

## Update on Lyme Disease

### The Hidden Epidemic

#### ABSTRACT

Lyme disease is the most common vector-borne disease in the United States. Diagnosis is problematic for many reasons, including unsatisfactory laboratory tests and confusion about test interpretation. When Lyme disease is diagnosed early, treatment is usually successful with oral antibiotics. Unfortunately, the diagnosis is often missed, allowing the infection to disseminate and affect every body system. When Lyme disease affects the central nervous system, it is often treated with intravenous antibiotics in the home setting. Infusion nurses who are experienced with the myriad symptoms and treatment challenges of these complex patients will be a reassuring asset to patients and physicians alike.

Lyme disease was named in 1975 after an unusual outbreak of pediatric arthritis in New Lyme, Connecticut, but despite its recent recognition, the disease is not new. The first reported case of a similar condition occurred in Germany in 1883, with unidentified cases undoubtedly going back many decades or centuries. In 1909, a Swedish physician associated the typical bull's-eye rash, now considered diagnostic of Lyme disease, with the bite of an Ixodes tick. But it was not until 1984 that the causative organism of the disease was discovered by Dr Willy Burgdorfer: a spirochete or spiral-shaped bacterium that was subsequently named *Borrelia burgdorferi* (Bb). Today, Lyme disease is the most common vector-borne disease in the United States.<sup>1</sup>

The tiny nymphal deer tick, which is the usual culprit for the spread of Bb, is no bigger than a poppy seed, making it very hard to detect on an unsuspecting victim. Although the disease-carrying ticks have been found in every state, areas of highest incidence include the northeastern states, northern California, and the Great Lakes

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states.<sup>2</sup> Reported cases of Lyme disease have risen yearly, but restrictive epidemiologic criteria, underreporting, and underdiagnosing make the current estimate of about 20,000 new cases yearly likely to be grossly underestimated.<sup>3</sup> Increased prevalence of the disease is directly related to the burgeoning increase of the deer population in civilized areas of the United States. Although the summer months are the time of highest incidence of Lyme disease, there is no time of the year when cases are not reported.<sup>3</sup>

The riskiest behaviors for contracting Lyme disease through the bite of an infected tick are sitting on a dead log, gathering wood, leaning against a tree, sitting in leaves and litter, and walking through tall grasses. More than half of tick bites occur on the arms and legs. Another 20% occur on the head and neck, with the remainder on the torso.<sup>4</sup>

Acute Lyme disease, also known as early localized Lyme disease, occurs during the month immediately after infection. This is the time when the disease is most easily treated, but unfortunately, the time when the disease is often missed. About half of the victims are not even aware that they have suffered a tick bite.<sup>5</sup>

The tick injects a substance that anesthetizes and decreases inflammation at the site of the bite, making the victim unaware as the tick takes its blood meal.<sup>6</sup> Furthermore, the erythema migrans rash (commonly known as the "bull's-eye rash" for its characteristic shape), which occurs soon after the bite and is diagnostic of Lyme disease, is not present in as many as 50% to 60% of infected patients.<sup>7</sup> When it is present, it can take many shapes and forms and is frequently misdiagnosed as ringworm or cellulitis. The nonspecific symptoms of acute Lyme, such as headaches, body aches, joint pain, and low-grade fever, can easily be dismissed as a virus. Thus, the unsuspecting victim who misses the presence of the tiny tick and the distinguishing rash may go on to have disseminated or chronic Lyme disease, in which symptoms are severe and diverse and treatment is complex and protracted.<sup>8</sup>

Chronic Lyme disease may present with either primarily musculoskeletal symptoms (such as fixed or migratory arthropathies and myopathies) or primarily neurological symptoms. Neurological symptoms vary in severity and may include cognitive impairments, balance and coordination problems, dizziness, and neuropathies.<sup>1</sup> Moreover, the chronic or disseminated form of Lyme

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disease can affect any and every body system. A century ago, the adage regarding syphilis, an illness caused by another spirochete, *Treponema pallidum*, was "to know syphilis is to know medicine." Today, the same could be said of syphilis' close cousin Lyme disease, where knowledge of rheumatology, neurology, cardiology, gastroenterology, dermatology, urology, ophthalmology, endocrinology, and psychiatry are necessary to understand and treat this complex disease. For a list of typical Lyme symptoms, by body system, see Table 1.<sup>4,8</sup>

