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Review Article

Lyme Carditis: A Rare but Lethal Condition (A Practical Review of Lyme Disease: Past, Present, and Future)

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Abstract

Lyme disease was first identified in the late 1970s by a consortium of scientists investigating individuals residing in Old Lyme, Connecticut (in the Northeastern U.S.) who experienced symptoms of unknown origin. The scientists from Yale School of Medicine and the Connecticut State Department of Health discovered that a tick bite caused the patients' symptoms. It was later determined that the causative pathogen was Borrelia. The disease is endemic in the Northern Hemisphere with infection rates spiking in the warmer and summer months.

In 70–80% of infected individuals, the disease is characterized by the hallmark (painless) erythema migrans (EM) rash or lesion, occurring about 3–30 days post-tick bite. In the early stages after infection, symptoms may include myalgia, arthralgia, regional lymphadenopathy, headache, and fever. Symptoms may progress to secondary skin lesions, malaise, headache, neck stiffness, chills, and arthralgia. If left untreated, neurological and cardiac-related complications can occur (such as meningitis, subtle encephalitis, cranial neuritis, neuropathy, ataxia, myelitis, presyncope, syncope, dyspnea, arrhythmia or angina, accompanied by pyrexia and myalgia). Lyme carditis, although rare, can be fatal. Also, specific psychological symptoms and disorders can be aggravated or provoked by Lyme disease.

To combat the *Borrelia* pathogen, specific oral or intravenous (IV) antibiotics are prescribed. Most Lyme disease cases respond favorably with a 10–28 days course of antibiotics. However, in 10–20% of the treated cases, post-treatment Lyme disease syndrome (PTLDS) develops—the etiology and treatment of which is currently undecided.

The most effective prevention against Lyme disease is avoiding a tick-bite, wearing appropriate clothing, using anti-tick sprays, and performing a body inspection, preferably with a mirror. Novel treatment regimes—as yet not medically-recognized or endorsed—consist of herbal remedies and herbal-drug combinations. There is no vaccine against the disease, although research into a universal vaccine continues.

Keywords: *Deer; Fever; Malaise; Outdoors; Rash; Tick*

Abbreviations

ASD: Autism Spectrum Disorder; EM: Erythema Migrans; ECM: Erythema Chronicum Migrans; EIA: Enzyme Immunoassay; EPA: Environmental Protection Agency; FDA: U.S. Food and Drug Administration; HGA: Human Granulocytic Anaplasmosis; IFA: Indirect Fluorescent Antibody; IgM: Immunoglobulin M; IgG: Immunoglobulin G; IV: Intravenous; NIAID: National Institute of Allergy and Infectious Diseases; OspA: Outer Surface Protein A; OspB: Outer Surface Protein B; OspC: Outer Surface Protein C; POWV: Powassan Virus; PTLDS: Post-treatment Lyme Disease Syndrome; SCID: Severe Combined Immunodeficiency

Introduction

General information

Lyme disease, also referred to as Lyme borreliosis, is a tick-borne bacterial infection. It is prevalent in woody and grassy areas where ticks of the Ixodes genus are commonly found. The disease is endemic in the Northern Hemisphere, including parts of the United States, Europe, and Asia [1]. Infection rates spike between June and September [2]. This is the period when human outdoor activities are at their peak, and coincide with the specific stages of the tick's life cycle. During this period, ticks are more likely to attach to a human host.

A historical perspective

In 1975, two mothers from Old Lyme, Connecticut suffered arthritis and juvenile arthritis within their families, as well as other families in their town. These family members approached the Connecticut State Department of Health and the Yale School of Medicine for help. Allan C. Steere (MD, a first-year fellow), Stephen E. Malawista (MD, Department Head from the Rheumatology Department of the Yale School of Medicine), David R. Snydman, and Francis M. Steele (the latter two being attached to the Connecticut State Department of Health), led the investigation regarding the cause of the affliction of these Old Lyme residents. The investigators performed extensive physical examinations and blood tests on the patients. A comprehensive history of each patient was collected by interviewing the treating physicians and the patients' family members. Nearly 25% of the patients who were studied by the investigating team reported a skin lesion with an expanding bull's–eye pattern about four or more weeks before the onset of arthritis. The lesion description matched that of erythema chronicum migrans (ECM) or erythema migrans (EM). This lesion was described in a European study and thought to be caused by a then-unknown infectious agent [1–3].

