JOURNAL OF NEUROLOGY AND PSYCHOLOGY RESEARCH

CASE STUDY Open Access

Lyme disease Neurological Implications: I. Symptomatology and Etiology

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Received date: September 19, 2023, **Accepted date:** September 25, 2023, **Published date:** October 01, 2023.

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Abstract

Lyme disease is the most commonly occurring vector-borne infection spread by ticks. It is caused by Borrelia burgdorferi and other closely related species of bacteria. It is the most commonly occurring vector-borne infection spread by ticks in the Northern Hemisphere and the sixth most commonly reported notifiable infectious disease. This series of articles is interested in the neurological implications of this disease. Accompanying diseases may be chronic axonal polyneuropathy or encephalopathy accompanied by cognitive disorders such as sleep disturbance, fatigue, and personality changes. Morbidity can be severe, chronic, and disabling. Lyme can also manifest as a disease of the nervous system in addition to the musculoskeletal and cardiovascular systems. Borrelia and other infections attack the brain and central nervous system unimpeded. Early neurologic manifestations include lymphocytic meningitis; cranial neuropathy, especially facial nerve palsy; and radiculoneuritis. I will discuss Lyme disease per se, chronic Lyme disease, and chronic Lyme disease complex. Here, the bacteria are able to cross the protective blood-brain barrier and create new problems that may mimic other diseases. They can inhabit glial cells and neurons, and render them dysfunctional, leading to anxiety and depression. They may also interfere with the host's neurotransmitters, disrupting the production and use of dopamine, and causing what can look like (but is not!) Parkinson's disease (PD). Further, they can increase the production of the octopamine neurotransmitter, accumulate in the brain, raise blood pressure, and cause headaches. Lastly, when this insidious microorganism is killed, it sheds parts of itself as endotoxins, which may interfere with the brain's chemistry. A buildup of toxins can give intense brain fog and memory issues.

Abbreviations

AB3CE: Anaplasmosis, Babesiosis, Bartonellosis, Borreliosis, Colorado tick fever, Ehrlichiosis; AC2MPQ:

Anaplasmosis, Chlamydia pneumonia, Coltivirus disease, Mycoplasma pneumonia, Powassan virus disease, Q-Fever; ACA: Atrophic Chronic Acrodermatitis; AD: Alzheimer's Disease; ALS: Amyotrophic Lateral Sclerosis; BBB: Blood-brain barrier; CAP: Chronic Axonal Polyneuropathy; CFS: Chronic Fatigue Syndrome; CLD: Chronic LD; CLD-U: Untreated CLD; CLD-PT: Previously treated CLD; CNS: Central Nervous System; EBV: Epstein-Barr Virus; EM: Erythema Migrans; FJAB: Fatigue, Joint pain, Autoimmune diseases, and Brain fog; GBBS: Garin-Boujadoux-Bannwarth Syndrome; HHV: Human Herpes Virus; ILAD: International Lyme and Associated Diseases Society; JIRA: Juvenile Idiopathic Rheumatoid Arthritis; LD: Lyme Disease; LMR: Lymphocytic Meningo-Radiculopathy; MS: Multiple Sclerosis; PD: Parkinson's Disease; RMSF: Rocky Mountain Spotted Fever; STARI: Southern tick-associated rash illness: TBRF: Tick-borne relapsing fever; XFS: Chronic Fatigue Syndrome.

Keywords

Alzheimer's disease; Amyotrophic lateral sclerosis; Axonal polyneuropathy or encephalopathy; Brain chemistry; Lyme disease; Chronic Lyme disease; Multiple sclerosis; Neurotransmitters disruptions; Parkinson's disease; Post-traumatic Lyme disease syndrome; Memory impairment.

Background

In the U.S., Lyme disease (LD) was discovered in 1975 after a mysterious outbreak of what appeared to be juvenile rheumatoid arthritis in children who lived there. Also called juvenile idiopathic rheumatoid arthritis (JIRA), the disease is the most common form of arthritis in children and adolescents. (Juvenile, in this context, refers to an onset before age 16 while idiopathic refers to a condition with no defined cause, and arthritis is the inflammation of the joint's synovium.) JIA is an autoimmune, non-infective, inflammatory joint disease of more than 6 weeks duration in children less than 16 years of age. The disease commonly occurs in children from the ages of 1 to 6, but it may develop as late as 15 years of age. It is a subset of arthritis seen in childhood, which may be transient and self-limited or chronic. It differs significantly from arthritis commonly seen in adults (osteoarthritis, rheumatoid arthritis), and other types of arthritis present in childhood that are chronic conditions such as, for example, psoriatic arthritis and ankylosing spondylitis. It affects about one in 1,000 children in any given year, with about one in 10,000 having a more severe form. However, there is no relationship between that outbreak of JIRA and LD for which it was originally mistaken and misnamed.

Introduction

In the U.S., LD was diagnosed as a separate condition for the first time in 1975 in Old Lyme, Connecticut. It is the most commonly occurring vector-borne infection spread by ticks in the Northern Hemisphere and the sixth most commonly reported notifiable infectious disease. Annually, it is estimated to affect about 300,000 people in the U.S. and 85,000 people in Europe.

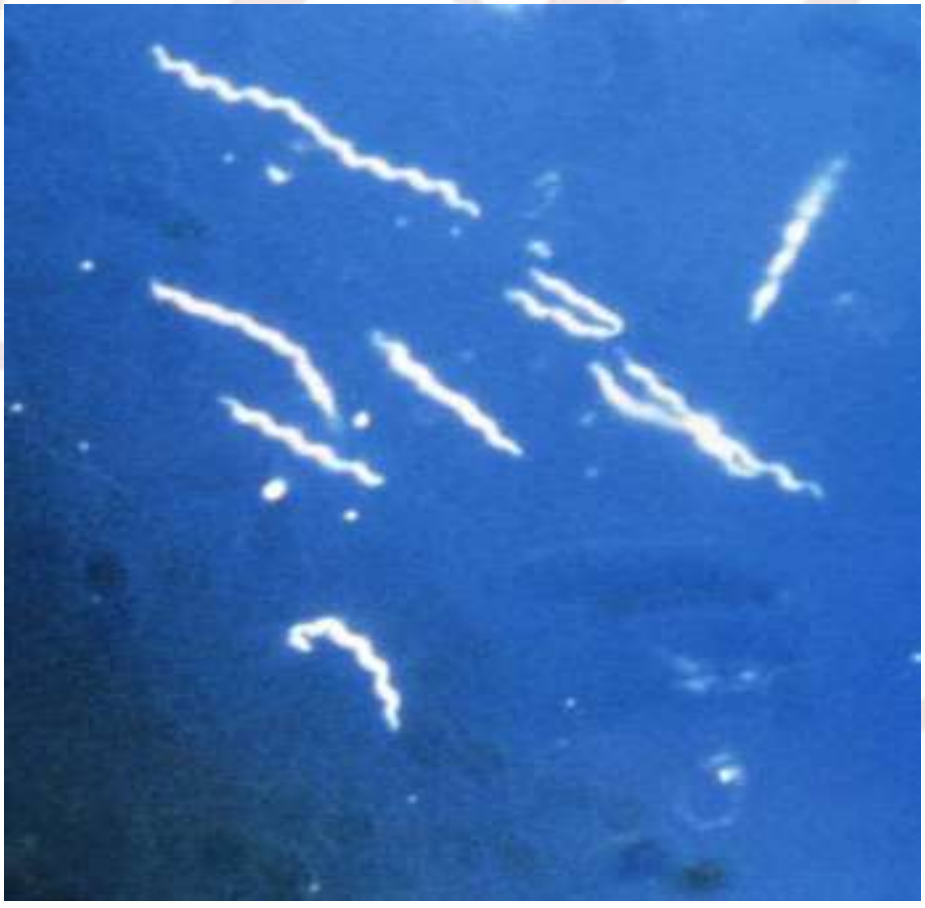
A brief history of LD

Borrelioses have long existed! The existence and evolution of Borrelia burgdorferi in the U.S. have been reconstructed, suggesting it dates back more than 60,000 years, long before the arrival of humans in the Americas. The first known man (named Otzi) having the disease was identified about 5,300 years ago from the residual bacterial DNA recovered from his cadaver. However, the manifestations of the disease had been described, albeit sparsely, in Europe since the end of the 19th century. Thus, in 1883, a German physician in Breslau, Alfred Buchwald, described it as a skin anomaly which resembled what we today would call atrophic chronic acrodermatitis (ACA) but did not link it to a tick bite. That borreliosis was different from LD

proper as the dominant borrelia was different from those found in Eurasia or North America. In 1909, a Swedish dermatologist, Arvid Afzelius had noted the apparition of a ring-like lesion following a bite by the Ixodes tick and called it erythema migrans. A few years thereafter, an Austrian dermatologist, called it a "migrant chronic erythema".