Recognizing and diagnosing chronic Lyme disease is challenging because of several factors: (1) most clinicians are not familiar with the disease's myriad signs and symptoms; (2) symptoms can occur years to decades after the patient's tick exposure, when association with a tick bite is unlikely to be suspected; (3) clinicians are not aware of the insensitivity of the blood tests for Lyme disease and are likely to rule out disease based on a negative test result; (4) the criteria for positivity on the Lyme Western blot were meant for epidemiological purposes rather than diagnostic purposes and, therefore, are stringent and exclusive. A patient may test negative according to reporting criteria, but still have the disease; and (5) most clinicians are not aware that the Centers for Disease Control and Prevention (CDC) states that diagnosis of the disease should not be based on a test result anyway, but on the clinical impression of the healthcare provider.<sup>1-4</sup> Thus, many patients go undiagnosed or are misdiagnosed with illnesses that have no cure. These common misdiagnoses are listed in Table 2.<sup>2</sup>

## TESTING

Clinicians are taught to screen for Lyme disease using the enzyme-linked immunosorbent assay (ELISA) test. This test should be reevaluated as a screening tool, however, because the sensitivity is only about 50% and there is great laboratory-to-laboratory variability.<sup>7</sup> The Western blot, usually considered a confirmatory test, is a better diagnostic tool, although still far from ideal. The Western blot is highly specific but still fairly low in sensitivity. Unfortunately, most laboratories report only the bands required to meet the criteria established by the CDC for epidemiologic purposes, leaving out bands that, although not included in the CDC criteria, are highly specific for the presence of Bb. The polymerase chain reaction blood test, which looks for genetic material of Bb itself, is extremely specific but very insensitive. Furthermore, it is expensive and considered by many to be experimental. Thus, testing for Lyme disease remains a dilemma.<sup>9</sup>

Diagnosis of neurologic Lyme disease is based primarily on symptom presentation because the recovery of Bb or its antibodies in cerebral spinal fluid is unreliable. Magnetic resonance imaging or single-photon emission computed tomography scans often show abnormalities,

but these are not consistent or specific and are, therefore, not helpful as diagnostic tools. In about 50% of neurologic Lyme patients, magnetic resonance imaging show focal white-matter lesions resembling other demyelinating diseases such as multiple sclerosis. SPECT scans show areas of hypoperfusion in the frontal and temporal lobes, subtle enough to be missed or discounted by the untrained radiologist.<sup>5</sup>

## THE NATURE OF *B. BURGdorferi*'S RESISTANCE TO TREATMENT

*B. burgdorferi* is a genetically sophisticated bacterium, with over 1500 gene sequences and at least 132 functioning genes (in contrast to the 22 functioning genes found in syphilis bacterium *T. pallidum*) Bb has 21 plasmids, 3 times more than any known bacteria.<sup>6</sup> Plasmids contain bits of genetic material that enable the bacteria to survive under all sorts of adverse conditions. The survival techniques of Bb are phenomenal because of a stealth pathology that evades the immune response. The bacterium has pleomorphic forms that enable it to change its structure to avoid whatever type of attack it is facing.<sup>8</sup> Thus, when a patient takes an antibiotic that works by attacking the bacterial cell wall, Bb will quickly change into a cell wall-deficient form to survive the attack. In its latent cyst form, Bb can remain dormant in the body indefinitely or until the immune system is caught off guard. An entire chapter could be written on the many other complex methods these bacteria have for survival.<sup>8</sup>

## TREATMENT OF LYME DISEASE

If Lyme disease is diagnosed in its early stage, treatment is straightforward and successful within a month of taking either oral doxycycline or amoxicillin. However, as previously mentioned, the trick is in diagnosing and treating the disease before it has been able to disseminate deep into areas that are difficult to reach with oral antibiotics. For the clinician, a "better safe than sorry" approach is best when it comes to possible Lyme disease, as early diagnosis and treatment can eliminate years of suffering and disability. Furthermore, the risk of a missed diagnosis far outweighs the risk of taking a month of oral antibiotics.<sup>6</sup>

When Lyme disease becomes chronic or disseminated, the controversy regarding diagnosis and treatment begins. There are 2 published standards of care for the diagnosis and treatment of Lyme disease that represent divergent and conflicting viewpoints and approaches.<sup>6,7</sup>

