COVER STORY

Confronting the misnomer of chronic Lyme disease

Infectious Diseases in Children, June 2017

An estimated 329,000 cases of Lyme disease occur annually in the United States, according to the CDC, with the highest prevalence observed in the Northeast and Midwest regions, where 14 states account for 96% of reported cases. As the most commonly reported tick-borne illness in the U.S., Lyme disease has become increasingly infamous nationwide, due to both its growing incidence and its expansion beyond its historically-endemic range.

While the majority of patients with Lyme disease can be identified by the telltale erythema migrans rash, some patients may only exhibit symptoms of fever, fatigue or muscle/joint pain, which leave the clinician to piece together the diagnosis after confirming whether the patient was in a Lyme-endemic area. If symptoms are vague, the pediatrician or primary care provider may order a blood test, which, if confirmed, is followed with a 2- to 4-week course of antibiotics, according to current Infectious Diseases Society of America guidelines.

Although Lyme disease is an infection that does clear following antibiotic treatment, 10% to 20% of patients experience fatigue, musculoskeletal pain and insomnia that may continue for more than 6 months after the infection has resolved. Officially known as ‘post-treatment Lyme disease syndrome’, the loose confederation of nonspecific symptoms associated with this condition has unexpectedly provided a rallying point for patients with similarly vague symptoms seeking a concrete diagnosis.

Many patients whose symptoms overlap heavily with those of post-treatment Lyme disease syndrome, including fibromyalgia and chronic fatigue syndrome, have adopted the term ‘chronic Lyme disease’ for their condition. Communities of patients and patient advocates have emerged with the belief that their symptoms are the result of a persistent Lyme disease infection that has gone undiagnosed, despite the fact that many of these patients show no objective evidence they were previously infected.

Compounded by misinformation shared through internet forums, chronic Lyme disease has become a new fixture in the debate between patients and providers regarding medically unexplained symptoms. To explore the chronic Lyme disease phenomenon and how it fits into the health care landscape, *Infectious Diseases in Children* spoke with several infectious disease and Lyme specialists concerning the pervasive misnomer of chronic Lyme disease, the furor of the Lyme community, and how pediatricians and physicians can better prepare themselves for treating people with medically unexplained symptoms.

Photo by: Tufts Medical Center

H. Cody Meissner, MD, chief of the division of pediatric infectious disease at Tufts Medical Center, noted that many symptoms

The rise of chronic Lyme

often associated with chronic Lyme disease are also found in people who exhibit no sign of prior Lyme infection.

First diagnosed in Connecticut in 1975, Lyme disease remained an etiologic mystery until the discovery of the spirochete, a corkscrew-shaped bacterium named *Borrelia burgdorferi*, which is primarily transmitted through the bite of the blacklegged tick, otherwise known as the common deer tick.

“Lyme disease is most common from Virginia up through northern New England, with a secondary focus in Minnesota and Wisconsin — however, the range is clearly expanding,” **Paul M. Lantos, MD, MS,** assistant professor of internal medicine and pediatrics at Duke University, told *Infectious Diseases in Children*. “Every year, the geographical range seems to be increasing, with cases in the Midwest extending into the Dakotas and southward into Illinois. With new reports showing Lyme disease in Michigan, it appears to be filling in the gaps between the Midwest and the east. It has also expanded west through New York and Pennsylvania, north into southern Canada, and south through Virginia.”

While location within the deer tick range remains the most significant risk factor for Lyme disease, the amount of time spent outdoors in wooded or overgrown areas where ticks thrive comes in close behind. Because they are physically lower to the ground and more prone to play on the ground outdoors, children are at particular risk for tick exposure and subsequent infection.

“Children between the ages of 5 and 10 years have the highest incidence of Lyme disease of any age group — nearly twice as high as incidence among adults,” **Eugene Shapiro, MD,** professor of pediatrics and epidemiology at the Yale School of Medicine and an *Infectious Diseases in Children* Editorial Board member, said in an interview. “As a result, especially within the deer tick range, Lyme disease is a very common infection among children.”

However, it is the childhood prevalence of this infection — coupled with the range of vague ‘flu-like’ symptoms such as fever, malaise, and muscle and joint pains — that has given rise to the popular belief that a persistent ‘hidden’ Lyme disease infection is responsible for an overwhelming number of conditions with similar chronic, nonspecific symptoms.

