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ABSTRACT

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MODERN VIEWS ON THE EPIDEMIOLOGY, ETIOLOGY, AND CLINICAL PRESENTATION OF LYME DISEASE

Relevance. Lyme disease (LD) is the most prevalent tick-borne infectious disease and poses a significant health risk in countries in the northern hemisphere. Unlike other zoonoses, LD causes significant medical, social, and economic damage due to its high incidence and the severity of its clinical course. Complications can lead to disability and necessitate long-term dispensary observation and costly examinations.

Objective: To find out the current scientific views on the peculiarities of epidemiology, clinical course of Lyme disease, and mechanisms leading to multiorgan damage.

Materials and methods. We analyzed scientific articles and studies on Lyme disease, covered in the databases PubMed, Medline, Cochrane Library, Center for Public Health of the Ministry of Health of Ukraine, Karger, RKI, Onlinelibrary, CDC, Ecdc. Particular attention was paid to studies that investigated the etiology, prevalence, and clinical features of LD. The articles published from 2016 to 2025 were analyzed using the methods of systematic literature review, comparative analysis of clinical outcomes, and meta-analysis to ensure the relevance and accuracy of the conclusions.

Results. Surveillance of LD in Europe is carried out in only 25 out of 52 countries (48.1%) and is hampered by differences in national standards and reporting agreements.

The introduction of standardized case definitions in surveillance systems in Europe will be important to establish the true incidence of LD and to track its burden in relation to future interventions, including vaccination. To this end, a review of national surveillance strategies is urgently needed, with wider adoption of standardized case definitions to optimize their utility before a vaccine is available.

The development of new methods of disease risk control and prediction for better targeted control interventions requires an understanding of pathogen and disease course, so it is desirable to create

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maps of the distribution of Ixodes ticks and the extent of their infection.

In order to confirm the diagnosis of LD in patients with peripheral or central nervous system disorders, it is recommended to detect antibodies in the blood serum rather than PCR, since PCR should be performed using cerebrospinal fluid.

When diagnosing heart rhythm disorders in endemic areas, patients should be examined to exclude or confirm the disease as a cause of carditis.

In patients with LD and high fever or characteristic laboratory abnormalities, the possibility of coinfection with A. phagocytophilum and/or B. microti in endemic areas should be excluded and other infectious agents should be considered.

KEYWORDS: Lyme disease, Borrelia burgdorferi, ticks, tick-borne infections, surveillance, lyme arthritis, lyme carditis, neuroborreliosis, atrophic acrodermatitis, co-infection, good health and well-being.

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РЕЗЮМЕ

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СУЧАСНІ ПОГЛЯДИ НА ЕПІДЕМІОЛОГІЮ, ЕТІОЛОГІЮ ТА КЛІНІКУ ХВОРОБИ ЛАЙМА

Актуальність. Хвороба Лайма (ХЛ) є найпоширенішою трансмісивною інфекцією, що передається кліщами, та становить проблему для охорони здоров'я країн північної півкулі. На відміну від інших зоонозів, завдає найбільш істотний медико-соціальний та економічний збиток, що обумовлено не лише високим рівнем захворюваності, але і тяжкістю клінічного перебігу, можливістю хронізації, ускладненнями, що призводять до інвалідизації, потребує тривалого диспансерного спостереження та високовартісного обстеження.

Мета. З'ясувати сучасні наукові погляди щодо особливостей епідеміології, клінічного перебігу хвороби Лайма, механізмів, що призводять до поліорганних уражень.

Матеріали та методи. Здійснено аналіз наукових статей та досліджень щодо ХЛ, висвітлених у базі даних PubMed, Medline, Cochrane Library, Центра громадського здоров'я МОЗ України, Karger, RKI, Onlinelibrary, CDC, Ecdc. Особливу увагу приділено дослідженням, що вивчали етіологію, розповсюдженість, клінічні особливості ХЛ. Проаналізовано статті, опубліковані з 2016 до 2025 року, із застосуванням методів систематичного огляду літератури, порівняльного аналізу клінічних результатів та метааналізу для забезпечення актуальності й точності висновків.

Результати. Епіднагляд за ХЛ у Європі здійснюється лише у 25 з 52 країн (48,1 %) і йому перешкоджають відмінності у національних стандартах і угодах щодо звітності.

Впровадження стандартизованих визначень випадків у системах епіднагляду в Європі буде важливим для встановлення справжньої захворюваності на ХЛ та відстеження його тягаря у зв'язку з майбутніми втручаннями, у тому числі вакцинацію. З цією метою вкрай необхідний перегляд національних стратегій епіднагляду, ширше впровадження стандартизованих визначень

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випадків для оптимізації їх корисності, перш ніж з'явиться вакцина.