In 1976, new cases emerged during the summertime of that year. The investigating team referred to the condition as "Lyme arthritis" (named for the town) and concluded that EM was its early diagnostic hallmark [1,2].

In 1978, after a thorough epidemiological analysis, an association between deer ticks and Lyme disease was confirmed [2,3]. Steere., *et al.* (1978) continued to study the disease's various clinical manifestations through the late 1970s and early 1980s. Their studies showed that Lyme disease was able to spread deep into the skin and affect the nervous system [2–5], heart [2,6], and joints [2,7–9]. Although the researchers established an association between the deer ticks and Lyme disease, the bacterial agent responsible for the infection remained elusive until the early 1980s.

Burgdorfer., *et al.* (1982) isolated the Spirochete bacterium responsible for Lyme disease from the deer tick for the first time [10]—later named *Borrelia burgdorferi* (*B. burgdorferi*) [11,12]. The researchers dissected Ixodes ticks obtained from Shelter Island, New York (a hotspot for Lyme disease). Gram-negative spirochetes were isolated from the midgut region of these ticks. Indirect immunofluorescence revealed that only the serum extracted from Lyme disease patients reacted positively with the bacteria and not the serum from control patients. Thus, by the early 1980s, the link between Lyme disease and *B. burgdorferi* was firmly established [2,10]. The mystery of the strange arthritic cases from Old Lyme, Connecticut was solved by identifying the vector and bacterial agent directly responsible for the infection.

Discussion

Epidemiology of Lyme disease

Although the number of Lyme disease cases reported annually in the U.S. is about 33,000 (Table 1), it is believed that many cases go unreported or undiagnosed. Thus, by some experts' opinions, the actual disease burden may be 10 times higher [1,13].

Country	Year	Number of cases reported
USA [13]	2018	33,666
Canada [14]	2018	1487
Europe [16]	Per year estimate	65,400
Disease burden data from Asia was not available		

Table 1: *Number of lyme disease cases reported across the United States, Canada, and Europe.*

Most of the U.S. Lyme disease cases are reported as coming from the New England, Mid-Atlantic, and Upper Midwest Regions [1]. Lyme disease is on the rise in Canada as well. In 2009, 144 cases were reported, to an upsurge of 1487 cases in 2018 [14]. Researchers consider climate change to be a chief contributor to the northward spread of Lyme disease. The temperature at the higher altitudes has witnessed an increased due to global warming. Regions that were unaffected earlier have now become vulnerable to the tick vectors and the reservoir of animal hosts [15].

Due to the absence of uniform case-reporting protocols across Europe and Asia, tracking Lyme disease cases in these continents has been problematic. Germany, Austria, Slovenia, and Sweden reported the greatest number of cases on the European continent [16]. Cases have also been reported in China [17], Mongolia [18,19], Japan [20], Korea [20], Russia [19,21], Nepal [22], and India [23].

Region-specific tick species and the pathogens they harbor are listed in Table 2 (below). The list is for representative purposes only and not exhaustive. Different vectors, the various pathogen species they carry, and the regions where they are found across different geographies are depicted below.

Country	*Borrelia* spp.	Tick (vector) species
USA [13,24]	*B. burgdorferi, B. mayonii* (rarely)	*Ixodes scapularis* (Northeastern, Mid-Atlantic, and Northcentral United States) *Ixodes pacificus* (Western Pacific Coast)
Canada [14]	*B. burgdorferi*	*Ixodes scapularis* (Southeastern and Southcentral Regions of Canada) *Ixodes pacificus* (British Columbia)
Europe [24,25]	*B. afzelii* *B. garinii* *B. burgdorferi sensu stricto* *B. spielmanii*	*Ixodes ricinus*
Asia [1,25]	*B. garinii* *B. afzelii*	*Ixodes persulcatus*

Table 2: *Tick and Borrelia spp. found in different regions.*

Signs and symptoms

Clinically, Lyme disease is categorized as an early-localized, early-disseminated, or late-stage disease, depending on the presentations and symptoms [26].

Early–localized disease: In this stage, nearly 70–80% of the patients present with the characteristic EM rash. The eruption of the rash occurs about 3–30 days after a tick bite [13]. The bull's-eye pattern of the rash is due to the pathogen's movement through the skin [26]. The rash is painless, and pruritis is absent. Patients may experience symptoms, such as myalgia, arthralgia, regional lymphadenopathy, headache, and fever [13].

