her opening remarks, "When I was very sick, I really did lie in my bed and wish that someday a group of scientists might come together to take interest in the plight of all of us who live with infection-associated illness."

Lorraine Johnson, CEO of LymeDisease.org and principal investigator of MyLymeData.

And here they all were, in one place, paying rapt attention to the results of patient-led research, presented by Hannah Davis and Lisa McCorkell (long COVID) and Lorraine Johnson (Lyme disease).

In addition, academic researchers delivered presentations on various factors relevant to all infection-



associated diseases, including immune dysfunction, autonomic dysfunction, brain inflammation, and the role of the microbiome.

Discussions explored the strong connection between Epstein-Barr virus and multiple sclerosis, the persistence of pathogens in COVID-19 and Lyme disease, and the occurrence of postural orthostatic tachycardia syndrome (POTS) in both ME/CFS and long COVID. (We know that POTS is experienced by lots of folks with Lyme as well.)

Other speakers looked at possible treatments, including repurposing current drugs as well as developing new ones, along with better ways of helping patients cope with pain and fatigue.

Breaking down the silos

The various presentations demonstrated that there's already a wealth of valuable information out there — but much of it is locked up in research silos. The term "silo" originally meant a tower for storing grain. Now it's used metaphorically to describe organizations that operate independently and keep their discoveries to themselves.

There seemed to be consensus in the group for abolishing the silos and moving forward cooperatively. After a speaker floated the idea of creating a division of the National Institutes of Health devoted specifically to infection-associated chronic illness, an affirmative buzz moved through the audience

Later, Rear Admiral Michael Iademarco, a high-ranking official at the Department of Health and Human Services, commented near the close of the event that "words matter."

I wholeheartedly agree with that assessment. Uniting all these conditions under the term infection-associated chronic illness could be precisely what's needed to make progress.

We are at a turning point. National health officials and research institutions are finally poised to give these debilitating conditions the attention they deserve. It's what the patient community has long been fighting for.

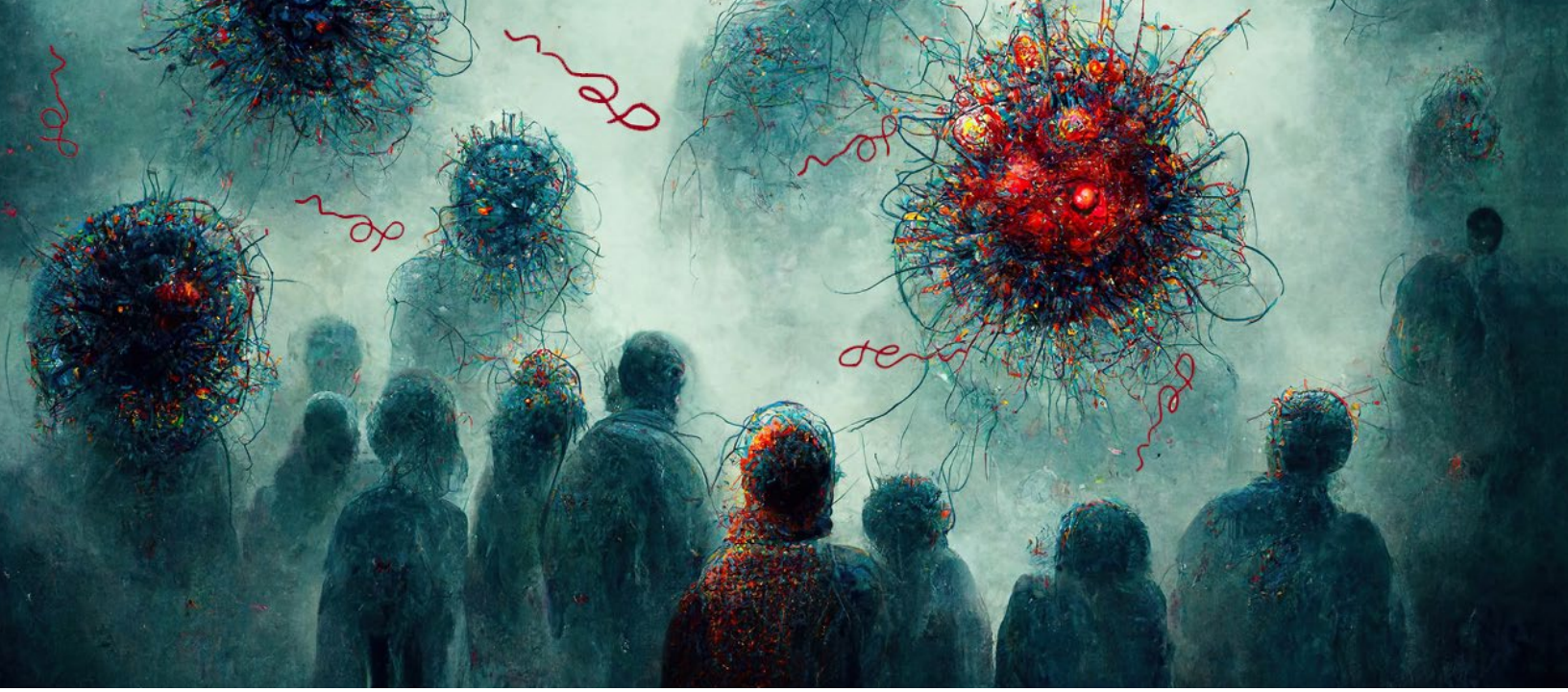
I feel hopeful in a way I haven't felt before.

This event was put together with major support from the Steven and Alexandra Cohen Foundation, which has long supported Lyme disease research. The community owes them a huge debt of gratitude.

Rear Admiral Michael Iademarco serves as senior advisor to the Assistant Secretary for Health.

Watch replay of NASEM conference

The recordings are broken up into 11 segments. Click on the image below to view each segment's video and to view the list of who is speaking during that segment.



Let's Establish an NIH Office for Long-haul Diseases Such as Long COVID and Long Lyme

Journalist proposes consolidating research on seemingly unrelated conditions that emerge from an infectious origin

By Ryan Prior

More than three years out from the beginning of the COVID-19 pandemic, scientific authorities continue to monitor long COVID, the syndrome comprising the disabling aftereffects of SARS-CoV-2 that can last for months and years after one's initial infection.

If public health policymakers are to fully learn the profound lessons about human biology and pandemic resilience that this crisis has presented, it means grappling with the reality of complex, chronic illness as an outcome of any infection, whether it be viral or bacterial.

To do so, it's time to establish and fully fund an Office at the National Institutes of Health (NIH) solely dedicated to researching infection-associated chronic illness.

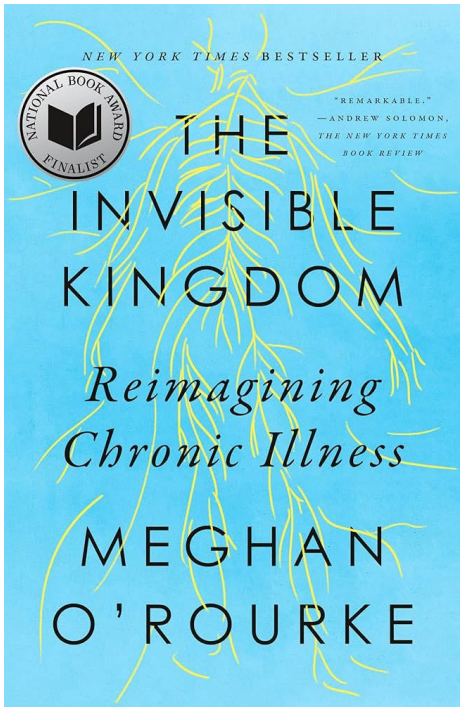
The need for such an office at the NIH is clear. Long COVID is the new face of a similar set of conditions occurring in the wake of infections and well-documented in the scientific literature. Such effects are associated with polio, Lyme, Epstein-Barr, Ebola, SARS, MERS, Ross River virus, Q fever, chikungunya, and other infections. They will undoubtedly occur from the future epidemics and pandemics that are bound to strike in the coming years and decades.

A New Office for a New Paradigm

This summer, the National Academy of Science, Engineering and Medicine held a landmark workshop intended to establish a national research agenda for infection-associated chronic illnesses.