Paul M. Lantos

Although the IDSA maintains that an antibiotic course of 21 days is sufficient to eradicate Lyme infection, the International Lyme and Associated Diseases Society (ILADS) — an advocacy group consisting of physicians, patients and laboratory personnel — contends that a longer course of therapy is required, and that chronic Lyme conditions are the result of a persistent infection that remained following initial antibiotic treatment.

In its alternative diagnostic guidelines for chronic Lyme disease, ILADS included many of the staple symptoms of post-treatment Lyme disease syndrome (PTLDS), such as musculoskeletal pains, disrupted sleep and lack of typical mental functions; however, the group also included several nebulous symptoms not customarily associated with *B. burgdorferi* infection, such as night sweats, sore throat, myalgia, diarrhea, jaw pain, tinnitus and vertigo.

While the IDSA and the National Institutes of Health have been careful to differentiate diagnosis and treatment for patients with well-documented Lyme disease from those who have no record of prior Lyme infection, patients and advocate groups — most commonly for neurologic and rheumatologic diseases — have continued to point to Lyme disease as a culprit for a range of unexplained symptoms.

“The media coverage of chronic Lyme disease is almost sensationalism, and has resulted in many people expanding upon what we recognize as Lyme disease to include symptoms that are likely not a result of the disease or even the infectious process,” **H. Cody Meissner, MD,** chief of the division of pediatric infectious disease at Tufts Medical Center, said in an interview.

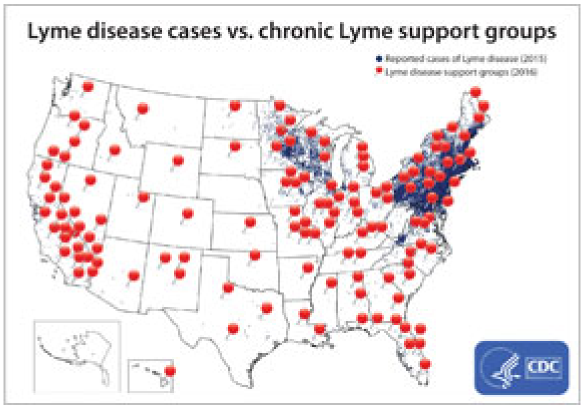
“In cases of PTLDS, oftentimes there is nothing abnormal on the physical exam nor laboratory values that can be used to guide us in the diagnosis; therefore, we don’t know if this subjective syndrome is any more common after Lyme disease than other infectious disease or if it occurs among people who don’t have Lyme disease,” Meissner noted. “While we recognize that these symptoms can be functionally disabling, how often do these symptoms occur in someone who does not have Lyme disease?”

Growth of Lyme communities

When patients suffering from debilitating yet vague symptoms are unable to obtain a concrete diagnosis from their physician due to the lack of objective evidence, inevitably they will go looking for information on their own. The internet has provided not only a way to link together patients with comparable symptoms lacking diagnoses into supportive networks, but also facilitated the spread of inaccurate medical information and unsubstantiated treatment advice through online forums.

The burgeoning online chronic Lyme community not only consists of patients who are symptomatic and Lyme disease activists, but also by groups of physicians who specialize specifically in diagnosing and treating these patients, even if the treatments suggested have minimal scientific backing.

“‘Lyme-literate doctors’ are what the chronic Lyme disease advocacy community calls doctors who specialize in the diagnosis and treatment of chronic Lyme disease,” Lantos said. “The doctors referred to as ‘Lyme-literate’ MDs often offer treatments that have not been substantiated by high quality research. These include prolonged or unorthodox antibiotic courses, including antibiotics that are not typically used to treat Lyme disease.”



Although many chronic Lyme activists insist Lyme disease is a chronic infection requiring extended duration of antibiotics, clinical trials have never born this out. In a recent double-blind, placebo-controlled trial published in *The New England Journal of Medicine*, Berende and colleagues demonstrated that long-term antibiotic treatment with ceftriaxone and doxycycline did not improve health outcomes among patients with persistent symptoms of Lyme disease.

“The evidence is fairly clear at this stage that there are no benefits from a prolonged course of antibiotics beyond what is generally recommended by IDSA guidelines,” Meissner said in an interview. “Whatever the explanation, PTLDS is not responsive to additional antibiotics, which, unfortunately, has led to some very unorthodox therapies that physicians are trying to discourage."