Early–disseminated disease: In this stage, patients may present with secondary skin lesions and symptoms of malaise, headache, neck stiffness, fever, chills, and arthralgia. If untreated, the disease may precipitate neurological complications, such as meningitis, subtle encephalitis, cranial neuritis, neuropathy, ataxia, or myelitis—indicating pathogen progression into the central and peripheral nervous systems [26]. Patients may also exhibit cardiac symptoms, such as light-headedness, fainting, shortness of breath, heart palpitations, or chest pain, accompanied by fever and body ache. Such symptoms are suggestive of Lyme carditis [13]. Although most Lyme carditis patients recover within six weeks post-treatment, about eleven carditis-related fatalities have been reported globally between 1985 and 2019 [13].

Late-stage disease: Patients may present with arthritis-like symptoms during this stage—indicating the pathogen has spread to the bones and joints. Late-stage symptoms manifest more than a month after the initial infection. Typically, large joints (particularly the knee) are most affected. Neurological symptoms worsen during this stage [26]. According to Lantos., *et al.* (2020), earlier reports indicated a 60% incidence rate of Lyme arthritis in untreated patients. However, with enhanced diagnosis in the early stages and surveillance of the disease, newer data have suggested that the incidence rate has declined to about 30% [27].

Comorbidities

According to Bransfield (2018), there is growing evidence of a connection between Lyme disease and psychological disorders. Lyme disease gives rise to metabolic and immune responses, gradually leading to a range of neuropsychiatric symptoms and conditions: autism spectrum disorder (ASD), generalized anxiety disorder, eating disorder, sleep disorder, schizoaffective disorder, developmental disorder, decreased libido, cognitive impairment, dissociative episode, bipolar disorder, anxiety disorder, derealization, opioid addiction (and other addiction disorders), violent behavior, dementia, seizure, anhedonia, depersonalization, depression, and suicide [28].

Diagnosis

The early diagnosis of Lyme disease remains challenging and is based primarily on clinical findings. Clinical diagnosis, rather than laboratory testing, is recommended in patients with suspected tick exposure who present one or more characteristic EM lesions. The National Institute of Allergy and Infectious Diseases (NIAID) (2019) supports this rationale, owing to the seronegative results obtained at this stage [29]. Laboratory confirmation of Lyme disease is determined by two-step serum antibody testing. This procedure involves an enzyme immunoassay (EIA) or indirect fluorescent antibody (IFA) test followed by immunoglobulin M (IgM) and immunoglobulin G (IgG) immunoblots. Alternatively, a modified two-tiered protocol may be employed in which two different EIAs are performed in tandem or one after the other [13,27].

Laboratory testing involves detecting antibodies; however, this testing consumes more time, allowing the infection to progress. Scientists are trying to identify specific biomarkers of Lyme disease to facilitate its earlier diagnosis. Molins., *et al*. (2015) developed a metabolic profile of specific biomarkers of Lyme disease found in the serum of early-stage Lyme disease patients. These biomarkers are a potential diagnostic aid with high specificity and sensitivity in detecting early-stage Lyme disease [29,30].

Transmission

According to the U.S. Centers for Disease Control and Prevention (CDC): "The lifecycle of black-legged ticks (*Ixodes scapularis* and *Ixodes pacificus*) generally lasts two years. During this time, they go through four life stages: egg, six-legged larva, eight-legged nymph, and adult. After the eggs hatch, the ticks must have a blood meal at every stage to survive" [13]. The pathogen contamination may occur at any stage of the life cycle.

The tick's life cycle is synchronous with seasonal changes. Adult female ticks lay eggs in the spring, hatching in late summer, and forming larvae. Larvae typically attach to small hosts, such as the white-footed mouse. The nymphs are formed during spring to early summer when the larvae molt. The nymphs are minuscule, eventually molting into adult ticks in the fall.

Adult ticks attach to, feed, and mate on large animals like the deer [13]. Transmission to human hosts occurs during the nymph or adult stage. When attached to the human host, the ticks require 36–48 hours or more to transmit Lyme disease—by transmitting the *Borrelia* pathogen to the host. Nymphs are notably smaller than adult ticks; hence, they are more likely to go unnoticed [13].