A study from Harvard economist David Cutler estimates the five-year economic burden of long COVID to the U.S. economy at $3.7 trillion. Such an enormous toll must catalyze ever more ambitious and creative policymaking that tackles the core biological issues head on.

Held on June 29 and 30 in Washington, D.C., the event brought together scientists and advocates working on a host of infection-associated chronic diseases, including long COVID, multiple sclerosis, persistent Lyme disease, myalgic encephalomyelitis, and fibromyalgia.



One expert, Meghan O'Rourke, the author of 2022's National Book Award-nominated *The Invisible Kingdom: Reimaging Chronic Illness,* delivered remarks during an early session, invoking ideas from philosopher Thomas Kuhn, who popularized the notion that scientific progress occurs when one outdated paradigm of thinking gives way to a new paradigm that is able to encapsulate new data or observations.

"Paradigm shifts in medicine do not happen by slow and steady incremental change," O'Rourke said. "They happen when a change in perception allows us to see what was already there. And that often happens when people new to fields come in with fresh eyes."

To this point, the research on these diseases has been in crisis. It is underfunded, disjointed, and riven by controversy and distrust sown among scientists, providers, and patients desperate for answers. The arrival of Long COVID as a mass-disabling event has begun to alter national perception of chronic illness. An Office of Infection-Associated Chronic Illness Research would send a signal that public health policymakers intend to resolve the crisis and welcome this paradigm into mainstream medical thinking.

These long-term effects of infections should become a cornerstone of scientific understanding, not unlike cell theory or germ theory in centuries past.

Historic Precedent

In recent decades, the NIH has created new structures as it has evolved to meet needs that are new and pressing, or to correct neglected concerns of marginalized communities. Several historic examples illustrate similar circumstances that led to institutional innovation, establishing new offices which act to coordinate NIH activities on a certain set of priorities across all its institutes and centers.

The agency created its Office of AIDS Research in 1988, as HIV/AIDS became a burgeoning pandemic.

Later, in 1990, the agency built out its Office of Research on Women's Health, to remedy a longstanding problem that women were not properly included in clinical research, and thus many women's health issues were poorly understood.

The most recent example to draw from is the Office of Autoimmune Research, formally created in April 2023. Its origin story can be traced as far back as 1999, when then-Senator Joe Biden first proposed legislation to create such an office. Since then, more than two decades of advocacy culminated in 2022, when the National Academy held a symposium on autoimmune diseases. Its subsequent report recommended that Congress create an Office of Autoimmune Research. About 8 percent of the U.S. population lives with an autoimmune disease—including lupus, rheumatoid arthritis, and irritable bowel disease—and 80 percent of patients are women. Therefore, the office is housed within the Office of Research on Women's Health.

In the wake of June's historic meeting on infection-associated chronic illnesses, policymakers must prioritize a similar recommendation to consolidate research on the seemingly disparate conditions all into a single office based around the idea that they emerge from an infectious origin.

An Emerging Consensus

In an opinion essay about long COVID last summer, the *New York Times*' Zeynep Tufecki called for the creation of a "National Institute for Postviral Conditions," modeled after the National Cancer Institute.

Such a bold vision is admirable. But homing in on the specific category of conditions is critical. While those with long COVID are experiencing a post-viral condition, those with post-treatment Lyme disease syndrome were sickened by *Borrelia burgdorferi,* which is a bacterium rather than a virus. Further, if Lyme and long COVID are driven by pathogens capable of persisting in reservoirs in the body—as a growing

body of research seems to point—the conditions might not be post-infectious at all. They may be the result of hidden pathogens that biomedical science has so far just not yet had the tools to detect.

Finally, many people living with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) either cannot identify the original virus that threw their nervous systems and immune systems into a yearslong tailspin, or do not know whether another type of trauma—such as a divorce or car wreck—may have provided the systemic shock similar to an infection that disrupted their immune systems.

Similarly, a report by the Center for Economic Policy Research (CEPR) and the Congressional Progressive Caucus Center last year called for Congress to "establish and adequately fund a National Institute on Complex Chronic Conditions."

Like Tufecki's proposal, the CEPR proposal is worthy as well. Yet the definition of a "complex chronic" condition may well be too broad, encompassing nearly anything from cancer to diabetes. It might risk drifting into a catch-all category rather than a precision strike against the conditions long COVID has illuminated.

Large funders and advocacy groups are organizing around the idea as well. The long Covid Alliance, in partnership with Solve M.E., recently launched a new push for what it calls the Office of Infection-Associated Chronic Illness Research, or "Office of IACIR." That effort could have galvanizing power, as the CDC Foundation recently awarded a grant for patient advocacy organizations for the various diseases to create partnerships and convene meetings to set a common advocacy agenda.

As these groups organize over the next year, they'll continue to distill the idea into its best form, while building necessary momentum around it in the press and with members of Congress.

Recommendations for New Steps

Within the NIH, an office could be established with an investment of $10 million, and serve as the initial step in a longer-term policy process. If successful, policymakers should consider growing the Office into a Center, and then, if warranted, into a whole new Institute.

The NIH is currently composed of twenty-seven institutes and centers, as prescribed by law. Creating a twenty-eighth institute would require an act of Congress, a tall ask. To start, policymakers should urgently move to create an office, given the need.

An office could also introduce cost savings by coordinating and synergizing research across multiple institutes. Currently, each institute is using its own funding to investigate elements of these illnesses, potentially duplicating other work.

The agency has other mechanisms for stoking the fires of necessary medical innovation. One avenue toward creating a new NIH structure for infection-associated chronic illnesses could be via the NIH's Common Fund, which supports bold, scientific programs that catalyze discovery across biomedical and behavioral science and which are designed to be accomplished in five to ten years. Those proposals must be transformative, catalytic, synergistic with NIH's goals, and cut across multiple institutes and centers.

One of the most successful fruits of this process in recent years was the Undiagnosed Diseases Network, a network of clinical and research sites across the country serving the 25 million Americans living with a rare diseases, which often require specialized care, and for which there may only be a few clinicians in the country with the necessary expertise.

Since its humble beginnings as a laboratory at Staten Island's New York Marine Hospital in 1887, the NIH has continually evolved to meet new challenges. The world's leading agency counts more than 80 Nobel Prizes having been awarded for work it supports. Should a new office lead to breakthroughs on chronic illness, it may be an opportunity for another one.

With the burgeoning crisis around long COVID and related conditions, policymakers again have an opportunity to build on this legacy and seed new discoveries that could revolutionize the understanding of human immunology.

Doing so could help unlock the dreams and potential of the tens of millions of Americans struggling with these conditions every day.

*This article was originally published by **The Century Foundation**, where journalist Ryan Prior is a fellow. Prior is also the author of The Long Haul: Solving the Puzzle of the Pandemic's Long Haulers and How They Are Changing Healthcare Forever.*

Making Sense of Lyme Research – What Does Science Say?

After her husband died of Lyme-related causes, Nicole Bell applied her engineering skills to analyzing the state of Lyme research

By Nicole Danielle Bell

Venturing out in nature can introduce us to a silent adversary: ticks. When I finally realized that my husband's early-onset Alzheimer's was caused by Lyme disease and other co-infections, I tried to use my engineering background to make sense of it all.

I very quickly found myself lost. An excerpt from my memoir about our experience shows how confused I was as a newly minted caregiver.

January 2018 – Lost in the literature

(Excerpt from *What Lurks in the Woods: Struggle and Hope in the Midst of Chronic Illness*)

I poured every spare moment into research. Of course, I started where everyone starts: the Internet. I quickly realized what I already knew. The Internet was a dangerous place to get information. My searches left me more confused than when I started.

Half of the articles insisted that chronic Lyme didn't exist. The Centers for Disease Control and Prevention, the CDC, claimed Lyme could be treated with two to four weeks of antibiotics. After that, anyone still sick didn't have chronic Lyme; they had Post-Treatment Lyme Disease Syndrome or PTLDS. But the causes of PTLDS were unknown. It could be an autoimmune response triggered by the bacteria. It could be a persistent but difficult to detect infection. It could be other issues unrelated to Lyme. As I read their position over and over again, it didn't make sense. One of their explanations for PTLDS was a "persistent but difficult to detect infection." Um, okay. Why couldn't that be Lyme?