Розробка нових методів контролю та прогнозування ризику захворювань для кращого цілеспрямованого втручання у боротьбу вимагає розуміння динаміки патогенів та захворювань, тому бажано створити карти розповсюдження іксодових кліщів та ступеня їх інфікування.

З метою підтвердження діагнозу ХЛ при обстеженні пацієнтів з ураженням периферичної або центральної нервової системи рекомендовано проводити виявлення антитіл у сироватці крові, а не ПЛР, оскільки саме ПЛР доцільно проводити з ліквором.

При діагностуванні порушень серцевого ритму у ендемічних районах обстежувати пацієнтів з метою виключення чи підтвердження недуги, як причини кардиту.

У пацієнтів із ХЛ і високою лихоманкою або характерними лабораторними відхиленнями слід спростовувати можливість коінфекції з *A. phagocytophilum* і/або *B. microti* в ендемічних регіонах та пам'ятати про інших інфекційних агентів.

КЛЮЧОВІ СЛОВА: хвороба Лайма, борелії, *Borrelia burgdorferi,* кліщі, кліщові інфекції, епіднагляд, лайм-артрит, лайм-кардит, нейроборелиоз, атрофічний акродерматит, коінфекція, міцне здоров'я та благополуччя.

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INTRODUCTION

Lyme disease (LD) is classified as a natural focal disease with a transmissible mechanism of transmission. It is spread by ticks of the genus *Ixodes* and caused by bacteria of the *Borrelia burgdorferi sensu lato* complex. The disease is characterized by a polymorphic clinical presentation, staged progression, and a tendency toward chronic and recurrent courses, due to the activation of a powerful complex of inflammatory and immunological reactions, even despite etiological therapy [1]. Despite significant progress in understanding this relatively new disease, ongoing research continues to expand our knowledge of its epidemiology, clinical manifestations, and immunological mechanisms. This is essential for improving the diagnosis, treatment, and prevention of tick-borne diseases [2–4].

Individual symptoms of the disease were described long before the discovery of the causative agent. The first mentions of them appeared more than 140 years ago. As early as 1883, A. Buchwald described the symptoms of chronic atrophic acrodermatitis under the name "diffuse idiopathic atrophy of the skin." In 1894, Czech dermatologist Ph. J. Pick introduced the new term "Pick's erythromelia." In 1902, K. Herxheimer proposed the term "chronic atrophic acrodermatitis."

In 1909, at a meeting of the Swedish Dermatological Society in Stockholm, A. Afzelius, in his presentation, mentioned the term "chronic migrating erythema," and in 1914 – Lipschütz did as well. The erythema became known as "Afzelius-Lipschütz erythema," which was accompanied by pain along the peripheral nerves, paralysis, or meningitis.

In 1922, the term "Garin-Bujadoux-Bannwarth syndrome" appeared, and in 1943, Bäferstedt described benign cutaneous lymphocytoma.

Another mention of the disease occurred in 1975, when an outbreak of rheumatoid and juvenile arthritis was registered in the town of Old Lyme, Connecticut, and rheumatologist A. C. Steere introduced a new variant of a crossover syndrome of idiopathic rheumatoid arthritis – Lyme disease.

In 1976, a link was found between the occurrence of migrating erythema and the subsequent development of arthritis, and the ring-shaped erythema was officially recognized as the first stage of Lyme disease.

Only six years later, in 1982, W. Burgdorfer and his colleagues discovered Borrelia in the salivary glands of *Ixodes dammini* ticks [5].

Despite a 50-year history since its discovery, Lyme disease is still classified among the so-called "new" nosologies and requires detailed study [2, 4, 6].

LD is found on all continents of the globe and is the most common tick-borne transmissible infection, posing a significant public health concern in the countries of the Northern Hemisphere. In terms of the rate of spread, the disease ranks second only to HIV infection in the

countries of Central and Eastern Europe. Unlike other zoonoses, it causes the most substantial medical, social, and economic damage, manifested not only by a high incidence rate but also by the severity of its clinical course, the potential for chronic progression, complications that lead to disability, the need for prolonged medical follow-up, and the requirement for high-cost diagnostic procedures [7–9].

Objective. To find out the current scientific views on the peculiarities of epidemiology, clinical course of Lyme disease, mechanisms leading to multiorgan damage.