Reinfection and coinfection

In a mouse model, Bhatia., *et al.* (2018) reported that the reinfection rate with the same strain of *Borrelia* pathogen was low [31]. The researchers determined that pre-existing antibodies from previously infected mice could attenuate the effects of the same strain of *Borrelia* pathogen when the tick fed on the mice's blood [29,31]. However, reinfection of the mice with a different strain of *Borrelia* pathogen was observed [29,31], suggesting that patients who have had Lyme disease in the past could become reinfected if they are bitten by a tick harboring a different strain of *Borrelia* pathogen.

Studies by Lantos., *et al*. (2020) suggested that, in addition to *B. burgdorferi*, the *Ixodes* ticks may also harbor other pathogens, such as *Anaplasma phagocytophilum* (rickettsial bacterium), *Babesia microti* (protozoan parasite), *B. miyamotoi*, *B. mayonii*, *Ehrlichia muris eauclairensis* (earlier known as *Ehrlichia muris*-like agent), and Powassan virus (POWV), also known as deer tick virus. Among these, *Anaplasma phagocytophilum*—the causative agent of human granulocytic anaplasmosis (HGA)—and *Babesia microti*—the causative agent of babesiosis—are most commonly associated with *B. burgdorferi*, with coinfection ranging between 2–11.7% [27]. Their research was indeterminate regarding whether Lyme disease coinfection with HGA presents more severe complications than Lyme disease alone. Nevertheless, Lyme disease coinfection with babesiosis was found to increase the severity of early-stage Lyme disease. On the other hand, Lyme disease does not appear to affect the severity of babesiosis [27].

Immunity

Lyme disease elicits a humoral response for clearing the spirochete. Seiler and Weis (1996) found infected mice serum defensive when passively shared with a naive mouse earlier or at the infection period [38]. Mice with severe combined immunodeficiency (SCID) phenotype—deficient of mature B cells and T cells—are fractionally protected from infection by transmitting whole splenocytes and B cells, but not T cells. Even though serum antibodies for flagellin and outer surface protein C (OspC) occur early in the infection, spirochetes persevere in the presence of these antibodies [38,39].

The late-stage disease is due to a more significant multifaceted antibody reaction pattern accompanied by spirochete persistence. Antibodies against outer surface protein A (OspA) and outer surface protein B (OspB) have an unrelenting cytocidal effect on *B. burgdorferi.* Vaccination studies revealed that these antibodies offer protection from infection during the tick bite by removing spirochetes from the vector. However, these antibodies appear later in the *B. burgdorferi's* infection process and, thus, do not ameliorate the disease [32].

Vaccination

In 1998, the U.S. Food and Drug Administration (FDA) approved a recombinant vaccine, LYMERix®, for treating Lyme disease. However, shortly thereafter, the vaccine's manufacturer discontinued its production due to low and insufficient sales [13,33].

Currently, there is no vaccine available to prevent Lyme disease. However, ongoing studies are funded by the NIAID to develop strategies to vaccinate intermediate tick hosts, such as mice. According to the NIAID, such reservoir-based approaches would minimize the *Borrelia* spp pathogen's transmission from infected intermediate reservoir hosts to ticks. Subsequently, the transmission to humans would be reduced [29]. Scientists (collaborative research between NIAID, CDC, and Ventria Bioscience) are investigating novel vaccine delivery systems, such as rice plants containing vaccine components. When fed to mice, these plants would control *Borrelia* infection in the rodent population [29].

Apart from these reservoir-based approaches, there are currently two human vaccine candidates under investigation. One vaccine is being developed by Valneva and Pfizer against the North American and European strains of *Borrelia* and are presently under clinical trial testing . The other vaccine is being developed by MassBiologics (FDA-licensed non-profit vaccine manufacturer, managed by the University of Massachusetts Medical School). The latter vaccine is a seasonal vaccine, recommended to be taken before each tick season, and is being prepared for a Phase-I clinical trial [13].

Management and treatment

Oral or intravenous (IV) antibiotics, which are effective against the *Borrelia* pathogen, are currently used to treat Lyme disease. The goal of treatment is to ensure complete resolution of symptoms, prevent disease progression and relapse. Oral antibiotic therapy is preferred over IV therapy due to its lower cost and comparable efficacy. When clinically indicated, hospitalized patients are administered IV antibiotics. Lantos., *et al.* (2020) cited the following factors governing antibiotic choice: the patient's age, presence of extracutaneous symptoms, allergies, coinfection with other pathogens, the possibility of differential diagnosis of cellulitis, and cost [27].