The other half of the articles blamed Lyme for nearly every chronic disease on the planet: fibromyalgia, arthritis, chronic fatigue syndrome, multiple sclerosis, myocarditis, Parkinson's, Alzheimer's, scleroderma, depression, schizophrenia. The bacteria was invading our immune system and wreaking havoc. It infected joints, brain tissue, and cardiac tissue. It triggered autoimmune conditions, dementia, and mental illness. The disease was way under-reported and globally prevalent, not only in the American Northeast.

So, what to believe? Frustrated, I turned away from Internet articles and turned toward scientific articles on PubMed. The messages there were equally mixed. I scanned through titles and abstracts. For each article I found supporting chronic Lyme's existence, I found another attempting to debunk it. Clearly, I needed to read the articles to form my opinion, so I dug in. I found observational studies with no controls, failed attempts to reproduce past results, citations to other papers that didn't say what was claimed. The more I read, the more frustrated I became.

I had long been a steward of science. "In God we trust; all others must bring data." The quote from W. Edwards Deming was frequently touted at the FDA and always made me smile. I agreed. Data was pure. Data had no agenda. Data was just data.

But my career taught me this wasn't true. Data collected was only as good as the methods used. Science used mice and cell cultures that may not represent the complexity of a human. Researchers interpreted the data, and often their bias skewed the results. I'd seen engineers interpret the same results in opposite ways. Plus, people made mistakes.

I once struggled for over a month with an experiment, having no idea why the results didn't match the theory. Then, I spent the day with my technician and realized that every time I instructed her to do a step for a minute and a half, she entered one minute and fifty seconds into the machine, completely trashing my analysis. Data wasn't always pure. It could be flawed.

I saw this debate raging in the medical community, and I didn't know whether to feel vindicated for finally finding my answers or crazy for believing in something so clearly outside mainstream medicine. Organizations like the CDC and the Infectious Disease Society of America should know what they are talking about, right?

On the other hand, mainstream thinking always evolves, even in science. If it didn't, we would still think the world was flat or that lobotomies were the best way to treat mental illness. No one believed that the bacteria H. pylori caused stomach ulcers, so Dr. Barry Marshall infected himself to prove it. Nutritional guidelines in the 1980s told us a low-fat diet was best. Now, leading experts tout that a high-fat, ketogenic diet is better for overall health. I needed to navigate a complex infectious disease, and I couldn't get a straight answer on eggs. Good for me? Bad for me? Different doctors, different answers. Argh! I was in the middle of a debate where my husband's life hung in the balance. I had the desire to learn and the skills to understand, but I was more lost than ever.

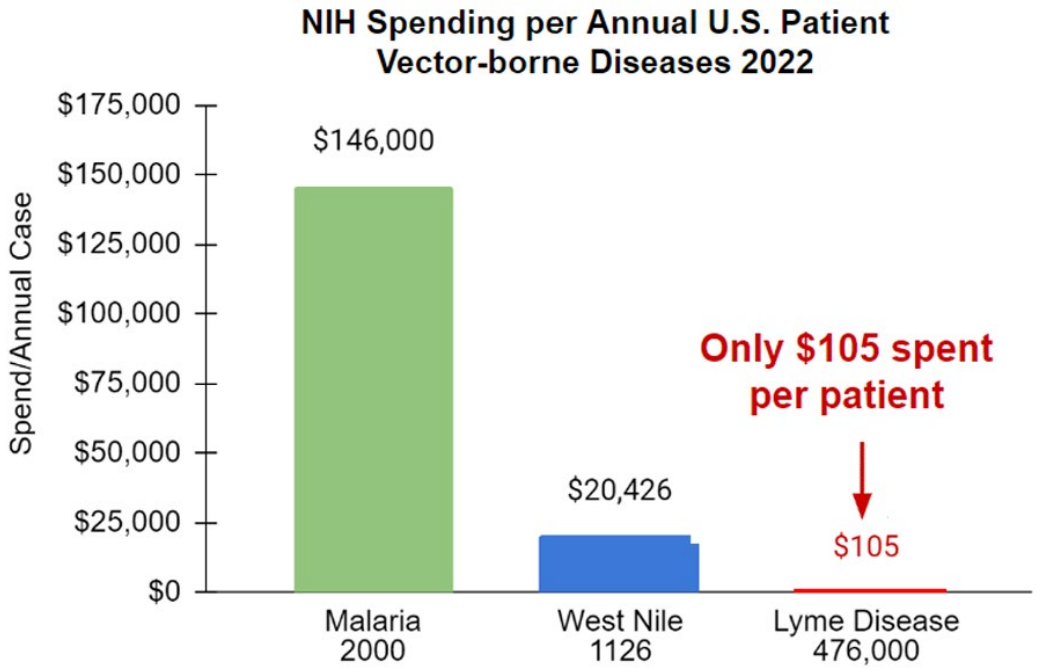
October 2022 – A second chance to make sense of it all

My husband's story didn't end well. He lost his battle with tick-borne illness and passed away in January of 2022, a broken shell of the man he once was. Devastated, I turned my energy into sharing our story and driving change for future patients.

My networking efforts connected me with researchers striving to develop new diagnostics and therapies, philanthropists funding new approaches and studies, and advocates seeking to raise awareness and funds for this critical problem. One of those advocates was Bonnie Crater, a co-founder of the Center for Lyme Action.

Bonnie explained that part of the reason the available Lyme literature and information was so confusing and incomplete was that federal research funding is insufficient. Lyme disease accounts for the vast majority of vector-borne illnesses in the United States; however, it is funded at a fraction of other diseases.

The CDC estimates that 476,000 Americans are diagnosed and treated for Lyme annually; however, funding at the National Institutes for Health (NIH) for Lyme Research was only $50M in 2022. This calculates to $105 per patient, representing 0.1% and 0.5% of the per-case funding for malaria and West Nile virus, respectively.



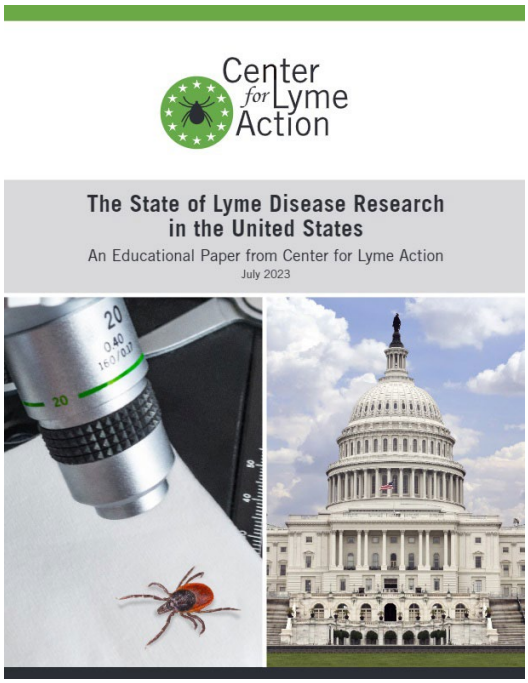
The Center for Lyme Action was established to change this funding scenario. For their 2023 efforts, they wanted a paper summarizing "The State of Lyme Disease Research in the United States." This document would review the evidence and highlight government action and research funding opportunities. But the project needed a writer, and after reading my book, Bonnie was convinced that writer was me.

I was honored by Bonnie's confidence, but I wasn't so sure. It was a daunting project, and flashbacks to my previous attempt to dig into the research haunted me. But the more I thought about it, the more I realized I had to do it.

I had to do it for my husband, Russ, who had needed this summary in 2018 – or sooner. I had to do it for the millions of patients struggling with their chronic symptoms. And I had to do it for the millions of people who will become infected and fail to get a timely and accurate diagnosis.

Fortunately, the evidence has evolved since my time as a caregiver. Panels of experts weighed in as part of the Federal Tick-Borne Disease Working Group (TBDWG). The TBDWG was a six-year process, issuing reports in 2018, 2020, and 2022, reviewing the status of the research, and making recommendations for government action.

Per the recommendations of their 2018 report, the National Institutes of Health (NIH) convened a trans-NIH strategic planning team. In 2019, this team released a comprehensive Strategic Plan to improve tick-borne disease diagnosis, prevention, and treatment. I could leverage all of this work in the paper. Finally, Bonnie agreed to connect me to a network of leading Lyme researchers to guide and review the document.