MATERIALS AND METHODS

We analyzed scientific articles and studies on Lyme disease, covered in the databases PubMed, Medline, Cochrane Library, Center for Public Health of the Ministry of Health of Ukraine, Karger, RKI, Onlinelibrary, CDC, Ecdc. Particular attention was paid to studies that investigated the etiology, prevalence, and clinical features of LD. The articles published from 2016 to 2025 were analyzed using the methods of systematic literature review, comparative analysis of clinical outcomes, and meta-analysis to ensure the relevance and accuracy of the conclusions.

RESULTS

Global warming in recent years has led to an earlier onset of the tick activity season and their attacks on humans. The first tick bites are recorded as early as late March, coinciding with the appearance of spring thaw patches. In addition, it is important to consider the possibility of simultaneous infection of a person with multiple infectious agents through a single tick bite [3, 10]. Artificial expansion of forest plantations, which is part of land use practices aimed at obtaining sustainable yields, leads to the creation of conditions favorable for ixodes ticks in areas where their presence was not previously recorded [11].

The migration of domestic and wild animals, as well as birds, contributes to the introduction of vectors into new areas that were previously uncharacteristic for their existence. This creates favorable conditions for the survival of vectors and pathogen reservoirs, and for the formation of anthropurgic foci of Lyme disease. Alongside the increasing incidence of Lyme disease in North America and Eurasia, there is also a sharp rise in other tick-borne infections such as tick-borne viral encephalitis, human granulocytic anaplasmosis, human babesiosis, and others [5, 12].

EPIDEMIOLOGICAL AND ETIOLOGICAL ASPECTS OF LYME DISEASE

LD is the most common tick-borne illness in the temperate regions of North America, Europe, and Asia, and the number of reported cases has increased in many areas due to landscape changes. Land reclamation and reforestation have led to an increase in the population of hoofed animals and a decline in predators, which has affected the ecosystem. In the United States, the number of reported cases has tripled over the past 20 years and has also increased in some regions of Europe [13].

National-level estimates of LD incidence were available for 25 out of 52 (48.1%) European countries. This included 8 out of 13 (61.5%) countries in Eastern Europe, 10 out of 13 (77%) in Northern Europe, 3 out of 17 (17.6%) in Southern Europe, and 4 out of 9 (44.4%) in Western Europe. In the subregions of Northern Europe, information was available for all Baltic countries, 2 out of 5 (40%) Northern European countries, and 100% of the United Kingdom and Ireland. Due to varying surveillance systems and case definition criteria used by the European countries included in our study, there are limitations in comparing incidence estimates between countries and European regions [14].

The functioning of natural foci of Lyme borreliosis (LB) with high epidemic potential is influenced by the infection rate of ixodid ticks with Borrelia, tick population density, species diversity and abundance of reservoir animals, as well as the degree of their infection. More than 200 species of vertebrate animals serve as reservoirs of Borrelia, including 130 rodent species (such as forest mice, tree rats, voles, squirrels, chipmunks, and rats), insectivores (shrews, hedgehogs), raccoons, and 100 species of birds. Domestic animals also play an important role as spirochete reservoirs in synanthropic foci of LB [15].

In Europe and Ukraine, the vectors of LB are ticks of the species *Ixodes ricinus*, and *Dermacentor reticulatus*. In forest biotopes across the three natural-geographical zones of Ternopil region, ticks are infected with *B. burgdorferi* s.l., *B. miyamotoi*, *Babesia* sp., and *A. phagocytophilum*. The dominant parasite is *I. ricinus*, with eight species of mouse-like rodents acting as hosts [16].

Currently, 23 genospecies of the *Borrelia burgdorferi* sensu lato (s.l.) complex have been identified and studied, at least ten of which have been isolated from patients. The primary genomic differences between various *Borrelia* genospecies lie in the presence or absence of certain plasmids, which result in differences in the range of hosts they can infect and the human organs they tend to disseminate to. The genospecies pathogenic to humans include *B. afzelii*, *B. garinii*, *B. burgdorferi* sensu stricto (s.s.), *B. bavariensis*, and *B. spielmanii* sp. nov. The geographical distribution of *Borrelia* genospecies, their vectors, and their hosts explains some important differences in the clinical manifestations of the disease across regions: *B. afzelii* and *B. bavariensis* are

maintained in rodent and small mammal reservoirs, *B. valaisiana* and most serotypes of *B. garinii* are associated with birds, while *B. spielmanii* is linked to dormice (family Gliridae) [17, 18].

The different habitats and species diversity of the pathogen contribute to variations in the clinical and epidemiological features of Lyme borreliosis across continents. Climate change is often cited as a major factor contributing to the rising incidence of tick-borne diseases, including Lyme borreliosis [19].