Patients presenting with EM may be treated with oral antibiotic therapy (Table 3) [13]. The CDC noted that macrolide antibiotics, such as azithromycin, have a lower efficacy against *Borrelia* and should be reserved for patients who cannot tolerate doxycycline, amoxicillin, or cefuroxime [13].

The CDC also noted that patients displaying neurologic, cardiac, or arthritic symptoms may be considered for a longer duration (14–28 days) of oral or IV antibiotic therapy. Patients with carditis may require a temporary pacemaker [13].

The CDC and Lantos., *et al.* (2020) went on to state that patients who are suffering from post-treatment Lyme disease syndrome

Antibiotic	Duration of therapy (days)
Doxycycline	10
Amoxicillin	14
Cefuroxime	14
Azithromycin*	5–10 days (7 days preferred)
*: Is used as a second-line therapy reserved for patients who cannot take doxycycline or β–lactam antibiotics.	

Table 3: *Antibiotics that may be used to treat patients presenting EM [13].*

(PTLDS) should not be prescribed prolonged antibiotic therapy [13,27]. Instead, healthcare practitioners should treat patients on a case-by-case basis as there is no specific recommended treatment for PTLDS. One hypothesis for PTLDS posits that drug tolerance to existing antibiotics leads to persistent bacteria. Thus, studies are being conducted to identify new drug candidates that are effective against *Borrelia* and can, subsequently, be used to treat PTLDS.

Pothineni., *et al*. (2020) identified one such molecule, azlocillin, which has been shown to destroy doxycycline-tolerant *B. burgdorferi* during in vitro experiments [34]. Although this particular study is in a preliminary stage, the collaboration of other similar studies in the future should facilitate the development of effective treatment options for PTLDS patients.

Post-treatment Lyme disease syndrome (PTLDS)

Most Lyme disease cases can be well managed with a short (10–28 days) course of antibiotics [13]. However, in 10–20% of the treated cases, symptoms of fatigue, pain and cognitive difficulty persisted for up to 6 months after antibiotic treatment. As mentioned previously, this condition is referred to as post-treatment Lyme disease syndrome or PTLDS [13]. Such chronic presentation of symptoms has been problematic for scientists and researchers. Several hypotheses have been put forth regarding PTLDS; however, their is lack of consensus on the exact cause of the syndrome. Some experts posit PTLDS as being consequential to an autoimmune response triggered by the infection [13,29]. Similar autoimmune responses have been seen in several other infections, such as the Guillain–Barre syndrome (following *Campylobacter* infection), rheumatic heart disease (following strep throat), and Reiter's syndrome (following *Chlamydia* infection) [13]. Other explanations have included the persistent, yet clinically undetectable, *Borrelia* infection . Which causes an entirely an entirely distinct illness unrelated to the original *Borrelia* infection [13]. Pothineni., *et al.* (2020) have put forth that persistent infection may be due to drug-tolerant bacteria remaining dormant in the body and triggering late symptoms as seen in PTLDS [34].

A study by Uhde., *et al.* (2018) suggested a role of distinct inflammatory mechanisms, evidenced by the elevated levels of C–reactive protein in PTLDS patients compared to those with a history of Lyme disease and PTLDS–associated symptoms [29,35].

Although the symptoms associated with PTLDS are chronic and debilitating, data from specific and extensive studies do not support prolonged antibiotic treatment for these patients. There has been no difference in patients' long-term outcomes when treated with antibiotics over a prolonged period verus placebo control. Moreover, Lyme disease's protracted antibiotic treatment has been associated with other adverse outcomes [13,27].

Medicines and mechanisms of action

Doxycycline, a tetracycline, inhibits the inflammatory process of several infections. Pachner and Steere (1984) established that tetracyclines exercised a limiting-control over inflammation provoked by *B. burgdorferi* besides their antimicrobial function [4]. Wormser., *et al.* (2006) employed the human monocytic cell line THP-1 of rhesus monkey brain astrocytes and microglia. The researchers excited the cells using live or sonicated *B. burgdorferi* or the OspA lipoprotein in the presence of cumulative concentrations of minocycline or doxycycline. They found that the antibiotics resulted in a reduction of IL-6, IL-8, and TNF-α in a dose-reliant manner in all cell types [36].