July 2023 – The summary I wish I'd had and changing tides

So I put on my big girl pants and agreed to do it. I dug into the research, interviewed experts, and assembled what I learned. And this week, after several months of research and writing, the summary I wish I'd had over five years ago went public.

The process of producing it was invaluable, not only because of what I learned but also because it demonstrated to me and hopefully others that the problems Lyme disease patients face ARE solvable.

Research shows that Lyme IS linked to chronic conditions across multiple body systems. New diagnostics and treatments ARE promising, but more funding is needed to get them out of the research lab and into the clinic.

And the tide is turning in mainstream thinking. The Department of Health and Human Services (HHS) has begun using the term "infection-associated chronic illness," and the National Academies of Sciences, Engineering, and Medicine recently held a workshop to discuss these conditions, including persistent Lyme disease.

And the tide is also turning on a disease near and dear to my heart, Alzheimer's. New research reported at the Alzheimer's Association International Conference in 2021 found associations between COVID-19 and persistent cognitive deficits, including the acceleration of Alzheimer's disease pathology and symptoms.

These findings have rekindled scientific interest in the link between neurological infections and the progression of dementia, with the National Institute of Aging offering a virtual workshop on the Infectious Etiology of Alzheimer's Disease in October of 2021.

In addition, last month, a consortium of scientists called for the establishment of a consensus protocol to explore the role of infections, such as Lyme disease, in patients with mild cognitive impairment and Alzheimer's disease – a battle I fought with neurologists only a few years before.

The future – what you can do to drive change

"The State of Lyme Disease Research in the United States" aims to educate Congress on the breadth of the problem and how they can fix it. The NIH Strategic Plan released in 2019 was comprehensive, and that plan and the recommendations of the Tick-Borne Disease Working Group need to be funded and implemented.

So what can you do? You can sign onto the Center for Lyme Action mailing list at CenterForLymeaction.org. Scroll to the bottom of the home page, and you'll get a pop-up form for sign-up. Several times a year, you'll get notifications of activities and actions you can take to grow federal funding for Lyme and tick-borne disease. By signing up, you will also be invited to participate in the annual "Lyme Fly-In," an opportunity to speak directly with your Senator or Member of Congress's office.

But I hope that "The State of Lyme Disease Research in the United States" goes beyond congressional action. If you are a patient or a caregiver, I hope it provides the scientific evidence you need to understand that you aren't crazy, and it's not in your head. I hope you give a copy of the paper to your doctor and it helps your doctor understand the realities of Lyme disease and the status of the research. And I hope it helps you or your loved one get a timely diagnosis and effective treatment.

Nicole Bell is the author of *What Lurks in the Woods: Struggle and Hope in the Midst of Chronic Illness.*

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)

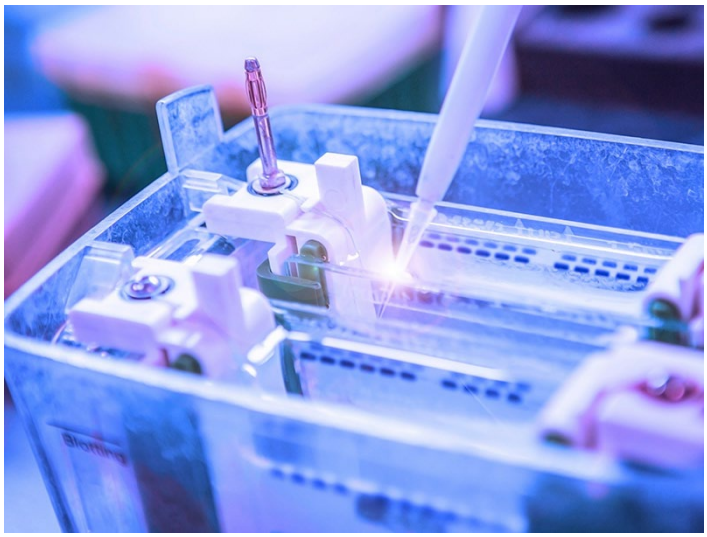
Like the ELISA, the IFA methodology for Lyme disease testing is an indirect test that looks for antibodies formed against the bacteria that causes Lyme disease – Borrelia burgdorferi.

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.

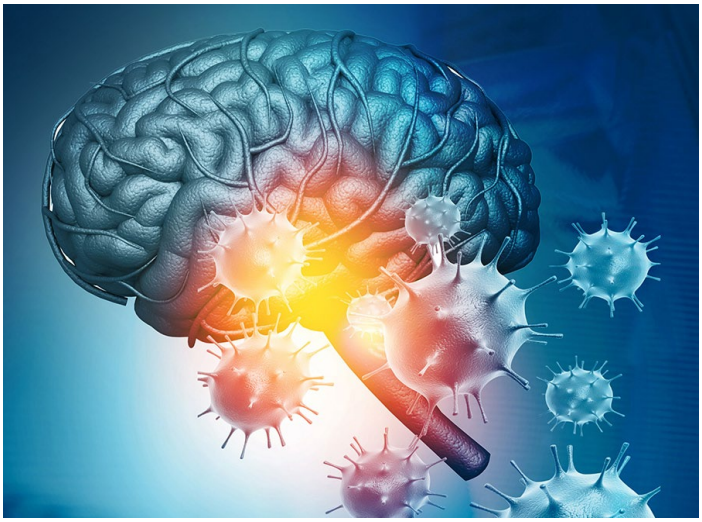
When specific foods trigger brain inflammation in children

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.

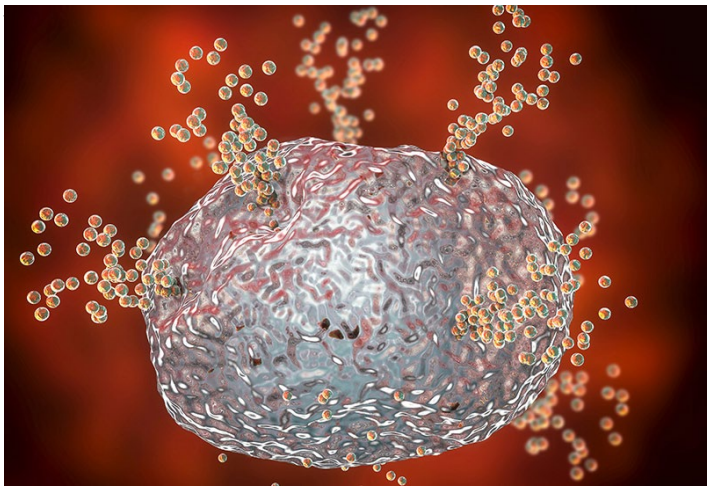
Mast Cell Activation Syndrome

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



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.

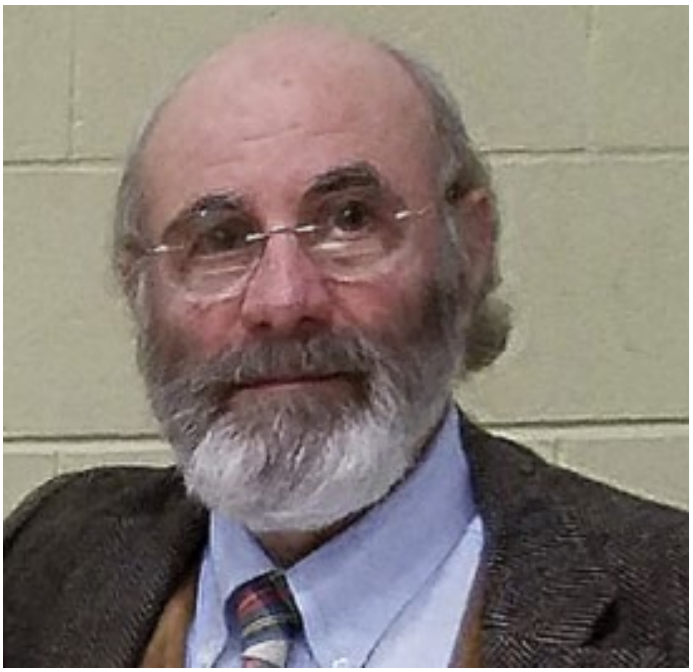
How a pioneering doctor uses disulfiram to treat persistent Lyme disease

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.)