In 1922, French physicians Garin and Bujadoux associated this dermatologic lesion with an incidence of paralysis "...more or less serious, at times deadly, consecutive to tick bites (Ixodes hexagonus)". They attributed this lymphocytic meningo-radiculopathy (LMR, a combination of meningitis and polyneuritis) to a "virus" to be found not in the blood but in nervous tissues. Subsequently, in 1934, in Germany, the erythema migrans was described in association with arthritis. In 1944, again in Germany, Alfred Bannwarth also associated the arthritis with LMR. The corresponding disease was therefore named the Garin-Boujadoux-Bannwarth syndrome (GBBS).

Later, in 1951, the beneficial effects of penicillin pointed to the bacterial origin of these other expressions of the disease. It is only in 1975, in Lyme. Connecticut, U.S.A. that the mysterious JIRA outbreak in children was recognized and misnamed LD. In 1981, Wilhelm "Billy" Burgdorferi first described the Borrelia burgdorferi pathogen (Figure 1).



Source: Scott Bauer, U.S. Department of Agriculture, Agriculture Research Service

Figure 1: Borrelia bacteria, the principal causative agents of Lyme disease

Symptomatology

Signs and symptoms of LD

LD is caused by Borrelia burgdorferi and other closely related species of bacteria. The infection is commonly contracted through a tick sting (although most people think of it as a bite, but technically it is a sting), which may not even be noticed. Within the first few days to weeks of the infection, a rash called erythema migrans (EM) may develop. It is generally red and circular but, as it subsides, it may present a "bull's-eye" pattern. Although the rash is a major sign of acute LD, many infected people do not get it, that is, while the rash is a definite indication for LD, its absence does not mean the absence of LD. During this early stage, it is referred to as "localized" because it has not yet spread to other areas of the body and seems like the flu (aches, pains, and swollen glands). Like other short-term infections, it may last a few weeks. It is easier to diagnose than treat. The recent history of the patient's exposure and a total body skin exam for rash are followed by a round of antibiotics after which the affected individual is usually (but not generally) well again within 4-6 weeks.

The initial culprit

There are two different LD pathogens, namely (1) Borrelia burgdorferi, which can be transmitted by either the tick Ixodes scapularis or/and the tick Ixodes pacificus (Figure 2) and (2) Borrelia mayonii transmitted by the tick Ixodes scapularis only. In 1982, Dr Burgdorfer discovered the tick-borne spirochete (a cousin of the syphilis family of diseases) as the long sought-after cause of LD and related disorders in the U.S. and Europe.

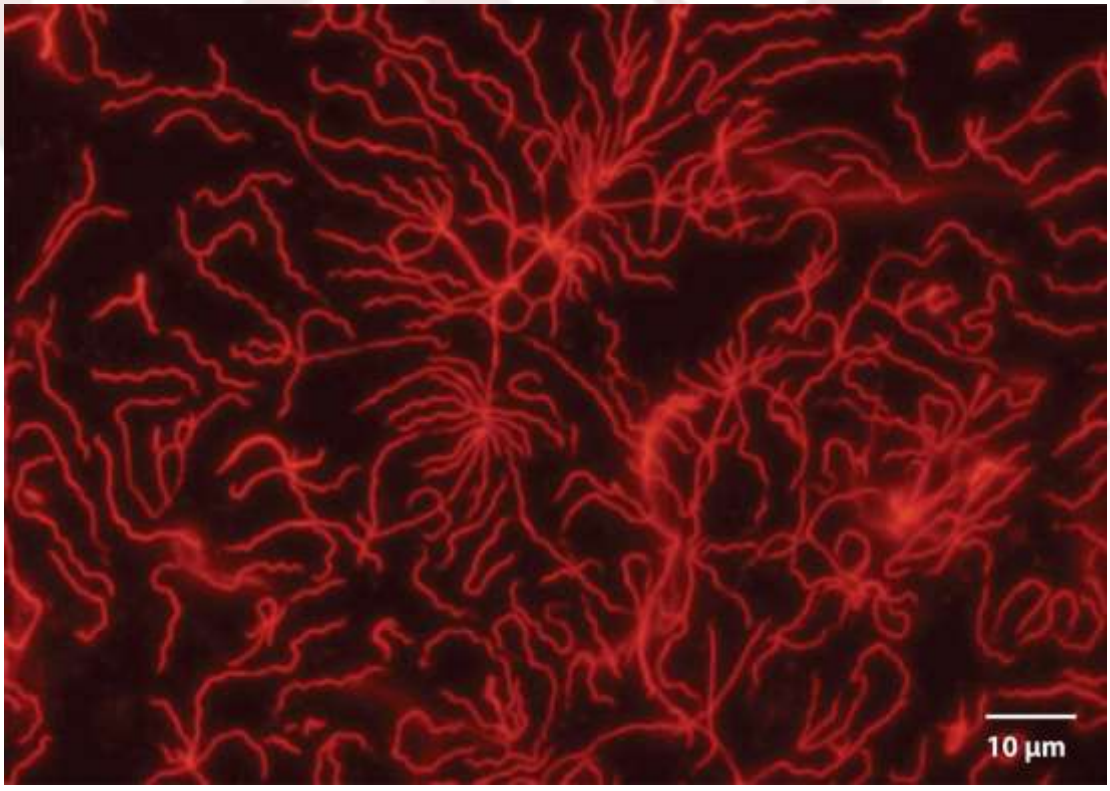


Figure 2: Live Borrelia burgdorferi sensu stricto stained with wheat germ agglutinin (Alexa Fluor®)

Clinical manifestations of the disease

Most often, LD is evidenced by a characteristic rash (called erythema migrans, EM) that is accompanied by nonspecific symptoms (e.g., fever, malaise, fatigue, headache, myalgia, and arthralgia). The incubation period from infection to onset of EM is typically 7-14 days but can be as short as 3 days or as long as 30 days. Some infected persons have no recognized illness in that their infection cannot be ascertained by a blood test. Others may manifest only nonspecific symptoms (e.g., fever, headache, fatigue, and myalgia) that preclude a definitive diagnosis.

If untreated or inadequately treated within weeks to months, the infection can progress from a "localized" or "early-disseminated" disease to a persistent disease (also called "late-disseminated" disease) that is manifested by intermittent swelling and pain of one or some joints (usually, the large, weight-bearing joints such as the knee). Accompanying diseases may be chronic axonal polyneuropathy (CAP), or encephalopathy accompanied by cognitive disorders such as sleep disturbance, fatigue, and personality changes. LD morbidity can be severe, chronic, and disabling. An ill-defined "post-Lyme disease syndrome" occurs in some persons after treatment for Lyme disease. Fortunately, LD is rarely, if ever, fatal.

Really,... what is LD?

Strictly speaking, LD is the disease transmitted to humans by the bite of infected black-legged ticks Ixodes scapularis (Figures 3 and 4), which transmits the bacterium Borrelia burgdorferi (less frequently, Borrelia mayonii). It can also be caused by Borrelia burgdorferi carried out by the western black-legged tick Ixodes pacificus.

From the site of inoculation, LD disseminates along three routes: cutaneous, lymphatic, and blood-borne. Early dissemination of the infection usually occurs days to weeks after the appearance of a solitary or secondary EM lesions. It can also manifest as a disease of the musculoskeletal system, the nervous system, or the heart. Musculoskeletal manifestations can include migratory pains of the muscles or the joints with or without joint swelling. Early neurologic manifestations include lymphocytic meningitis; cranial neuropathy, especially facial nerve palsy; and radiculoneuritis. Cardiac manifestations are rare but can include myocarditis and transient atrioventricular block of varying degree. There may be three possible manifestations: muscular, neurologic, and cardiologic.

Source: (U.S.) Centers for Disease Control & Prevention (CDC&P), Public Health Image Library PHIL #6631

Figure 3: The adult deer tick Ixodes scapularis, the primary vector of Lyme disease in Central and Eastern U.S. but also elsewhere such as in Europe

According to some scientists, some individuals with Borrelia burgdorferi can remain seropositive (that is, still have the bacteria in their blood) for decades, even after successful treatment with antibiotics and resolution of their clinical symptoms. By contrast, others believe that this is the normal humoral immune response and not a continuation of active chronic infection, especially if all key symptoms remain at bay.

Figure 4: Adult deer tick, Ixodes scapularis

The developmental stages of Ixodes scapularis

The developmental stages of Ixodes scapularis are illustrated in Figure 5. Beginning from the left and progressing to the right, these stages include the unfed larva, engorged larva, unfed nymph, engorged nymph, unfed male and female, and lastly the partially engorged female (at the bottom right). The nymphal stages are those of importance at the beginning of LD.