The philosophy of the Infectious Diseases Society of America (IDSA) is that Lyme disease is rare, difficult to contract, and straightforward to cure. It is the opinion of the IDSA that treatment with antibiotics for



**TABLE 1**

# Main Symptoms of Lyme Disease

Neurologic	Musculoskeletal	Cardiac	Endocrine	Gastrointestinal and Urinary	Other
Neuropathies	Joint pain	Exhaustion	Low body temperature	Abdominal pain and tenderness	Easy bruising
Paresthesias	Muscle pain and cramps	Palpitations	Sweats, chills	Bloating, gas	Hair loss
Dizziness	Muscle and joint stiffness	Shortness of breath	Irregular menses	Constipation	Recurrent sinusitis
Cognitive disturbances	Loss of muscle tone	Tachycardia	Loss of libido (sex drive)	Loose stools	Sore throat
Attention deficit	Back pain, stiffness	Hypotension	Worsening PMS	Nausea	Tender glands
Hypersensitivity to touch, sound, light, and smell	Neck pain, stiffness	Hypertension	Pelvic or testicular pain	Urinary frequency	Tooth pain
Bell's palsy	TMJD	Heart murmur	Milky breast discharge	Constant thirst	Unusual rashes
Tinnitus	NA	Abnormal ECG	Hypertriglyceridemia	Irritable bladder	Shooting pains throughout body
Restless leg syndrome	NA	Chest pain, tightness	Weight change (usually gain)	Urine control problems	NA
Drooping eyelid	NA	NA	NA	Bowel control problems	NA
Transient blurred vision	NA	NA	NA	NA	NA
New onset anxiety or panic attacks	NA	NA	NA	NA	NA
Clumsiness	NA	NA	NA	NA	NA
Depression	NA	NA	NA	NA	NA
Difficulty in chewing or swallowing	NA	NA	NA	NA	NA
Hallucinations	NA	NA	NA	NA	NA
Headaches	NA	NA	NA	NA	NA
Involuntary jerking or muscle twitching	NA	NA	NA	NA	NA
Irritability	NA	NA	NA	NA	NA
Poor balance	NA	NA	NA	NA	NA
Sleep disturbances	NA	NA	NA	NA	NA
Speech difficulty	NA	NA	NA	NA	NA
Weakness of limbs	NA	NA	NA	NA	NA

Abbreviations: ECG, electrocardiogram; NA, not applicable; PMS, premenstrual syndrome; TMJD, temporomandibular joint disturbances.

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- Lupus
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**TABLE 2**  
**Common Misdiagnoses**

Lyme disease is often misdiagnosed as
Chronic fatigue syndrome
Fibromyalgia
Depression, anxiety, and obsessive compulsive disorder
Somatization disorder
Lupus
Multiple sclerosis
Parkinson's disease
Amyotrophic lateral sclerosis (Lou Gehrig's disease)
Early-onset Alzheimer's disease
Ménière's disease
Viral syndrome
In children,
Failure to thrive
Autism
Attention-deficit disorder, attention-deficit/hyperactivity disorder
Learning disabilities

more than 1 month is very rarely necessary, and if a patient remains symptomatic after 1 month of treatment, the remaining symptoms are most likely due to a "post-Lyme syndrome" or autoimmune-like state induced by an immune system that has been unable to shut down. Recommended treatment is 30 days of intravenous ceftriaxone in cases of neurologic disease and, in all other cases, 2 to 4 weeks of a single oral antibiotic with the Food and Drug Administration indication for the treatment of Lyme disease (doxycycline, amoxicillin, or cefuroxime).<sup>6</sup>

Conversely, the International Lyme and Associated Diseases Society (ILADS) promotes that Lyme disease is prevalent, underdiagnosed, and difficult to cure.<sup>5</sup> Their approach is treatment with antibiotics until symptom resolution, maintaining that the bacteria are very hard to eradicate and symptoms are due to ongoing infection. The International Lyme and Associated Diseases Society further maintains that treatment is often complicated by tick-borne coinfections that must be addressed before the patient's Lyme disease can be cured. Treatment consists of high doses and combinations of various antibi-