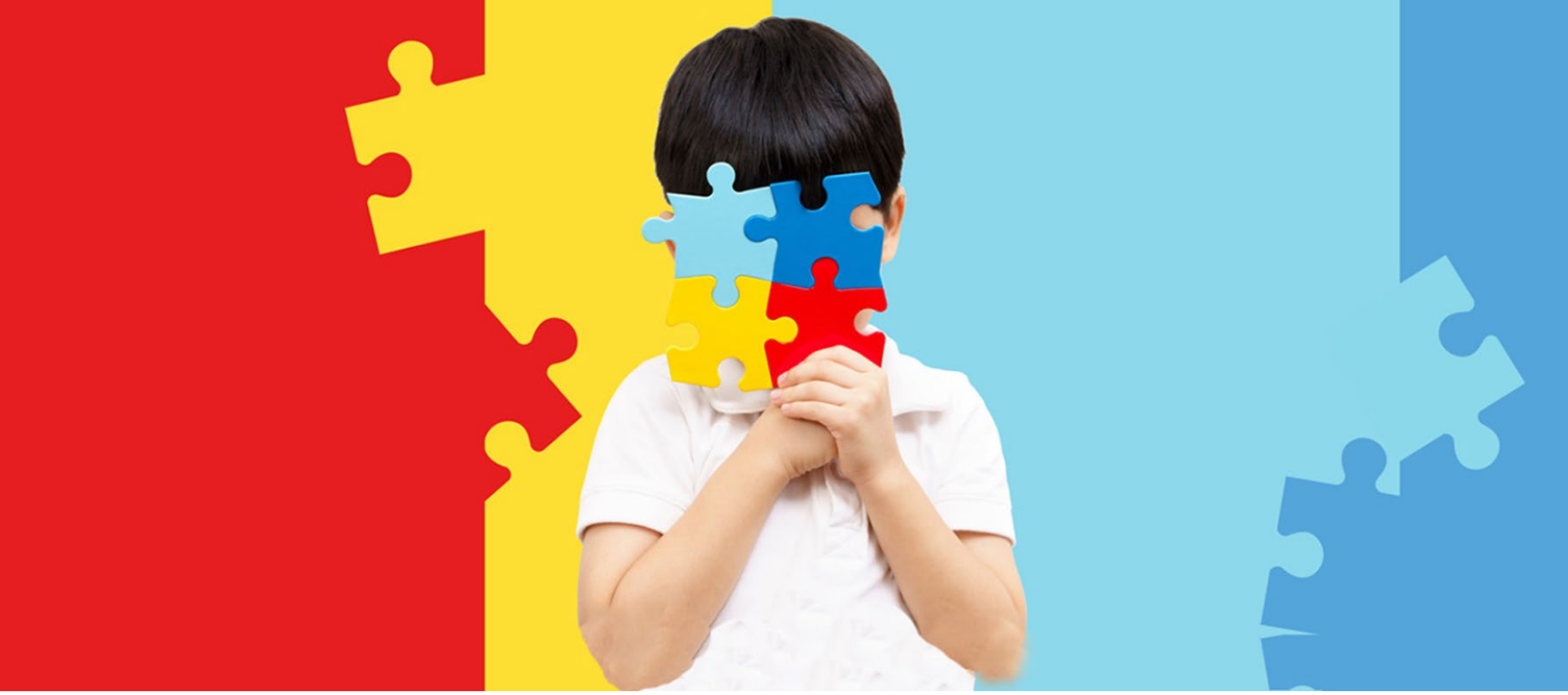
However, the randomized control trial I would like to do next year should be the bridge to allow other researchers and clinicians to take what we have found and improve upon the efficacy, looking at higher dosing of new and novel persister drugs.

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?

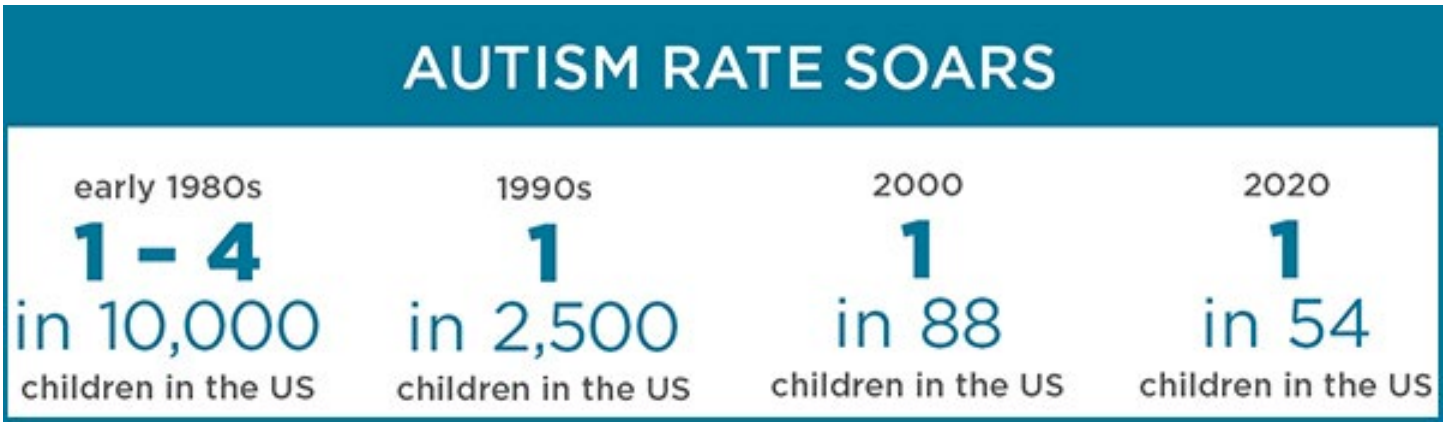
Studies indicate that approximately 25% of those with ASD show evidence of infection with Lyme disease.

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:

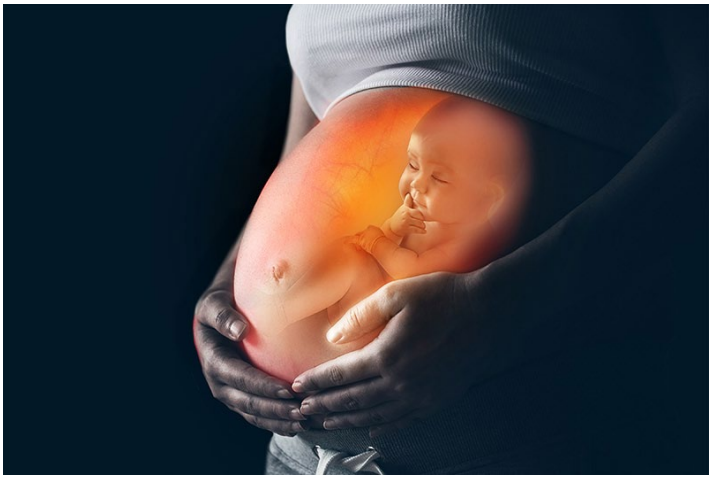
1. Significant temporal lobe dysfunction (the part of the brain involved in emotion, comprehension, memory, language, sensory input and vision) and
2. A predominance of findings in the white matter of the brain (which is important for learning and coordinates communication between different parts of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

FTo 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.