The life cycle of the deer tick Ixodes scapularis

The lifecycle of the Ixodes scapularis tick is diagrammed in Figure 6 following the seasons. The egg is laid down in Spring and, after one month, transforms itself into a larva, which feeds once every two days preferably on a mouse host from Summer to Fall. It then hibernates through the Winter season till the next Spring when it transforms itself into a nymph. Until the next Fall, the nymph feeds itself 3-4 times a day, preferably on a mouse host.

Figure 5: Developmental stages of Ixodes scapularis

Sexual distinction then occurs between Fall and Winter when the nymphs become adults and mating takes place. Feeding is now once a day with a preferred shift from a mouse to a deer host. Following hibernation, and three weeks into Spring, eggs are deposited and the adults die. The biannual cycle then repeats itself.

On the other hand, the Ixodes persulcatus tick which spreads the Borrelia afzelii and Borrelia garinii spirochetes is thought more likely to bite humans in its adult stage, with the nymphs seemingly reluctant to bite humans. The larva is usually infected (<5%) and is unlikely to either feed on humans or transmit infection to humans.

A new view on LD

A new view on LD has recently been advanced in which rodents (not deers) hold the key to the annual risk of contracting LD. The ecological determinants of LD over a 13-year period in southeastern New York, a hot zone for the disease, were examined. Combining field data with computer simulations, trends in inter-annual variation were analyzed, yielding two powerful predictors of entomological risk of LD in any given year: (1) the abundance of tick hosts (white-footed mice and chipmunks) in the previous year and (2) the abundance of acorns (which sustain the rodents) two years out. These findings have upset the long-held view that deer and climate are the best indicators of disease risk.

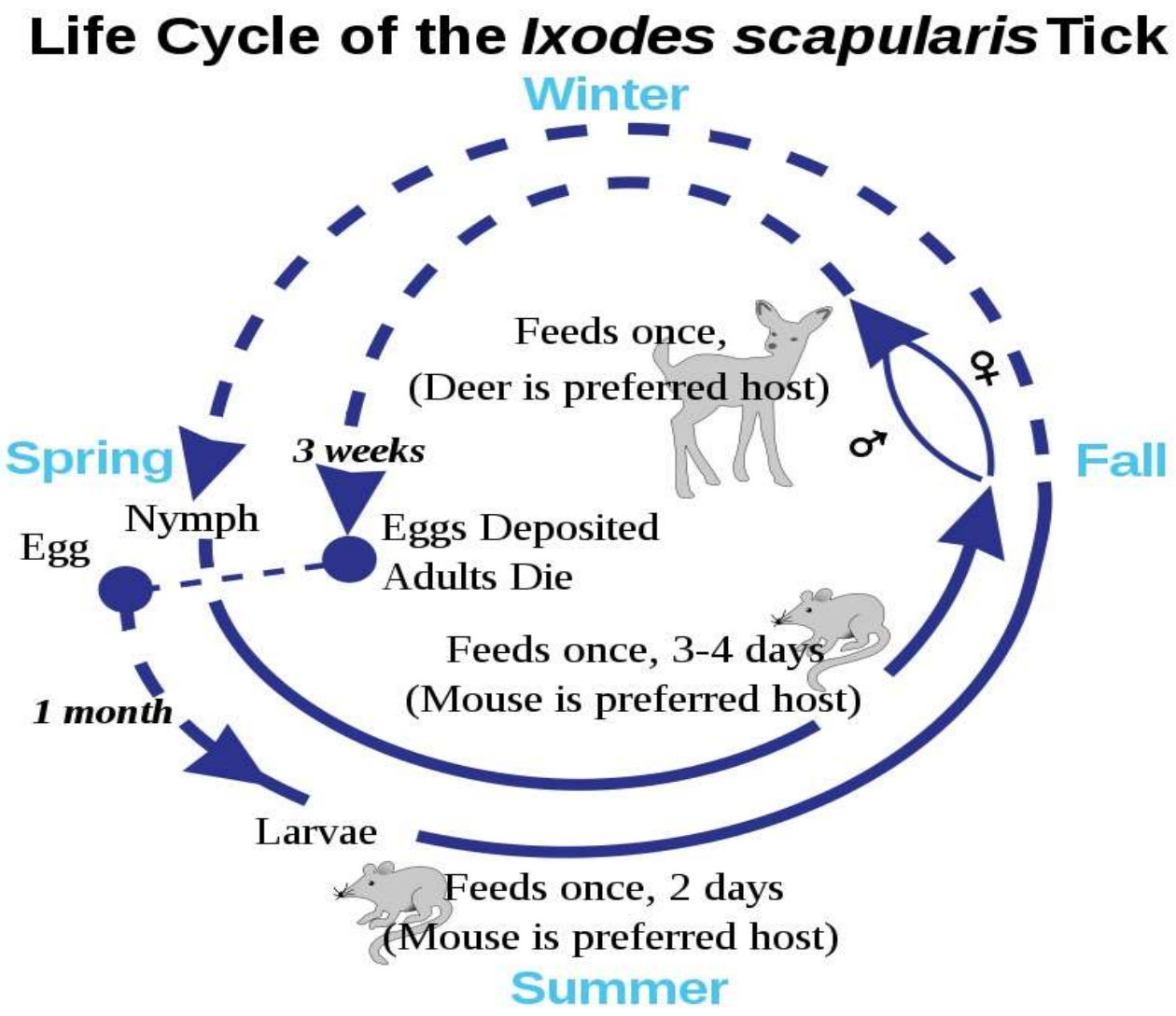


Figure 6: Life cycle diagram of the deer tick *Ixodes scapularis*

In this view, Ixodes scapularis larvae hatch in midsummer, and acquire infection after feeding on an infected mouse or other small animal. Larvae detach after several days of feeding, morph into nymphs, and enter a nearly year-long dormant stage. After another round of feeding, nymphs fall off and molt into adults, which prefer the blood of larger mammals. While larvae and nymphs can acquire and transmit infection, people are most likely to contract LD from nymphs.

While none of the climate variables influenced nymphal infection prevalence, higher temperatures in the previous year and precipitation patterns in the current year had weak, though unexpected, effects on total density and density of infected nymphs. It is thought that higher temperatures keep tick populations down, but the models showed them increasing both total density and density of infected nymphs.

Although tick survival is expected to rise with precipitation, the models found the highest tick numbers at intermediate precipitation levels. These inconsistencies can be explored by incorporating other variables with documented effects into the approach outlined here. Also, surprisingly, the researchers found that even a 3-fold variation in deer numbers had no impact on subsequent nymph abundance.