**TABLE 3**  
**Antibiotic Treatment Options for Lyme Disease**

1. Doxycycline, 400 mg/d
2. Minocycline
3. Macrolide (clarithromycin, azithromycin) + beta-lactam
4. Macrolide (clarithromycin, azithromycin) + metronidazole or tinidazole
5. Ketolide + beta-lactam or metronidazole

otics that are Food and Drug Administration–approved but used off-label for the treatment of Lyme disease. The ILADS approach is based on years of clinical experience of physicians from many specialties who have elected to focus on the treatment of tick-borne diseases and from animal studies showing persistence of the spirochete after treatment.<sup>5-7</sup>

Generally, when there is more than 1 treatment approach to an illness, options are explained to the patient to facilitate a treatment choice based on educated and informed consent. The 2 sides of the Lyme disease debate and the 2 consequent approaches to

**TABLE 4**  
**Treatment Options for Coinfections**

Babesia (treat this coinfection first, and treat for at least 4 months) <sup>10,11</sup>
Atovaquone + azithromycin
Metronidazole + azithromycin
Clindamycin + hydrochloroquine
Lariam + doxycycline
Bartonella <sup>12,13</sup>
Ciprofloxacin or levaquin
Clarithromycin + DS sulfa
Rifampin + doxycycline
Ehrlichia (many Lyme treatments will cover Ehrlichia too) <sup>14</sup>
Doxycycline 400 mg/d
More resistant cases, add rifampin to the doxycycline



treatment should be explained in detail to newly diagnosed patients. Because the IDSA approach is fairly straightforward, as outlined in the previous paragraph, the focus of the next paragraph will be the treatment principles promoted by the ILADS.

For musculoskeletal disease, 2 or 3 antibiotics from different classes are used simultaneously and sometimes at higher-than-normal dosages to achieve better tissue penetration. Length of treatment is until symptom resolution and, on the average, is about 18 months. Treatment protocols rotate every 2 to 3 months to allow for adaptation of the bacteria. Intramuscular benzathine penicillin G is used for mild neurologic disease and intravenous antibiotic therapy, usually with ceftriaxone, for more severe neurologic disease.<sup>5</sup>

Patients who are coinfecting with other tick-borne diseases—babesiosis, bartonellosis, anaplasmosis, or ehrlichiosis—require different antibiotics to specifically target those bacteria. See Table 3 for oral antibiotic combination therapies and Table 4 for coinfection treatment protocols.<sup>5</sup>

## WHAT INFUSION NURSES NEED TO KNOW

There are some specific considerations and complications involved in working with neurologic Lyme patients who are being treated with intravenous antibiotics. These patients are homebound but in many cases are mobile, so the elastomer positive-pressure ball is usually the delivery method of choice. Most patients are able to learn to independently manage their daily care.

An expected adverse effect of treatment is the Jarish-Herxheimer reaction, a symptom intensification reaction commonly known as “the Herx.” Unless the patient and nurse are prepared, this reaction can be alarming. The Herx will occur on about day 4 to 5 of treatment, again during week 4 of treatment, and periodically as treatment continues. The patient’s total white blood cell count may drop; transaminase levels may increase; there may be fever or a rash; and the pain, fatigue, mental confusion, and malaise become almost unbearable. All of the patient’s symptoms intensify and new, frightening symptoms may suddenly appear such as chest pain, shortness of breath, or irregular heartbeats.<sup>5</sup>

It is easy to confuse the Jarish-Herxheimer reaction with an adverse or allergic reaction to the antibiotic. Patients often say they feel toxic, which is understandable because the reaction is characterized by high levels of proinflammatory cytokines that are released as the immune system reacts to the die-off of the bacteria. There may even be neurotoxins released into the bloodstream as the bacteria die, although this is not clearly substantiated.<sup>8</sup>

Other important considerations for the infusion nurse who cares for neurologic Lyme patients are the

neuropsychiatric complications. Patients are often irritable or depressed and therefore require reassurance and a tolerant approach. Because of the cognitive impairments experienced by these patients, it is best to use simple, concise language when communicating, to put all instructions in writing, and to encourage a family member or caregiver to be present for all teachings.<sup>5</sup>

## CONCLUSION

As awareness increases regarding the widespread prevalence of Lyme disease, primary care providers will hopefully learn to recognize the early signs of the disease so that victims can be treated easily and effectively with oral antibiotics. However, because of the complexities of diagnosis reviewed in this article, there will unfortunately remain those with disseminated and neurologic complications who will require at-home intravenous antibiotics. Infusion nurses who are experienced with the myriad symptoms and treatment challenges of these complex patients will be a reassuring asset to patients and physicians alike.

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