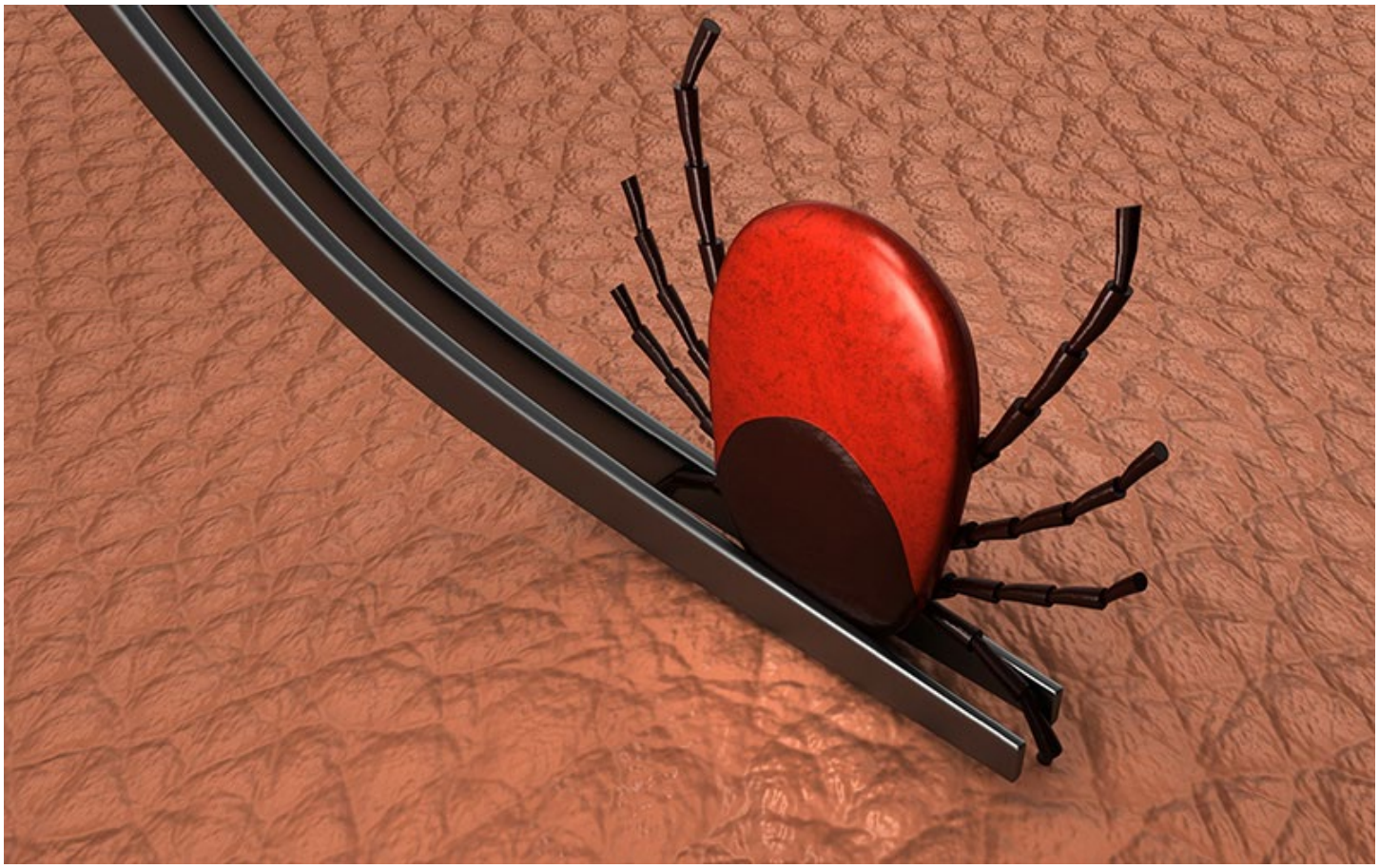
Recognizing and treating Lyme disease in young children

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.

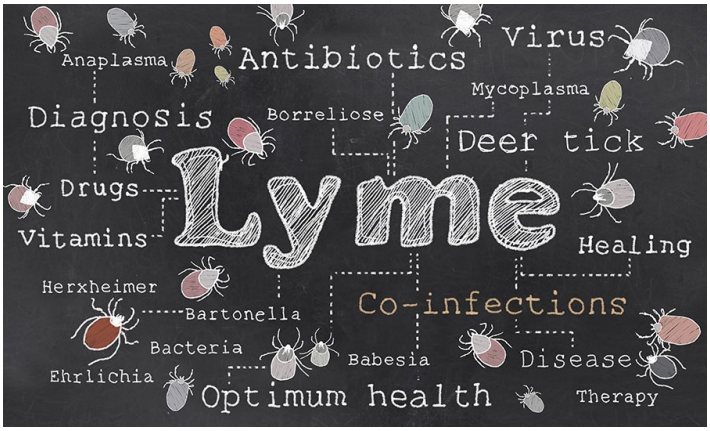
The American Academy of Pediatrics now says doxycycline can safely be used in children under 8 years for short durations, up to 21 days. Notably, doxycycline has long been the treatment of choice, regardless of age, for tick-borne rickettsial diseases such as Anaplasma, Ehrlichia, and Rocky Mountain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

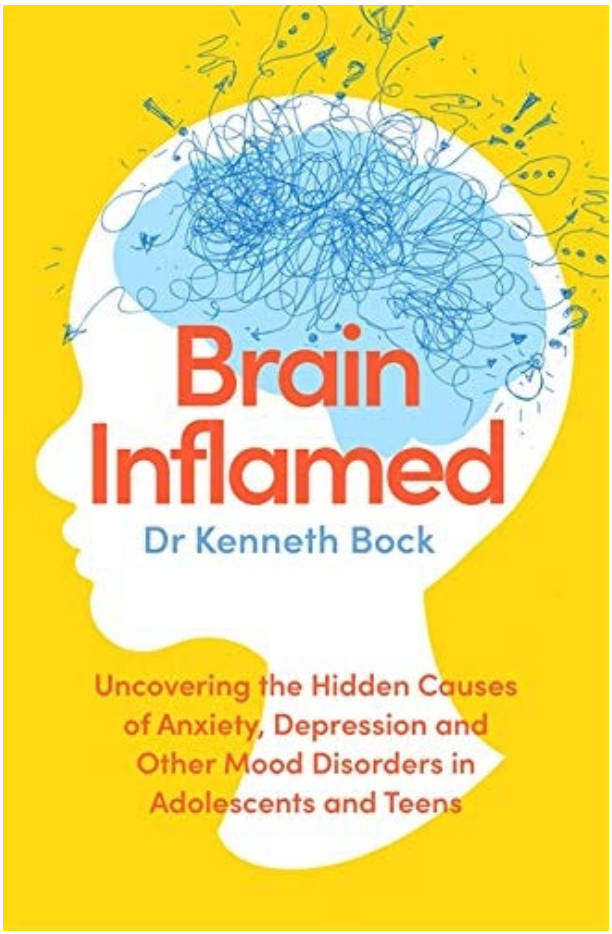
Rooting out hidden causes of anxiety, depression, mood disorders in teens

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:

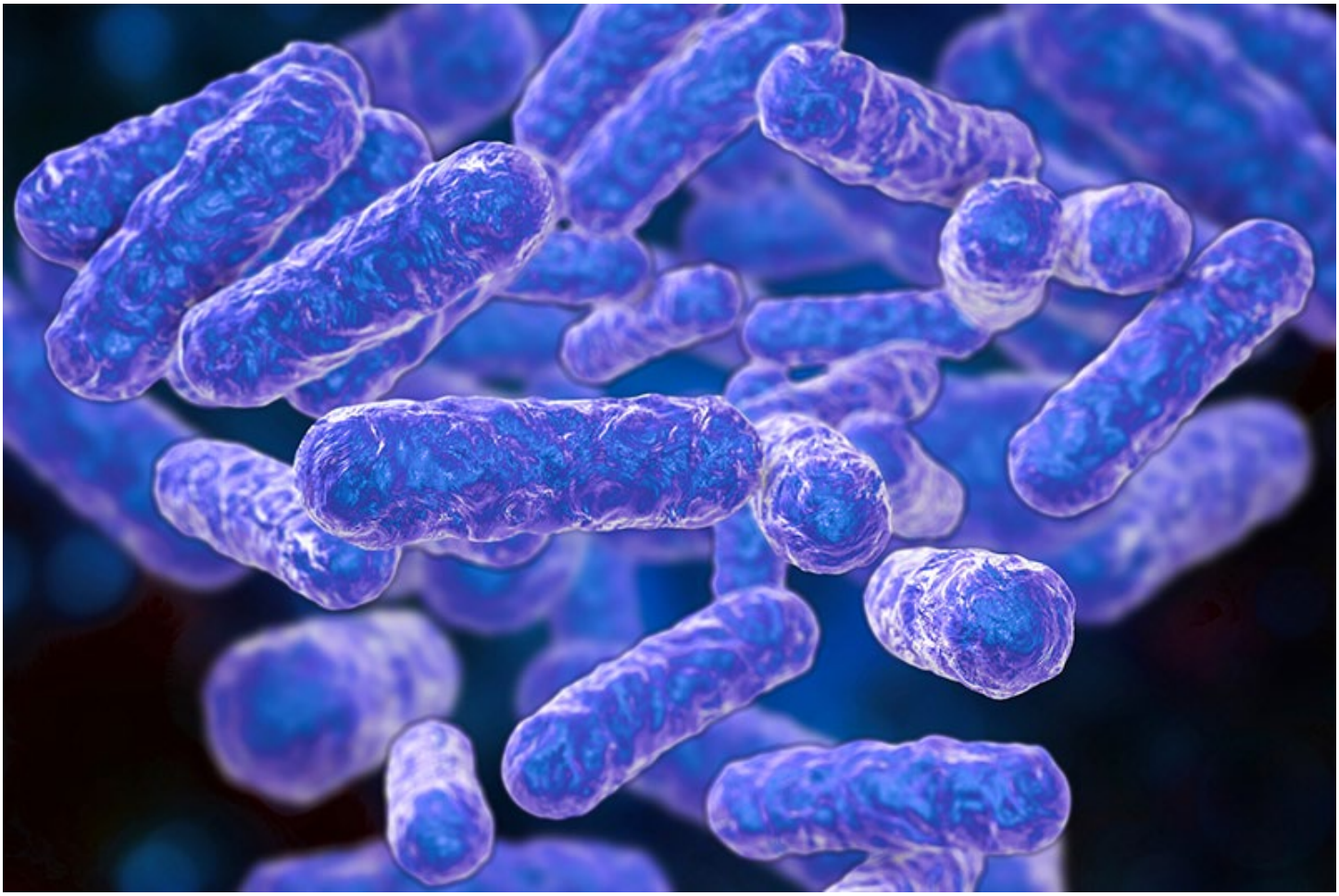
1. **CHRONIC INFECTIONS:** In addition to multiple strep infections, Stacey had battled chronic sinusitis since early childhood. So many infections suggested a compromised immune system.
2. **FOOD ALLERGIES:** At some point, a doctor suggested that Stacey had a sensitivity to dairy and possibly egg whites, 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