Moreover, they reported that microarray analyses regarding doxycycline effect on gene transcription in spirochete-stimulated monocytes, IKKα and NFκB genes were reduced. IκBα phosphorylation and binding of NFκB to target DNA were diminished in these cells [36]. Thus, the study strongly suggested that tetracyclines exhibited a dual therapeutic effect on Lyme disease.

Contraindications for specific Lyme disease medication

Doxycycline is contraindicated in patients with documented hypersensitivity to the drug, pregnant women, and children under 8 years [37].

Non-pharmacological treatments

Avoiding a tick bite is considered the best preventive measure against Lyme disease in people living in tick-infested areas, lacking a protective vaccine. Current prevention strategies include the following: usage of a tick pesticide (acaricide), control of the deer population, alter the infestation areas (making such areas incompatible with the support and survival ofticks), and personal protective measures, clothing, and gear [33].

Ticks shelter in grassy and bushy areas. People are advised to wear protective clothing during outdoor activities, which minimizes the risk of tick bites. Outdoor clothing and gear should be carefully inspected for ticks and treated with Environmental Protection Agency (EPA)-registered insect repellents. After use, clothes should be washed in hot water. Careful examination of the entire body in front of a mirror aids in identifying attached ticks. If a tick is spotted, it should be carefully removed with a pair of pointed tweezers and disposed of appropriately [13]. The risk of Lyme disease pathogen transmission is significantly reduced if the attached tick is removed promptly,

Novel treatments

Novel approaches for the treatment of Lyme disease have been developed in the past decade. One such approach, which has shown efficacy against *B. burgdorferi* persisters, comprises sulfa drugs, essential oils, cefoperazone, disulfiram, dapsone, daptomycin, bee venom/mellitin, and stevia extract. Within *in–vitro* biofilm forms of *B. burgdorferi*, specific herbal compounds, such as stevia, biocidin, oregano oil, monolaurin, and baicalein, were reported effective against the bacteria [38].

Conclusion

Data suggest that Lyme disease is spreading to new regions. Ehhanced surveillance of such regions is paramount to control and eradicate the vector and spread of the infection and disease. Lyme disease, its history, and the research surrounding it are remarkable. It was first identified as a tick-borne illness in the late 1970s and the early 1980s in the Northeastern Region of the U.S. (Old Lyme, Connecticut). Specific ticks were identified as the carriers.

About 36–48 hours (or more) after the tick's attachment to a human host, the the Borrelia pathogen is transmitted. In the early-localized disease stage, nearly 70–80% of the patients present with the characteristic EM rash, which occurs about 3–30 days after a tick bite. Patients may experience myalgia, arthralgia, regional lymphadenopathy, headache, and fever. In the early-disseminated disease state, patients may present with secondary skin lesions, malaise, headache, neck stiffness, fever, chills, and arthralgia. If untreated, neurological complications can occur, such as meningitis, subtle encephalitis, cranial neuritis, neuropathy, ataxia, or myelitis—as well as cardiac-related light-headedness, fainting, shortness of breath, heart palpitations, or chest pain, accompanied by fever and body ache. Such symptoms are suggestive of Lyme carditis, being rare but potentially fatal. In the late-stage disease state (> one month after the initial infection), patients may present with arthritis-like symptoms, typically affecting the large joints (particularly the knee). Neurological symptoms worsen during this stage. Also, specific psychological symptoms and disorders can be provoked.

Specific oral or IV antibiotics are currently prescribed against the *Borrelia* pathogen—the oral route being preferred, primarily based on cost and reduced risk to the patient. Most Lyme disease cases respond favorably and can be managed with a 10–28 days course of antibiotics. However, in 10–20% of the treated cases, specific symptoms persist, referred to as post-treatment Lyme disease syndrome— the cause, course, and treatment of which are not well understood. Some contraindications regarding doxycycline administration have been noted for patients with documented hypersensitivity to the drug, pregnant women, and children under the age of 8 years.

Avoiding areas of known tick infestations and deer populations and preventing tick bites (through appropriate clothing, anti-tick sprays, and body inspection) are the most effective preventive measures. Novel treatment regimes are on the horizon, comprised of herbal remedies and herbal-drug concoctions. The manufacturer for LIMERix discontinued the only approved vaccine for Lyme disease due to a lack of profitability—discouraging further investigations into a universal vaccine, although research in this regard continues.

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

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Volume 8 Issue 4 April 2021