Personal testimonials for alternative treatments capable of curing chronic Lyme disease are widespread throughout Lyme communities, many of which endorse scientifically untested and potentially hazardous remedies. For patients desperate for answers, patient testimonials – or even product promotions from alternative therapy providers – posted on Lyme discussion boards extolling the benefit of a particular treatment can be incredibly persuasive.

Among the more inexplicable therapies for Lyme disease was 'malariotherapy', said **Sunil Sood, MD,** professor of pediatrics at Hofstra Northwell School of Medicine and a pediatric infectious disease specialist with Cohen Children's Hospital.

"This involved injecting malaria parasites into their blood to induce a fever that could reach up to 106°F, purportedly to 'burn off' the *Borrelia* bacteria in their brain," Sood said. "After this practice came to the attention of the CDC about 25 years ago, physicians have been encouraged to report cases of self-induced malaria."

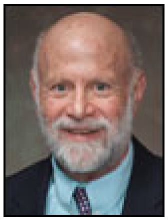
In a 2015 study published in *Clinical Infectious Diseases*, Lantos and colleagues identified more than 30 alternative therapies marketed for the treatment of chronic Lyme, including hyperbaric oxygen therapy, ultraviolet light therapy, herbal remedies, modified diet as well as vaginal or anal infusions of ozone. While these types of treatments may be supported by personal anecdotes and the recommendation of 'Lyme-literate' doctors, "there is no evidence that these are in any way beneficial," Shapiro told *Infectious Diseases in Children*.

"What drives patients to seek alternative explanations is the sense that the conventional medical community cannot offer them anything or that no one will listen to them," Lantos said. "This sense of futility is one of the things that drives patients away from infectious disease physicians, and conventional medicine in general, and probably lies behind the growth of the anti-vaccine movement and other alternative viewpoints."

Off the map

Medical misinformation is further reinforced by the vast network of support groups for chronic Lyme found nationwide – regardless of whether Lyme disease is endemic to the area.

According to the Lyme Disease Network, every state, except for Nebraska, hosts at least one support group. California, an area not typically affected by this disease, features 29 support groups available to those with chronic Lyme, the highest concentration of Lyme support groups demonstrated in any state. "Part of the chronic Lyme problem is that physicians ignore the epidemiology of Lyme disease," Sood said in an interview. "All one needs to do is look at the CDC map to observe the prevalence of Lyme disease — unless a patient has traveled or had significant exposure in an endemic area, Lyme disease will not occur."



Eugene Shapiro

That endemic range, however, could be changing. In 2016, **Rebecca Eisen, PhD,** from the CDC's Division of Vector-Borne Diseases, and colleagues published a study in the *Journal of Medical Entomology* which found that the blacklegged tick has experienced a population explosion within the past twenty years, doubling its established range. After compiling state and county tick surveillance data, researchers found that two species of blacklegged tick could now be found in 49% of all U.S. counties.

However, Eisen noted that while their surveillance map showed wide distribution of ticks “...the risk of people getting Lyme disease is not equal across areas of the country.”

More than ever, pediatricians and other primary care providers are finding themselves on the front line of Lyme disease, whether confirming a diagnosis and administering treatment, or providing additional counsel or referrals for parents of children whose chronic symptoms do not match the standard criteria for Lyme disease.

“For primary care providers in endemic areas, staying current with the literature is essential because the bulk of Lyme disease referrals — either for unambiguous Lyme disease or chronic symptoms attributed to Lyme disease — are showing up in the pediatrician’s office before they make their way to the infectious disease specialist,” Lantos said.

For pediatricians within newly established blacklegged tick ranges, educational offerings through the AAP’s *Red Book*, as well as an abundance of nationwide seminars, are available to familiarize themselves with the potential disease vectors in their area as well as how to efficiently diagnose the early symptoms of Lyme disease.

Most importantly, pediatricians need to be aware that chronic Lyme and its assortment of ill-defined symptoms are not a new phenomenon, but rather the most recent catch-all term for functional symptoms with no clear structural or pathophysiological causes. Before the discovery of Lyme disease, patients whose symptoms lacked objective physical findings attributed them to mononucleosis, and before that, to chronic candidiasis.