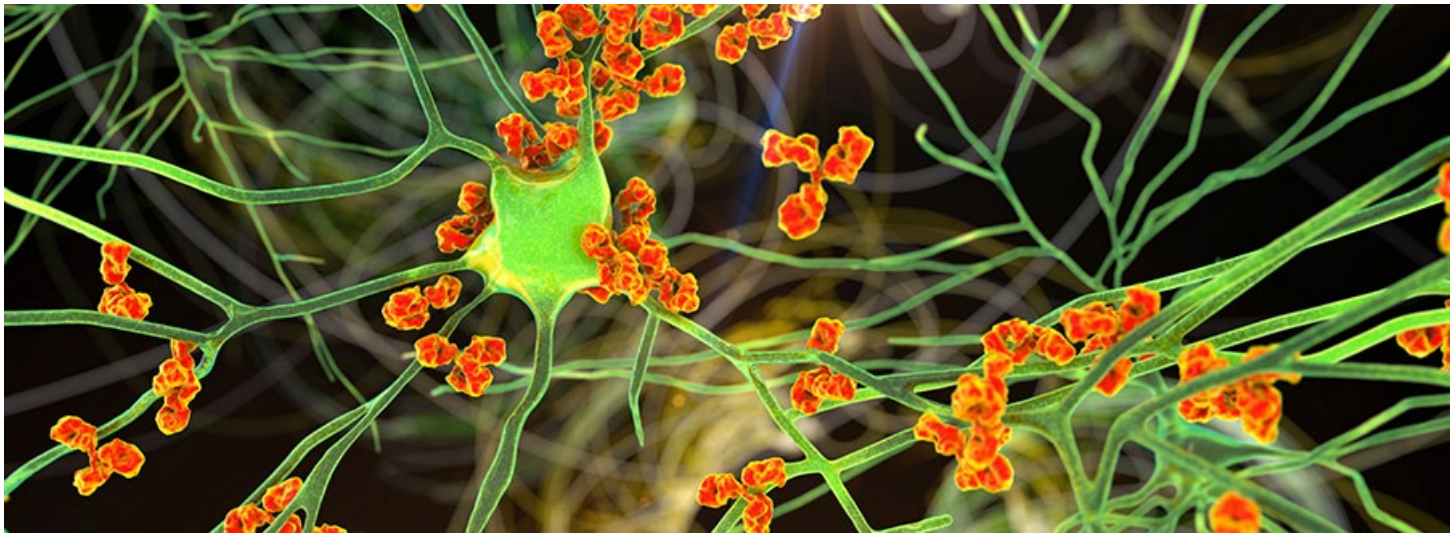
Stacey's explosive reaction to the ADHD and psych meds could have been caused by a new Bartonella infection if she'd been bitten by another tick. More likely, however, the cause was brain inflammation, which is often what I find in children who don't respond at all or have adverse reactions to psychiatric 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.

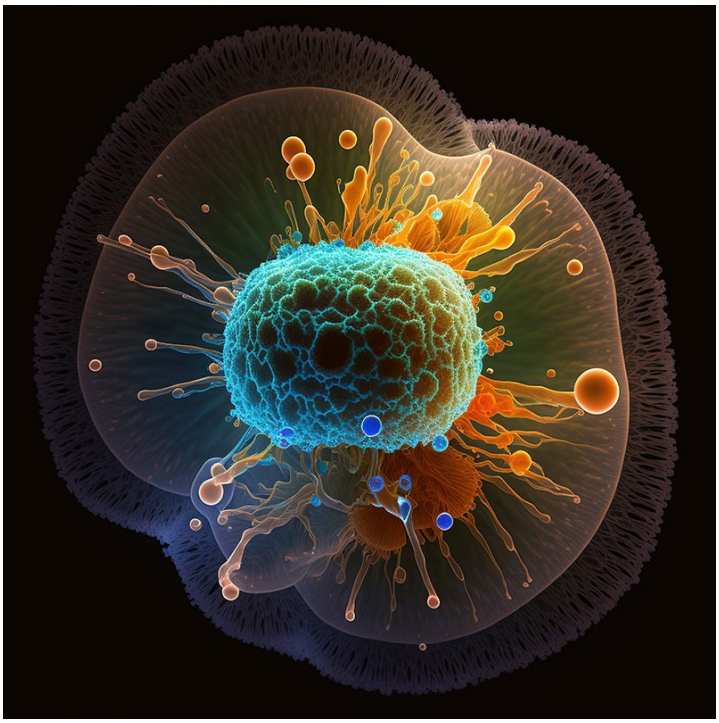
Let's take a look at inflammation in more detail, particularly chronic inflammation as it impacts people with Lyme disease, along with the best ways to quash it.

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.