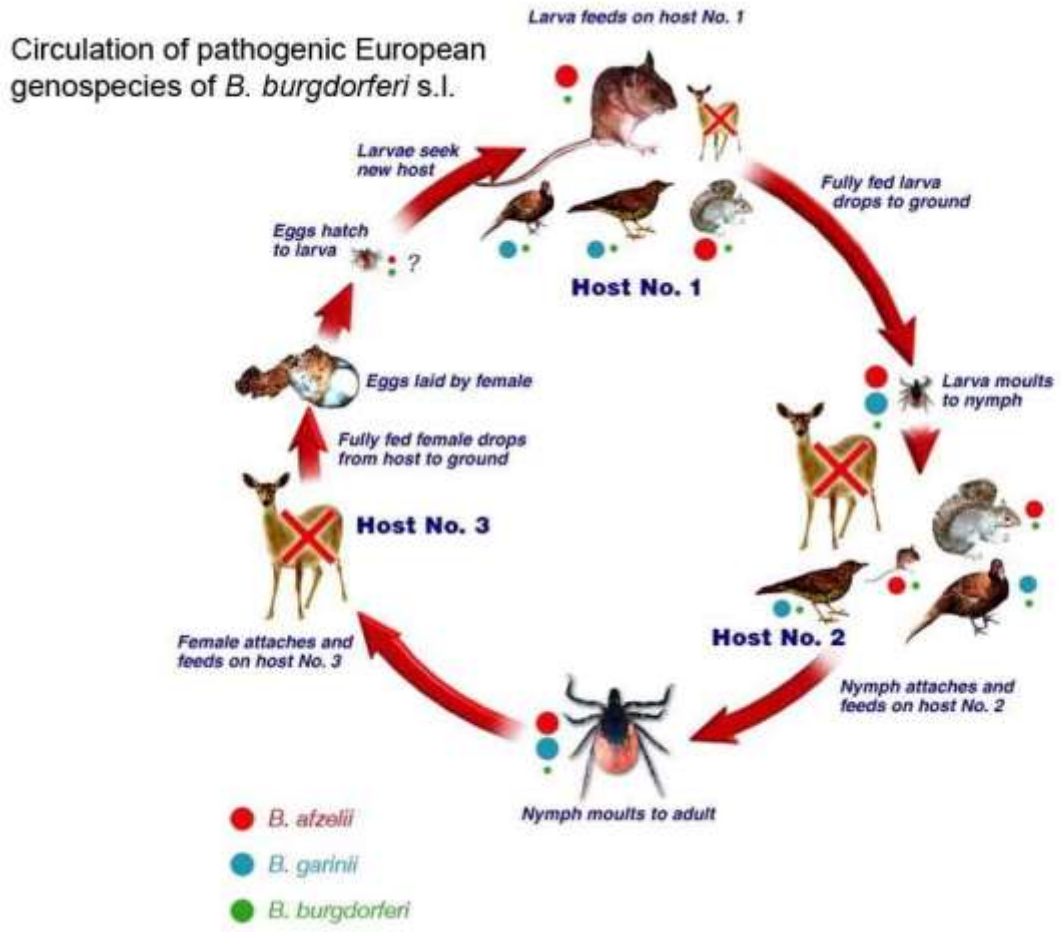


Figure 7: Circulation of pathogenic European genospecies of Borrelia burgdorferi sensu lato

Density of infected nymphs—the principal determinant of LD risk—varied significantly from year to year, fueled mostly by large fluctuations in total nymph density that, in turn, depended mostly on fluctuations in abundance of acorns, mice, and chipmunks. Interestingly, though chipmunk densities are generally lower than mice, their numbers were the best predictor of total nymph density in the subsequent year, likely reflecting their inferior grooming skills. Overall, the results found that acorns were the best predictor of LD risk—stemming from their crucial role in supporting white-footed mice, chipmunks, and likely other small animals, which provide large reservoirs for Borrelia burgdorferi. Acorns will not be a universal predictor of risk, the researchers acknowledge, since the disease can occur in areas without oaks. But the strength of these findings suggests that the observed link between increased LD risk and high rodent densities indicates that important food sources—or predators—of the rodent hosts of nymphs will be valuable predictors of disease risk.

What is chronic Lyme disease?

Chronic Lyme disease (CLD), also called “late” Lyme, is much different than the localized Lyme disease I alluded to above. The term “chronic Lyme disease” has been used to describe people with different illnesses.

While the term is sometimes used to describe illness in patients with LD, it has also been used to describe symptoms in people who have no clinical or diagnostic evidence of a current or past infection with *Borrelia burgdorferi*. Because of the confusion in how the term CLD is employed, and the lack of a clearly defined clinical definition, many experts in this field do not support its use.

Based on the combined expertise of its membership and its systematic review of 250 peer-reviewed papers in the international scientific literature, the International Lyme and Associated Diseases Society (ILADS) issued on 16 December 2019, a concept paper. That publication provided its "evidence-based" definition of CLD as a *"multi-system illness with a wide range of symptoms and/or signs that are either continuously or intermittently present for a minimum of six months. The illness is the result of an active and ongoing infection by any of several pathogenic members of the Borrelia burgdorferi sensu lato complex (Bbsl). The infection has variable latency periods and signs and symptoms may wax, wane, and migrate".* ILAD further subdivided CLD into two sub-categories (a) "untreated" CLD (CLD-U) and previously treated CLD (CLD-PT), the latter requiring that "CLD manifestations persist or recur following treatment and are present continuously or in a relapsing/remitting pattern for a duration of six months or more". It is hoped that use of this CLD definition, if accepted, will promote a better understanding and facilitate future research of this infection.

CLD is not an official diagnosis

The term "chronic Lyme disease" actually is not an official diagnosis. It categorizes patients who suffer from a wide variety of vector-borne diseases together with the primary and secondary infections. The most common co-infections include: *anaplasmosis, babesiosis*, *bartonellosis*, *Borreliosis*, Colorado tick fever, *ehrlichiosis* (my acronym AB3CE), and perhaps many others. Beyond AB3CE, other common primary co-infections that have been linked with CLD include chlamydia pneumonia, coltivirus disease, mycoplasma pneumonia, Powassan virus disease, Q-Fever (my acronym AC2MPQ), and perhaps others. CLD more accurately represents the wide range of infections patients can experience. It better illustrates the complexity and uniqueness of the condition burdening every single patient. Often, these patients will have a resistant *Borrelia* infection that is almost always followed by multiple other infections.

In CLD, signs of illness may appear gradually over time or may have never entirely subsided with earlier treatment. In some cases, major physical or emotional stress brings the disease to the forefront. Problems like joint pain, horrible fatigue, and trouble thinking may develop and become more debilitating over time.

Blood tests often miss this type of Lyme since the acute phase is past. Further, the infection can impair or even suppress the immune system so the body does not create enough antibodies to fight the infecting bacteria. The real source of poor health can remain a mystery, yet, the symptoms may be right there. When *Borrelia burgdorferi* is in the system for a while, it burrows its way into organs and tissues. This can give degenerative health issues that look like something else.

Signs and symptoms of CLD

The four most common symptoms are (my acronym **(FJAB)**:

• **Debilitating chronic fatigue (also called chronic fatigue syndrome, CFS):** Its cause is not known. It is due in part to the taxing of the immune system because the bacteria trigger the immune cells to produce chemicals called "cytokines" that generate inflammation to fight the infection. CLD is a last-resort diagnosis when a reason for it cannot be found. Though it may feel reassuring to get a diagnosis, the wrong one

can stand in the way of getting better. Nonetheless, for many (not all) people, the root cause of CFS could be undetected CLD.

• **Joint pain:** Irrespective of a previous healthy condition and active way of life, Lyme damages the joints accompanied by crippling pain. The bacteria colonize the joints and connective tissues (cartilage and ligaments), bind to collagen in these tissues, and break it down, destroying it as they multiply. Further, they interfere with the body's efforts to regenerate these tissues. Note that the bacteria are completely dependent on the individual for nutrients. Since they cannot make certain proteins, they siphon them from the joints leaving the ligaments brittle and the joints stiff and inflamed. It appears (but is not) arthritis.

• **Autoimmune Diseases:** The immune system attacks the tissues and the bacteria do whatever they can to protect themselves from it. They have learned to hide in the host's cells. This happens because some of the proteins in the bacteria look like the host's own. The immune system then starts to view healthy cells as foreign invaders and it attacks them thinking it gets rid of the Lyme. In some individuals, the problem can escalate to rheumatoid arthritis in which the body attempts to stomp out joint cells where the bacteria live. Separately, the tails of the bacteria look like the cells of the host's myelin sheath (these are the cells that cover and insulate your nerves). The bacteria can trick the immune system into attacking the healthy myelin cells and even block the body's ability to regenerate the myelin. Without this protective nerve covering, inflammation takes place with intense pain, a process that looks exactly like, but is not, multiple sclerosis (MS).

• **Brain fog and cognitive issues:** The bacteria are able to cross the protective blood-brain barrier (BBB) and create new problems that may mimic other diseases. After getting into the brain, they inhabit glial cells and neurons, and render them dysfunctional, leading to anxiety and depression. They may also interfere with the host's neurotransmitters or nerve messengers, disrupting the production and use of dopamine, and causing what can look like (but is not!) Parkinson's disease (PD). Further, the microbes can increase the production of another neurotransmitter (called octopamine) that can accumulate in the brain, raise blood pressure, and cause headaches. Lastly, when this insidious microorganism is killed, it sheds parts of itself as endotoxins, which may interfere with the brain's chemistry. A buildup of toxins can give intense brain fog and memory issues.

The potential for co-infections varies by location as well as exposure to various species of ticks. Since there is a potential for patients to experience several tick bites, including those of different species, additional microorganisms are also commonly transmitted via tick bites. Many of these other infections complicate treatment and increase the risk for auto-immune diseases, depending on the patient's genetic background. To repeat, patients with CLD never have just the one infection by Borrelia burgdorferi. They also have multiple co-infections that have gone untested and incompletely or totally untreated for extended periods of time. Like for viral, fungal, and parasitic infections, antibiotics are not effective for many of these infections that entered the body in the initial tick bite.

What is chronic Lyme disease complex?

Chronic Lyme disease complex (CLDC) is not just CLD. It involves the spirochete which causes *Lyme*, *Borrelia burgdorferi*, and also associated co-infections, which enter the body with it in the initial tick bite (my earlier acronyms AB3CE and C2MPQ). CLDC can also include secondary infections that occur as a result of a compromised immune state. This is important to keep in mind because antibiotics do not work against viral infections and, similarly, fungal infections require anti-fungal medication, and so on. The secondary and

co-infections must be identified in order for treatment to be effective. This is the number one reason why antibiotics alone cannot be used to treat these patients.