“What these patients want is a diagnosis. However, what often happens is that the subspecialist will say they do not have Lyme disease, but what the patient hears is that they are making it up or it is all in their head,” Shapiro told *Infectious Diseases in Children*. “A better approach for physicians is to be empathetic: Say that you are going over everything and that you think it is highly unlikely that what the patient has is Lyme disease. Be up front that you don’t know the cause of the symptoms, but it is unlikely to be something dangerous; highlight what is important is to figure out how best to manage the symptoms — whatever the cause — and get the patient back to normal life.”

Managing chronic Lyme at the root

In a study published in *Mental Health in Family Medicine*, Edwards and colleagues found that symptoms such as chest pain, fatigue, dizziness, headache, swelling, back pain, shortness of breath, insomnia, abdominal pain and numbness accounted for 40% of all primary care visits.

However, physicians were only able to identify a biological cause for these symptoms in 26% of patients. Without a medically identifiable cause, many patients become entangled with the label of Medically Unexplained Symptoms (MUS), which can have a variety of different causes.

“I believe that many of the patients who claim to have chronic Lyme disease do have the symptoms of which they are complaining, but the cause is not Lyme disease,” Shapiro said. “Our understanding of MUS is clearly imperfect, and unfortunately, it is likely due to combination of factors, such as genetic predispositions and/or psychological components. The problem is that most infectious disease specialists, and doctors in general, are not well-trained in managing symptoms without a diagnosis.”

In a 2014 *BMC Family Practice* survey of patients who identified themselves as having chronic Lyme disease, Ali and colleagues observed that patients were often unsatisfied with care in conventional settings. Patients reported that while conventional physicians were often dismissive of their diagnosis, responding to their inquiries with patronizing or condescending attitudes, consultations with ‘Lyme-literate’ MDs or complementary and alternative medicine practitioners were reported to be optimistic and supportive.

“I don’t blame people for getting caught up in the myth that there are two universes out there: one of doctors who don’t ‘believe’ in chronic Lyme disease, and the other of doctors who are chronic Lyme advocates and will actually help them,” Sood said. “Certainly, the physicians who diagnose chronic Lyme disease exhibit a whole lot of empathy for their patients. The problem is that their alternative therapies are not based on scientific fact, and can cause long-term harm.”

Furthermore, alternative doctors or ‘Lyme-literate’ MDs who rush to label a patient with chronic Lyme disease based on symptoms without performing a more thorough patient analysis may ultimately miss the true root of the patient’s problem.


Sunil Sood

“If a physician has a patient with well-documented, properly treated Lyme disease — with the acute illness resolved — and then the patient presents with vague symptoms, it is incumbent on the physician to consider all possibilities that might be causing these symptoms, such as depression or thyroid disease,” Meissner told *Infectious Diseases in Children*. “The physician should listen to the concerns of the parents and the child, and order appropriate tests to rule out other possible causes for these symptoms.”

However, Shapiro noted that informing a parent that their child’s symptoms are not the result of Lyme disease does not necessarily solve the problem. Parents want a concrete diagnosis and treatment when it concerns their children, and may feel frustrated when the physician refers them to a mental health professionals to address symptoms of depression, anxiety or other psychological concerns that a patient may be experiencing.

“[Treatment] gets complicated when it is the parent who is driving it, and the interaction between the child and the parent gets very complicated,” Shapiro said. “The goal is to get the child back to school, to seeing their friends. The things that seem to be effective, in addition to exercise and improved sleep, is to enter the patient into a long-term therapeutic relationship with some kind of provider — doctor, nurse, social worker, counselor, psychologist.”

While there remains considerable controversy between the medical community and advocacy groups over the prevalence and diagnostic criteria of Lyme disease — as well as the very existence of chronic Lyme disease — physicians continue to treat patients who claim to have chronic Lyme diagnoses. With Lyme advocacy groups disseminating medical misinformation through online forums, physicians can expect continued resistance to diagnoses that do not consider Lyme disease for chronic symptoms; ultimately, however, the focus should not be on the name associated with these symptoms but rather on the patient and their needs.

“When we are referred patients for Lyme disease, I don’t think we are doing our job if we make ourselves only adjudicators of a Lyme disease diagnosis,” Lantos said. “Some patients come to our office primarily concerned that they have Lyme disease; as with any other new consultation, however, our job should be to take a step back, perform the best clinical evaluation and determine the best medical explanation. In some cases, Lyme disease is the best explanation and in other cases it is not."– *by Katherine Bortz*

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Disclosures: Lantos, Meissner, Shapiro, and Sood reported no relevant financial disclosures.