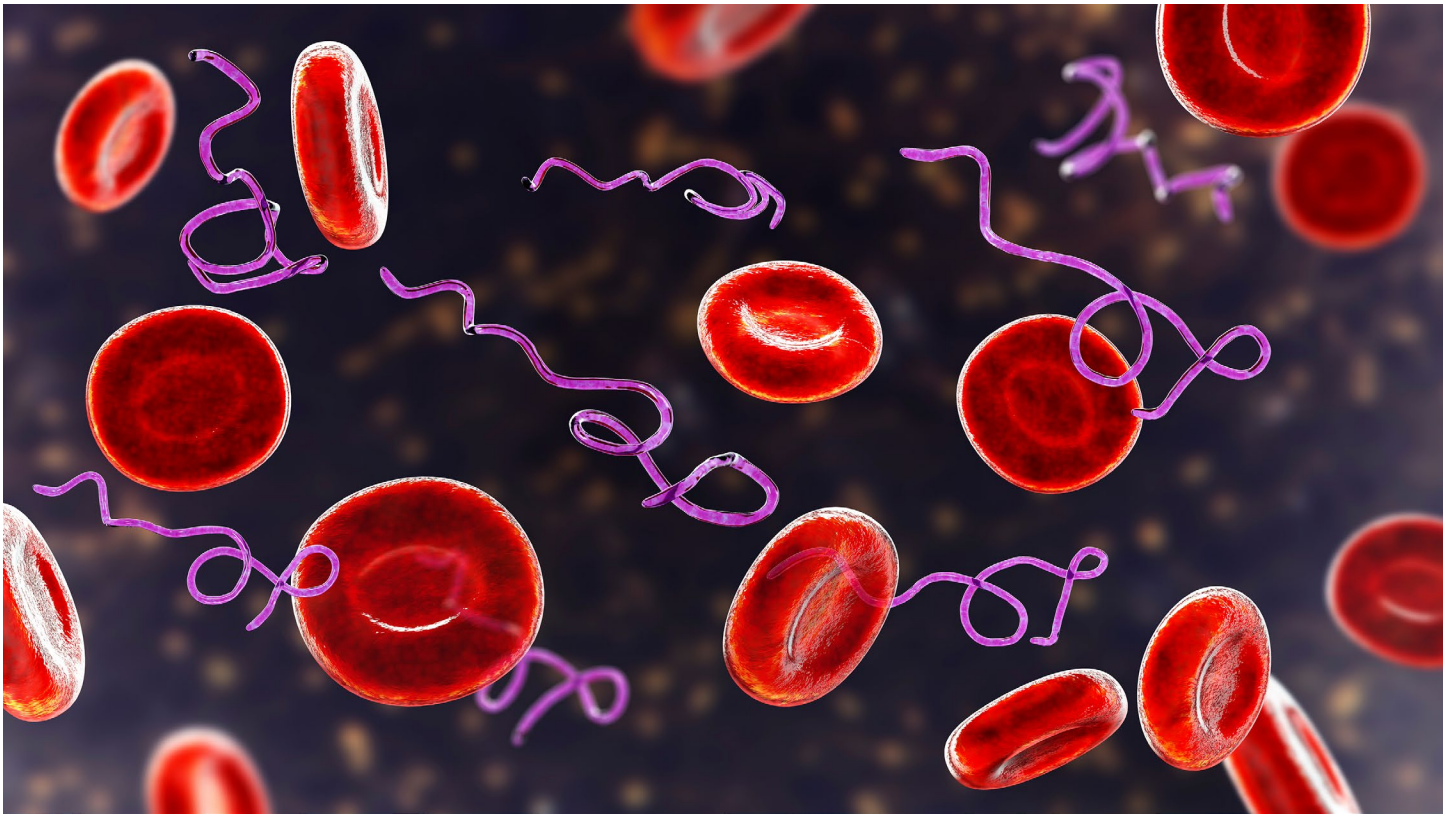


Once the injury is contained and the mess is cleaned up, WBCs migrate out of the area. Surviving cells repair damage from the injury and the inflammatory process itself. Gradually evidence of the injury disappears like nothing had ever happened.

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

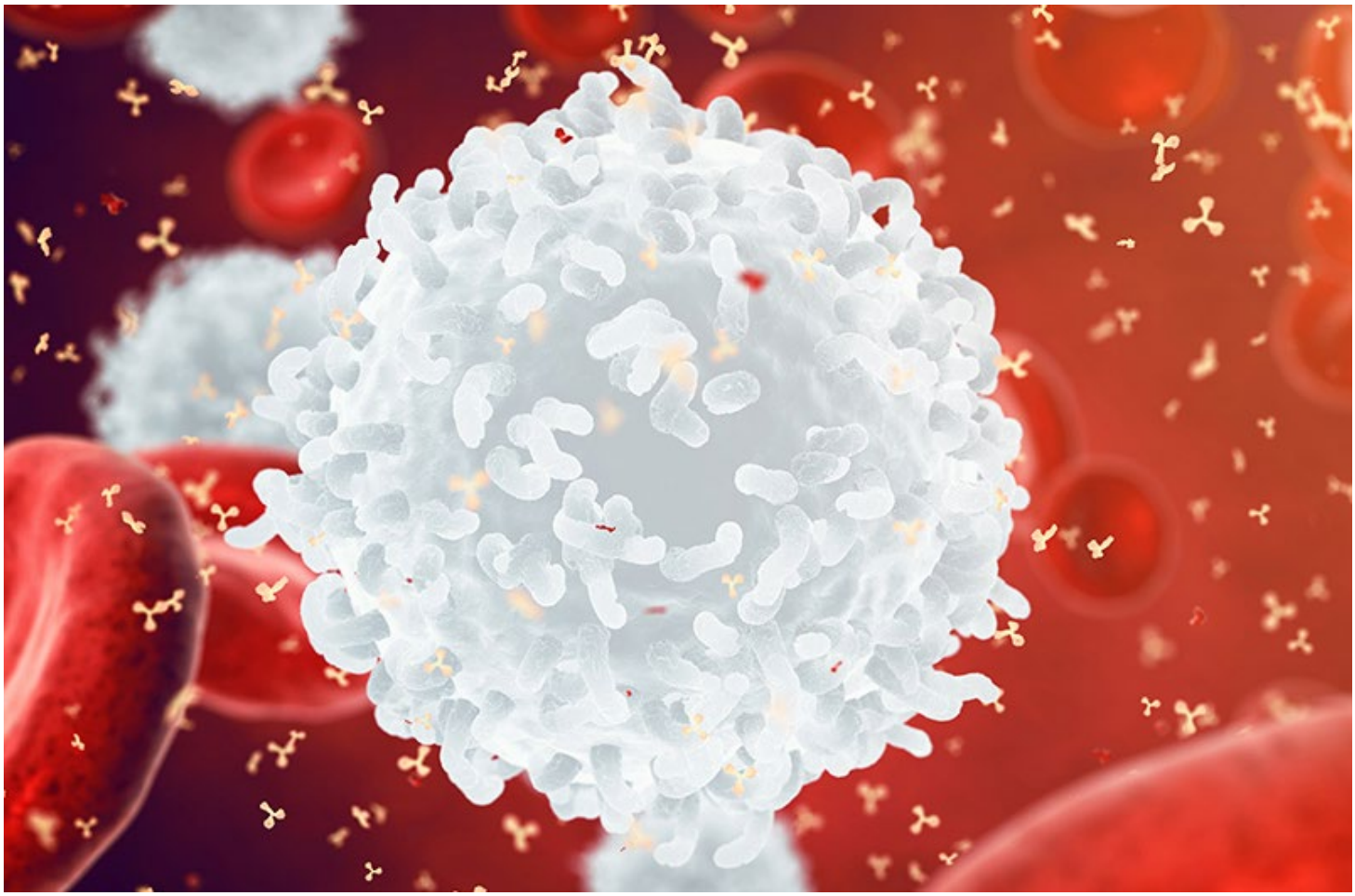
How all this plays out is a function of the health of cells as much as the aggressiveness of the bacteria: Cells that are weak from being chronically stressed are more vulnerable to invasion by bacteria. A healthy person with healthy cells who is bitten by a tick may not have much in the way of acute 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 phins 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: 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: 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.Of course, it helps when preaching to the choir.

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.

References:

1. *Feng J et al. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020 Feb 21;7:6. doi: 10.3389/fmed.2020.00006. eCollection 2020.*
1. *Xiao Ma, Jacob Leone, Sunjya Schweig, Ying Zhang. Botanical Medicines with Activity against Stationary Phase Bartonella henselae. bioRxiv 2020.08.19.256768; doi: https://doi.org/10.1101/2020.08.19.256768*
2. *Goc A, Rath M. The anti-borreliae efficacy of phytochemicals and micronutrients: an update. Ther Adv Infect Dis. 2016;3(3-4):75-82. doi:10.1177/2049936116655502*
3. *Cornejo E, Schlaermann P, Mukherjee S. How to rewire the host cell: A home improvement guide for intracellular bacteria. J Cell Biol. 2017;216(12):3931-3948. doi:10.1083/jcb.201701095*
4. *Randow F, MacMicking JD, James LC. Cellular self-defense: how cell-autonomous immunity protects against pathogens. Science. 2013;340(6133):701-706. doi:10.1126/science.1233028*
5. *Alberts B, Johnson A, Lewis J, et al. Molecular Biology of the Cell. 4th edition. New York: Garland Science; 2002. Cell Biology of Infection. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26833/*
6. *Thakur A, Mikkelsen H, Jungersen G. Intracellular Pathogens: Host Immunity and Microbial Persistence Strategies. J Immunol Res. 2019;2019:1356540. Published 2019 Apr 14. doi:10.1155/2019/1356540*
7. *Belkaid Y, Hand TW. Role of the microbiota in immunity and inflammation. Cell. 2014;157(1):121-141. doi:10.1016/j.cell.2014.03.011*