Further, as indicated in the sub-title of my book, Borrelia has a number of mechanisms for invading, evading, and distracting the immune system. It is capable of burrowing and spreading throughout most of the body's tissues, including the blood-brain barrier (BBB). Antibiotics cannot easily pass the BBB, but Borrelia and other infections attack the brain and central nervous system unimpeded. It implants itself in tissues and within individual cells to avoid being consumed and lysed by the immune system. The microbe is also adept at countering the adaptive immune system through constant variation in its surface proteins, or antigens, a feat enabled by its complex single chromosome and its circular DNA plasmids. Usually, by the time the body can create antibodies to target *Borrelia*, its surface has already changed so much that the new antibodies are no longer effective. In serum, *Borrelia* has the ability to inactivate C3, a protein marker which would normally trigger the immune response for free-floating microbes. When *Borrelia* does find a place to settle down and multiply, the microbe secretes a protein mesh called "biofilm" which shields it and its progeny from direct exposure to many antibiotics and other compounds that might otherwise harm the infection.

Thus, while the spirochete *Borrelia* is responsible for causing primary LD, it is usually not the only factor to consider when approaching treatment for CLDC. When a tick bites, various bacteria and parasites enter the wound besides just *Borrelia*. These simultaneous infections, called "co-infections", can include Babesia, Human herpes virus (HHV)-6, Epstein-Barr virus (EBV), and Rocky Mountain Spotted Fever (RMSF), to name just a few. They are able to gain a firmer foothold in the body and potentially become chronic since *Borrelia* excels at distracting and depressing the host immune system. "Secondary infections" can also be picked up after the initial bite due to a depressed immune response from the infected person. The result is a condition that is chronic and can linger for months or even years, typically worsening over time without proper treatment. The simultaneous presence of multiple different infections in the body seriously complicates any potential treatment, increases the risk for autoimmune diseases depending on the patient's genetic background, and can also be a precursor to various cancers. Treating these infections in their totality is essential to full recovery and for the patient to achieve health, which is why often antibiotics alone do not work clinically.

Again, to repeat, patients with CLDC never have just the one infection by the spirochete Borrelia burgdorferi. They also have multiple co-infections and secondary infections that have gone untested or/and insufficiently treated or even untreated for extended periods of time. Like for viral, fungal, and parasitic infections, antibiotics are not effective for many of these infections that entered the body in the initial tick bite.

What is post-treatment Lyme disease syndrome?

My purpose here is not to dwell on the Lyme alphabet soup, but it is important to distinguish between chronic Lyme disease (CLD) and post-treatment Lyme disease syndrome (PLDS). (PLDS was previously, though incorrectly, recognized as CLD, but the medical community no longer recognizes that diagnosis and it is now considered an outdated term.) Some healthcare providers claim that PLDS is caused by persistent infection, but this is not believed to be true because of the inability to detect infectious organisms after standard treatment. Rather, PLDS describes the continued ongoing resistance to antibiotics and continued symptoms. Further, PLDS does not define CLDC, which encompasses the breadth of infections present, regardless of whether standard-of-care treatment for Lyme Borrelia was given or not.

While CLD and PLDS may seem similar, they are very different from each other and knowing the difference may be essential for achieving symptom remission. I did not say cure …only symptom remission! PLDS is a diagnosis given to patients who continue to experience symptoms like depression, fatigue, and muscle/joint aches after being diagnosed and treated for LD with the recommended antibiotic regimen. In fact, the Lyme borrelia may not always be present in a CLD patient as the term refers to a wide range of tick-borne plus other secondary infections and complications that the patient may be dealing with. This infection load and the complications associated with it vary greatly from patient to patient. Like in most other areas of medicine wherein "one size does not fit all", a more personalized approach often leads to an improved patient outcome.

The problem with PLDS is that conventional medicine only recognizes Lyme borrelia as a causative factor, but provides no treatment for the primary and secondary infections and other complicating genomic risks. On top of that, PLDS only covers patients who have already been treated for LD. The PLDS diagnosis completely fails to address patients who are suffering from the many different infections seen clinically.

PLDS is always characterized by a Lyme borreliosis infection. While it may involve many other infections including viral, bacterial, and fungal, those infections are controversially not recognized as part of PLDS. These various infections are rarely tested properly and, while approximately 10% of those who are diagnosed and treated for LD with the standard antibiotic regimen will experience PLDS, there is no conventionally accepted treatment as the symptoms are expected to subside over time.

Dr. Burgdorfer was critical of the path LD research had taken over the past 30 years. He believed that *Borrelia burgdorferi* was a persistent infection, and that the current serological testing methodologies needed to be started anew without any knowledge of the results sought after.

Etiology

As indicated earlier (see also Table 1 in Appendix), LD can be caused in three separate ways by:

- Borrelia burgdorferi carried by the black-legged tick Ixodes scapularis;
- Borrelia burgdorferi carried by the western black-legged tick Ixodes pacificus; and
- Borrelia mayonii also carried by the blacked-legged tick Ixodes scapularis.

Note also that *Borrelia burgdorferi* can be transmitted by five species of Ixodes ticks within the Ixodes family. In North America, they are: *Ixodes scapularis, Ixodes pacificus, and Ixodes cookei*. In Europe and Asia, they are *Ixodes ricinus and Ixodes persulcatus*, respectively.

When discussing LD, it is helpful to identify which tick transmits which pathogen causing the disease. Often, the variety (1) above is the one generally discussed. However, varieties (2) and (3) also deserve consideration, particularly since they recognize two different ticks and two different pathogens.

Also, the same tick can carry several pathogens at the same time and cause several possible co-infections. For example, the black-legged tick Ixodes scapularis can transmit no less than seven pathogens and cause no less than six different diseases! Likewise, the western black-legged tick Ixodes pacificus can carry three different pathogens and cause three other infectious diseases, two of which (anaplasmosis, LD) being the same as for the tick *Ixodes scapularis*.

The multiplicity of pathogens transmitted by the several ticks further shows the number of other possible types of co-infectious diseases. While

geography and season may help in limiting the number of such possibilities, the task of reaching an accurate diagnosis for any given tick-borne pathogen remains daunting.

Can LD be inherited?

No! LD cannot be inherited. However, the risk of certain complications of the condition may be influenced by inherited genetic factors, but the inheritance pattern is unknown.

The terrible invader, evader... and great imitator

Borrelia is a terrible invader and evader in addition to being a great imitator:

- **Invader:** Borrelia is capable of burrowing and spreading throughout most of the body's tissues, including the blood-brain barrier (BBB) – that highly selective, semi-permeable border that separates the circulating blood from the brain and extracellular fluid in the central nervous system (CNS). The BBB allows the passage of some molecules such as glucose, water, and amino acids that are crucial to neural function but antibiotics cannot easily cross it. However, it allows Borrelia and other infections like Babesia to attack the brain and the CNS unimpeded. Borrelia implants itself in tissues and even within individual cells to avoid being consumed and lysed by the immune system. When it does find a place to settle down and multiply, the microbe secretes a protein mesh called a “biofilm” which shields it and its progeny from direct exposure to many antibiotics and other compounds that might otherwise harm the infection.

- **Evader:** The microbe is also adept at countering the adaptive immune system. Through several mechanisms, including a constant variation in its surface proteins (or antigens), it can distract and evade the immune system. Usually, by the time the body can create antibodies to target and neutralize Borrelia, its surface has already changed so much that the new antibodies are no longer effective. In serum. Borrelia has the ability to inactivate C3, a protein marker which would normally trigger the immune response for free-floating microbes.

- **Imitator:** LD is one of the most misunderstood and widely growing illness in the country and abroad. Because its symptoms resemble those of so many other diseases (and because the medical community remains misinformed or incompletely informed), it has been recognized as "the great imitator". It can mimic the symptoms of fibromyalgia, chronic fatigue syndrome (CFS), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS) or Lou Gehring disease, Parkinson's disease (PD), Alzheimer's disease (AD), as well as more than some 350 other diseases.

LD has also generally been misinterpreted. As a consequence, stricken patients are not diagnosed correctly and may not receive the treatment necessary to restore their health.

The Appendix provides a brief look at tick-borne diseases of the United States. My aim there is showing the multiplicity of such diseases and the associated difficulties in reaching the correct diagnosis.

Summary and conclusions

• Lyme disease, also known as Lyme borreliosis, is an infectious disease caused by the Borrelia bacterium. It was originally mistaken for juvenile rheumatoid arthritis. There are three varieties depending on the pathogen transmitted and the carrier tick.

• While Borrelia is responsible for causing primary Lyme disease, it is usually not the only factor. When one or several ticks perhaps from different species do bite, various bacteria and parasites also enter the wound causing other opportunistic infections. The overall disease caused by both the primary and secondary infections is referred to as chronic Lyme disease (or syndrome). The potential for co-infections varies by location as well as exposure to various species of ticks.

• Chronic Lyme disease can cause a significant burden on patients more so than Lyme disease alone. The infection can impair or even suppress the immune system so the body does not create enough antibodies to fight the infecting bacteria.

• When Borrelia burgdorferi is in the system for a while, it burrows its way into organs and tissues creating degenerative health issues. Many of these other infections complicate treatment and increase the risk for autoimmune diseases depending on the patient's genetic background. They can also be a precursor to various cancers and even neurodegenerative diseases.

• The four most common symptoms of chronic Lyme disease are: debilitating fatigue; joint inflammation and pain; autoimmune diseases; and brain fog and cognitive problems.

• Post-treatment Lyme disease syndrome is purportedly caused by persistent infection, but this is not believed to be true because we are unable to detect infectious organisms after standard treatment. Rather, it describes the continued ongoing resistance to antibiotics and continued symptoms.

• Through a number of mechanisms, the microbe is adept at countering, distracting, and evading the adaptive immune system. It is also capable of crossing the blood-brain barrier, infect the brain, and attack the central nervous system.

• Lyme cannot be inherited. However, the risk of certain complications of the condition may be influenced by inherited genetic factors, but the inheritance pattern is unknown.

• Two powerful predictors of entomological risk of LD in any given year were found to be: (1) abundance of tick hosts (white-footed mice and chipmunks) in the previous year and (2) abundance of acorns (which sustain the rodents) two years out. These findings upset the long-held view that deer and climate are the best indicators of disease risk.

• There are various tick-borne diseases encountered across the U.S. Their causal bacteria and the corresponding vector ticks have been summarized in Appendix 1 (Table 1). A brief look at tick-borne diseases in the U.S. can be found in Appendix 2.

Appendix 1
Ticks of the U.S. and their characteristics

The various ticks encountered in the U.S. and their associated diseases are summarized in Table 1, showing the tick common name, the bacterium, the vector carrying it, and the diseases transmitted, where found, and what are the high-risk seasons. (The pathogens of in interest and the diseases caused by them are highlighted in red font.)

Tick common name	Vector	Bacterium	Disease(s) caused	Where found in the U.S.?	High-risk seasons
Black-legged	***Ixodes scapularis***	**o *Borrelia burgdorferi* o *Borrelia mayonii*** o *Anaplasma phagocytophilum* **o *Borrelia miyamotoi*** o *Ehrlichia chaffensis, Ehrlichia ewingii, Ehrlichia muris eauclairensis* o *Babesia microti* o *Powassan* virus	***o Lyme disease*** ***o Lyme disease*** (newly discovered form) o Anaplasmosis o A form of relapsing fever o *Ehrlichiosis* o *Babesiosis* o Powassan virus disease	East, upper Midwest, and mid-Atlantic	Spring, Summer, Fall (any time when temperatures are above freezing) All tick life stages bite humans, but lymphs and adults are most commonly found on people
Western black-legged	***Ixodes pacificus***	o *Anaplasma phagocytophilum* **o *Borrelia burgdorferi*** o *Borrelia miyamotoi* (very likely)	o *Anaplasmosis* ***o Lyme disease*** o *Borrelia miyamotoi* disease (a form of relapsing fever)	Pacific Coast States	Larvae and nymphs often feed on lizards, birds, and rodents. Adults feed on deers. All life stages bite humans, but lymphs and adult females are most often reported
American dog	***Dermacentor variabilis***	o *Francisella tularensis* o *Rickettsia rickettsii*	o Rocky mountain spotted fever	East of the Rocky Mountains. Also, limited areas of the Pacific Coast	Bites most likely by adult females
Brown dog	***Ripicephalus sanguineous***	*Rickettsia rickettsii*	Spotted mountain fever	Southwestern and Western States along the border with Mexico	May bite humans and other mammals
Ground hog (aka Woodchuck)	***Ixodes cookei***	Powassan virus	Powassan virus disease	Throughout Eastern half of U.S. States	Feed on a variety of warm-blooded animals, including groundhogs, skunks, squirrels, raccoons, foxes, weasels, and occasionally on people and domestic animals
Golf coast	***Amblyomma maculatum***	*Rickettsia parkeri*	*Rickettsia parkeri rickettsiosis* (a	Southeastern, mid-Atlantic States, and	Larvae and nymphs feed on birds and small

			form of spotted fever)	southern Arizona	rodents. Adults feed on deers and other wildlife
Lone star (Very aggressive. Adult female distinguished by white dot or "lone star" on her back.) Note: Allergic reactions may be associated with consumption of red (mammalian) meat.	***Amphylomma americanum***	*o Ehrlichia chaffensis* *o Ehrlichia ewingii* *o Francisella tularensis* o Heartland virus o Bourbon virus o Southern tick	o *Ehrlichiosis* o *Ehrlichiosis* o *Tularemia* o Heartland virus disease o Bourbon virus disease o Southern tick-associated rash illness (STARI)	East, more common in the South	Early Spring through late Fall. Lymphs and adult females most frequently bite humans
Rocky mountain wood	***Dermacentor andersoni***	*o Rickettsia rickettsii* o Colorado tick fever virus *o Francisella tularensis*	o Rocky Mountain spotted fever o Colorado tick fever disease o *Tularemia*	Rocky mountain States	Larvae and nymphs feed on small rodents. Adults feed primarily on rodents and are primarily associated with pathogen transmission to humans
Soft	***Ornithodoros Spp***	*o Borrelia hermsii* *o Borrelia turicatae*	Tick-borne relapsing fever (TBRF)	Throughout the western half, rustic cabins, cave exposure	Emerge at night and feed briefly while people are sleeping

Source: Adapted from CDC&P (2018).

Table 1: Ticks of the United States and their characteristics

Appendix 2
A brief look at tick-borne diseases in the U.S.

In the U.S., several ticks carry pathogens that can cause human diseases including:

Anaplasmosis: This disease is transmitted to humans by tick bites primarily from the black-legged tick (Ixodes scapularis) in the northeastern and upper midwestern U.S. and the western black-legged tick (Ixodes pacificus) along the Pacific coast.

Babesiosis: This disease is caused by microscopic parasites that infect red blood cells. Most human cases of babesiosis in the U.S. are caused by Babesia microti, which is transmitted by the black-legged tick (Ixodes scapularis) and is found primarily in the Northeast and upper Midwest.

Borrelia miyamotoi: The bacterium Borrelia miyamotoi has recently been described as a cause of illness in the U.S. It is transmitted by the black-legged tick (Ixodes scapularis) and has a range similar to that of Lyme disease.

Bourbon virus disease: The virus has been identified in a limited number of patients in the Midwest and Southern U.S. At this time, we do not know if the virus might be found in other U.S. areas.

Colorado tick fever: This disease is caused by a virus transmitted by the Rocky Mountain wood tick (Dermacentor andersoni). It occurs in the Rocky Mountain states at elevations of 4,000 to 10,500 feet.

Ehrlichiosis: This disease is transmitted to humans by the lone star tick (Ambylomma americanum). It is found primarily in the south-central and eastern U.S.

Heartland virus disease: Cases of the disease caused by this virus have been identified in the Midwestern and Southern U.S. Studies suggest that Lone Star ticks can transmit the virus. It is unknown if the virus may be found in other areas of the U.S.

Lyme disease: The bacterium Borrelia mayonii has recently been described as a cause of illness transmitted by black-legged ticks (Ixodes scapularis). Borrelia mayonii is a new species that is the only species besides Borrelia burgdorferi known to cause Lyme disease in North America.

This disease is transmitted by the black-legged tick (Ixodes scapularis) in the Northeastern U.S. and upper Midwestern U.S. and the Western black-legged tick (Ixodes pacificus) along the Pacific coast.

Powassan disease: This disease is transmitted by the black-legged tick (Ixodes scapularis) and the groundhog tick (Ixodes cookei). Cases have been reported primarily from Northeastern states and the Great Lakes region.

Rickettsia parkeri rickettsiosis: This disease is transmitted to humans by the Gulf Coast tick (Amblyomma maculatum).

Rocky Mountain spotted fever (RMSF): This disease is transmitted by the American dog tick (Dermacentor variabilis), Rocky Mountain wood tick (Dermacentor andersoni), and the brown dog tick (Rhipicephalus sangunineus) in the U.S. The brown dog tick and other tick species are associated with RMSF in Central and South America.

Southern tick-associated rash illness (STARI): This disease is transmitted via bites from the lone star tick (Ambylomma americanum) found in the Southeastern and Eastern U.S.

Tick-borne relapsing fever (TBRF): It is transmitted to humans through the bite of infected soft ticks. TBRF has been reported in 15 states: Arizona, California, Colorado, Idaho, Kansas, Montana, Nevada, New Mexico, Ohio, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming) and is associated with sleeping in rustic cabins and vacation homes.

Tularemia: This disease is transmitted to humans by the dog tick (Dermacentor variabilis), the wood tick (Dermacentor andersoni), and the lone star tick (Amblyomma americanum). Tularemia occurs throughout the U.S.

364D rickettsiosis (alternative proposed name: Rickettsia phillipi): This disease is transmitted to humans by the Pacific Coast tick (Dermacentor occidentalis). This is a new disease that has been found in California.

Table 2 summarizes the several ticks causing the illnesses listed above. In particular, it is seen that LD bacteria are Borrelia burgdorferi and Borrelia mayonii that are both transmitted through the Ixodes scapularis tick. That disease can also be transmitted by the Ixodes pacificus tick.

Vector	Bacterium	Disease(s) transmitted
Ambyloma americanum (lone star tick)	*o Heartland virus*	o *Ehrlichiosis* *o Rickettsia parkeri rickettsiosis* o Southern Tick-Associated Rash Illness (STARI) o *Tularemia*
Ambyloma maculatum		o *Rickettsia parkeri rickettsiosis*
Dermacentor andersoni (wood tick)		o Colorado tick fever o Rocky Mountain spotted fever o *Tularemia*
Dermacentor occidentalis		o *364D rickettsiosis* (aka *Rickettsia philippi*)
Dermacentor variabilis (dog tick)		o Rocky Mountain spotted fever o *Tularemia*
Ixodes cookei (groundhog tick)		o Powassan disease
Ixodes pacificus (black-legged tick)		o *Anaplasmosis* o **Lyme disease**
Ixodes scapularis (black-legged tick)	*o Borrelia burgdorferi* *o Borrelia mayonii* *o Borrelia miyamotoi* o *Babesia microti X*	o **Lyme disease** o **Lyme disease** o *Anaplasmosis* o *Babesiosis* o Powassan disease
Lone star tick	*o Heartland virus*	o *Ehrlichiosis*
Rhipicephalus sanguineus		o Rocky Mountain spotted fever
Soft tick		o Tick-borne relapsing fever (TBRF)

Source: Adapted and augmented from "Tick-borne Diseases of the United States:

A Reference Manual for Health Care Providers", Fifth Edition (2018).

Table 2: Tick-associated diseases of the United States

An abridged geographical risk for the above diseases across the U.S. is also shown in Table 3 below:

U.S. Region	Pathogen	Disease
Eastern	*o Ehrlichiosis*	Southern tick-associated rash illness (STARI).
Gold coast	*o Rickettsia parkeri rickettsiosis*.	Powassan disease.
Individual States: Arizona, California, Colorado, Idaho, Kansas, Montana, Nevada, New Mexico, Ohio, Oklahoma, Oregon, Texas, Utah, Washington, and Wyoming		Tick-borne relapsing fever (TBRF).
Midwestern	*o Bourbon virus* o *Heartland virus*	
Northeastern	*o Anaplasmosis* *o Babesia*	**Lyme disease**
Pacific coast	*o Anaplasmosis* *o 364D rickettsiosis (aka Rickettsia phillipi).*	
Rocky Mountain States (at elevations of 4,000 to 10,500 feet)	*o Colorado tick fever* *o Rocky Mountains spotted fever (RMSF)* *(Note: RMSF is also present in Central and South America.)*	
South Central	*Ehrlichiosis.*	

Southern	*o Bourbon virus* *o Heartland virus*	STARI
Throughout U.S.	*o Tularemia*	
Upper midwestern	*o Anaplasmosis* *o Babesia,*	**Lyme disease**

Table 3: Geographical risks of tick-borne diseases across the U.S.

References

1. Agre F and Schwartz R (1993). "The value of early treatment of deer tick bites for the prevention of Lyme disease". Am J Dis Child 147(9):945-7.
2. Aguero-Rosenfeld ME, Nowakowski J, and Bittker S, (1996). "Evolution of the serologic response to Borrelia burgdorferi in treated patients with culture-confirmed erythema migrans". J Clin Microbiol 34(1):1-9.
3. Albert S, Schulze J, Riegel H, and Brade V (1999). "Lyme arthritis in a 12-year-old patient after a latency period of 5 years". Infection 27(4-5):286-8.
4. Alder J, Mitten M, Jarvis K, et al. (1993). "Efficacy of clarithromycin for treatment of experimental Lyme disease in vivo". Antimicrob Agents Chemother 37(6):1329-33.
5. Al-Robaiy S, Dihazi H, Kacza J, et al. (2010). "Metamorphosis of Borrelia burgdorferi organisms - RNA, lipid and protein composition in context with the spirochetes' shape". J Basic Microbiol 50(Suppl 1):S5-17.
6. Altman DG (2009). "Missing outcomes in randomized trials: addressing the dilemma". Open Med 3(2):51-3.
7. Asch ES, Bujak DI, Weiss M, et al. (1994). "Lyme disease: an infectious and post-infectious syndrome". J Rheumatol 21(3):454-61.
8. Aucott J, Morrison C, Munoz B, et al. (2009). "Diagnostic challenges of early Lyme disease: lessons from a community case series". BMC Infect Dis 9:79.
9. Aucott JN, Rebman AW, Crowder LA, Kortte KB (2013). "Post-treatment Lyme disease syndrome symptomatology and the impact on life functioning: is there something here?" Qual Life Res 22(1):75-84.
10. Bacon RM, Kugeler KJ, and Mead PS. (2008). "Surveillance for Lyme disease--United States, 1992-2006". MMWR Surveill Summ 57(10):1-9.
11. Barbour AG and Restrepo BI (2000). "Antigenic variation in vector-borne pathogens". Emerg Infect Dis 6(5):449-57.
12. Cairns V and Godwin J. (2005). "Post-Lyme borreliosis syndrome: A meta-analysis of reported symptoms". Int J Epidemiol 34(6):1340-5.
13. Cameron DJ (2008). "Severity of Lyme disease with persistent symptoms: insights from a double - blind placebo-controlled clinical trial". Minerva Med 99(5):489-96.
14. Cerar D, Cerar T, Ruzic-Sabljic E, et al. (2010). "Subjective symptoms after treatment of early Lyme disease". Am J Med 123(1):79-86.
15. Clark RP and Hu LT. (2008). "Prevention of Lyme disease and other tick-borne infections". Infect Dis Clin North Am 22(3):381-96.
16. Corapi KM, White MI, Phillips CB, et al. (2007). "Strategies for primary and secondary prevention of Lyme disease". Nat Clin Pract Rheumatol 3(1):20-5.
17. Costello CM, Steere AC, Pinkerton RE, and Feder HM Jr (1989). "A prospective study of tick bites in an endemic area for Lyme disease". J Infect Dis 159(1):136-9.
18. Coyle PK and Schutzer SE. (1991).

"Neurologic presentations in Lyme disease". Hosp Pract 26(11):55-66.discussion 66, 69-70 [Taylor & Francis Online].

19. Duray PH (1989). "Clinical pathologic correlations of Lyme disease". Rev Infect Dis 11(Suppl 6): S1487-93.
20. Duray PH, Yin SR, Ito Y, et al.(2005)."Invasion of human tissue ex vivo by Borrelia burgdorferi". J Infect Dis 191(10):1747-54.
21. Eikeland R, Mygland A, Herlofson K, and Ljostad U. (2011). "European neuroborreliosis: Quality of life 30 months after treatment". Acta Neurol Scand 124(5):349-54.
22. Embers ME, Ramamoorthy R, and Philipp MT (2004). "Survival strategies of Borrelia burgdorferi, the etiologic agent of Lyme disease". Microbes Infect 6(3):312-18.
23. Fallon BA, Levin ES, Schweitzer PJ, Hardesty D (2010). "Inflammation and central nervous system Lyme disease". Neurobiol Dis 37(3):534-41.
24. Frank C, Fix AD, Pena CA, and Strickland GT (2002). "Mapping Lyme disease incidence for diagnostic and preventive decisions", Maryland. Emerg Infect Dis 8(4):427-9.
25. Fymat AL (2017a). "Parkinson's disease and other movement disorders: a review", Journal of Current Opinions in Neurological Science 2(1):316-43.
26. Fymat AL (2017b). "Neurological disorders and the blood-brain barrier: 2. Parkinson's disease and other movement disorders", Journal of Current Opinions in Neurological Science 2(1)362-83.
27. Fymat AL (2018a). "Blood-brain barrier permeability and neurological diseases", Journal of Current Opinions in Neurological Science (Editorial).2(2):411-4.
28. Fymat AL (2018b). "Alzheimer's disease: a review", Journal of Current Opinions in Neurological Science 2(2);415-36,
29. Fymat AL (2018c). "Regulating the brain's autoimmune system: the end of all neurological disorders?" Journal of Current Opinions in Neurological Science 2(3):475-9.
30. Fymat AL (2018d). "Alzheimer's disease: prevention, delay, minimization and reversal", Journal of Clinical Research in Neurology 1(1):1-16.
31. Fymat AL (2018e). "Harnessing the immune system to treat cancers and neurodegenerative diseases", Journal of Clinical Research in Neurology 1(1):1-14.
32. Fymat AL (2018f). "Is Alzheimer's an autoimmune disease gone rogue"", Journal of Clinical Research in Neurology 2(1):1-4.
33. Fymat AL (2018g). "Dementia treatment: where do we stand?", Journal of Current Opinions in Neurological Science 3(1):1-3.
34. Fymat AL (2018h). "On dementia and other cognitive disorders", Journal of Clinical Research in Neurology 1(2):1-14.
35. Fymat AL (2018i). "Is Alzheimer's a runaway autoimmune Disease? and how to cure it?", Newsletter European Union Academy of Sciences Annual Report (2018).
36. Fymat AL (2019a). "Is Alzheimer's a runaway autoimmune disease? and how to cure it?" Proceedings of the European Union Academy of Sciences, Newsletter, pages 379-83.
37. Fymat AL (2019b). "Dementia: a review", Journal of Clinical Psychiatry and Neuroscience 1(3): 27-34.
38. Fymat AL (2019c). "The pathogenic brain", Journal of Current Opinions in Neurological Science 3(2);669-71.
39. Fymat AL (2019d). "On the pathogenic hypothesis of neurodegenerative diseases", Journal of Clinical Research in Neurology 2(1):1-7.
40. Fymat AL (2019e). "Dementia with Lewy bodies: a review", Journal of Current Opinions in Neurological Science 4(1);15-32.

41. Fymat AL (2019f). “Our two interacting brains: etiologic modulations of neurodegenerative and gastroenteric diseases”, Journal of Current Opinions in Neurological Science 4(2):50-4.
42. Fymat AL (2019g). “What do we know about Lewy body dementias?” Journal of Psychiatry and Psychotherapy (Editorial) 2(1)-013:1-4. doi:10.31579/JPP.2019/018.
43. Fymat AL (2019h). “Viruses in the brain...? any connections to Parkinson's and other neurodegenerative diseases?” Proceedings of the European Union Academy of Sciences, 2019 Newsletter.
44. Fymat AL (2019i). “Alzhei… Who? demystifying the disease and what you can do about it”, Tellwell Talent Publishers, pp 235, 2019. ISBN: 978-0-2288-2420-6 (Hardcover); 978-0-2288-2419-0 (Paperback).
45. Fymat AL (2020a). “Recent research developments in Parkinson's disease”, Current Opinions in Neurological Science 5(1):12-30.
46. Fymat AL (2020b). “The role of radiological imaging in neurodegenerative disorders”, Journal of Radiology and Imaging Science 1(1):1-14.
47. Fymat AL (2020c). “Parkin...ss...oo...nn: elucidating the disease and what you can do about it”, ISBN: 978-0-2288-2874-7 (Hardcover); 978-0-2228-2875-4, Tellwell Talent Publishers,
48. Fymat AL (2020d), “Lyme disease: The dreadful invader, evader and imitator, and what you can do about it”, ISBN: 978-0-2288-3198-3; 978-0-2288-3199-0, Tellwell Talent Publishers.
49. Gerber MA, Zemel LS, and Shapiro ED. (1998). “Lyme arthritis in children: clinical epidemiology and long-term outcomes”. Pediatrics 102(4 Pt 1):905-8.
50. Hartiala P, Hytonen J, Suhonen J, et al. 2008). “Borrelia burgdorferi inhibits human neutrophil functions”. Microbes Infect 10(1):60-8.
51. Haupl T, Hahn G, Rittig M, et al. (1993). “Persistence of Borrelia burgdorferi in ligamentous tissue from a patient with chronic Lyme borreliosis”. Arthritis Rheum 36(11):1621-6.
52. Hayes E. (2003). “Lyme disease”. Clin Evid (10):887-99.
53. Hodzic E, Feng S, Freet KJ, and Barthold SW (2003). “Borrelia burgdorferi population dynamics and prototype gene expression during infection of immunocompetent and immunodeficient mice”. Infect Immun 71(9):5042-55.
54. Institute of Medicine, (US) Committee on Lyme Disease and Other Tick-Borne Diseases (2011): “The state of the science”. In: “Critical needs and gaps in understanding prevention, amelioration, and resolution of Lyme and other tick-borne diseases: the short-term and long-term outcomes: workshop report”. National Academies Press; Washington, DC, USA.
55. Johnson L, Wilcox S, Mankoff J, and Stricker RB (2014). “Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey”. Peer J 2:e322.
56. Johnson RC, Kodner CB, Jurkovich PJ, and Collins JJ (1990). “Comparative in vitro and in vivo susceptibilities of the Lyme disease spirochete Borrelia burgdorferi to cefuroxime and other antimicrobial agents”. Antimicrob Agents Chemother 34(11):2133-6.
57. Klempner MS, Noring R, and Rogers RA (1993). “Invasion of human skin fibroblasts by the Lyme disease spirochete, Borrelia burgdorferi”. J Infect Dis 167(5):1074-81.
58. Kraiczy P, Skerka C, Kirschfink M, et al. (2002). “Immune evasion of Borrelia burgdorferi: insufficient killing of the pathogens by complement and antibody”. Int J Med Microbiol 291(Suppl 33):141-6.

59. Krause PJ, Telford SR 3rd, Spielman A, et al. (1996). "Concurrent Lyme disease and babesiosis: Evidence for increased severity and duration of illness". JAMA 275(21):1657-60.
60. Lawrence C, Lipton RB, Lowy FD, and Coyle PK (2012). "Seronegative chronic relapsing neuroborreliosis". Eur Neurol 35(2):113-17.
61. Liang FT, Jacobs MB, Bowers LC, and Philipp MT (2002). "An immune evasion mechanism for spirochetal persistence in Lyme borreliosis". J Exp Med 195(4):415-22.
62. Livengood JA and Gilmore RD Jr. (2006). "Invasion of human neuronal and glial cells by an infectious strain of Borrelia burgdorferi". Microbes Infect 8(14-15):2832-40.
63. Logar M, Ruzic-Sabljic E, Maraspin V, et al. (2004). "Comparison of erythema migrans caused by Borrelia afzelii and Borrelia garinii." Infection 32(1):15-9.
64. Logigian EL, Kaplan RF, and Steere AC. (1990). "Chronic neurologic manifestations of Lyme disease".N Engl J Med 323(21):1438-44.
65. Pollina DA, Sliwinski M, Squires NK, and Krupp LB (1999). "Cognitive processing speed in Lyme disease".Neuropsychiatry Neuropsychol Behav Neurol 12(1):72-8.
66. Stanek G and Reiter M (2011). "The expanding Lyme borrelia complex: clinical significance of genomic species?" Clin Microbiol Infect 17(4):487-93.
67. Steere AC, Bartenhagen NH, Craft JE, et al. (1983b). "The early clinical manifestations of Lyme disease". Ann Intern Med 99(1):76-82.
68. Stricker RB, Johnson L (2007). "Lyme disease: a turning point". Expert Rev Anti Infect Ther 5(5):759-62 [Taylor & Francis Online].
69. Szczepanski A and Benach JL (1991). "Lyme borreliosis: host responses to Borrelia burgdorferi". Microbiol Rev 55(1):21-34.
70. Thaisetthawatkul P and Logigian EL (2002). "Peripheral nervous system manifestations of Lyme borreliosis". J Clin Neuromuscul Dis 3(4):165-71.
71. Vazquez M, Sparrow SS, andShapiro ED. (2003). "Long-term neuropsychologic and health outcomes of children with facial nerve palsy attributable to Lyme disease". Pediatrics 112(2): e93-7.
72. Weder B, Wiedersheim P, Matter L, et al. (1987). "Chronic progressive neurological involvement in Borrelia burgdorferi infection". J Neurol 234(1):40-3.