In Europe, five genospecies of *B. burgdorferi* sensu lato circulate: *B. afzelii*, *B. garinii*, and less frequently *B. burgdorferi* sensu stricto, *B. spielmanii*, and *B. bavariensis*, whereas *B. burgdorferi* s.s. is the only *Borrelia* species pathogenic to humans in North America. *B. burgdorferi* from Europe and the United States represent different genotypes, which vary in their inflammatory potential and clinical manifestations of Lyme borreliosis. Despite greater genetic divergence among *Borrelia* species, the clinical features of *B. burgdorferi* infection in Europe are similar to those caused by *B. afzelii* or *B. garinii*, the most common *Borrelia* species in Europe [20–22].

The presence of a common transmission mechanism, reservoirs, and vectors of the pathogens determines the possibility of combined natural foci of vector-borne infections: tick-borne viral encephalitis, Mediterranean spotted fever, human granulocytic anaplasmosis, human monocytic ehrlichiosis, and human babesiosis [2, 23].

However, new tick-borne infections that are not widespread across the globe are also emerging. For example, in South America, as early as 1992, the first cases of a new disease that mimicked Lyme disease (LD) were described – Baggio-Yoshinari syndrome. This is a Brazilian infectious disease transmitted by ixodid ticks of the genera *Amblyomma*, *Rhipicephalus*, and *Dermacentor*. *Borrelia burgdorferi* has never been isolated in Brazil. However, analysis of patients' peripheral blood using electron microscopy revealed structures resembling spirochete-like microorganisms or latent forms of spirochetes (L-forms or cell wall-deficient bacteria). For these reasons, the Brazilian zoonosis has been classified as an exotic Brazilian infectious disease that develops and is transmitted by ticks, not belonging to the *Ixodes ricinus* complex. The Brazilian ecosystem, combined with its ticks and the biodiversity of its reservoir hosts, may have contributed to the emergence of this new zoonosis, which likely arose as a result of *B. burgdorferi* passing through exotic vectors and environments. Results of some antigenic, molecular, and epidemiological studies indicate that the disease is caused by latent spirochetes belonging to the *B. burgdorferi sensu lato* complex with atypical morphology, but at present, the pathogen has not yet been accurately identified, and the direct presence of *B. burgdorferi sensu lato* has not been proven [24].

Southern Tick-Associated Rash Illness (STARI), or Master's disease, is another emerging zoonotic illness characterized by a ring-shaped rash with central clearing, nearly identical to the erythema migrans seen in LD. However, it is transmitted through the bite of the *Amblyomma americanum* tick. This disease is caused by the spirochete *Borrelia lonestari* [25].

CLINICAL SIGNS OF LYME DISEASE

Lyme disease (LD), caused by *Borrelia burgdorferi*, *B. afzelii*, and *B. garinii*, is a chronic multisystem infection in which the spectrum of affected tissues varies depending on the pathogen strain. For example, infection with *B. garinii* is primarily associated with neurological manifestations, whereas *B. burgdorferi* is mainly linked to arthritis. OspC (outer surface protein C) is a highly variable protein of the pathogen that is essential for infectivity, and differences in OspC sequences are associated with variations in tissue invasiveness [26]. According to the European definition adopted at the WHO conference in Serócz in 1995, LD is diagnosed in patients who have experienced tick attachment followed by the development of typical signs and symptoms: involvement of the skin, nervous system, musculoskeletal system, and heart. Early and late stages of LD are distinguished. A pathognomonic symptom for LD is the erythema migrans (EM) rash, which appears in half of the patients after a tick bite and allows the diagnosis to be confirmed without additional laboratory tests [27].

There are three stages of the disease: the first is local infection, the second is dissemination, and the third is organ damage. However, this division is conditional. The disease can progress sequentially or manifest first at any stage, without the presence of the previous one [14].

All types of Borrelia cause the development of erythema migrans. However, Lyme arthritis (LA) is more characteristic of disease caused by *B. burgdorferi* sensu stricto, chronic atrophic acrodermatitis – *B. afzelii*, and Lyme neuroborreliosis – *B. garinii* (the 4th serotype of this genospecies, identified by the surface protein OspA, is characterized by pronounced neurotropism). Therefore, the development of autoimmune inflammatory reactions in the joints, which lead to antibiotic-resistant LA, is more frequently observed in the USA than in Europe. In Norway, 71.0% of cases are represented by Lyme neuroborreliosis. However, the existence of several genospecies of the pathogen within a single vector, which determines a polymorphic clinical picture, cannot be excluded [28].

Clinical signs of skin involvement in Lyme disease are diverse. At early stages, this is manifested as a specific erythema migrans [29]. However, at later

periods after infection, sclerotic-atrophic changes are possible – chronic atrophic acrodermatitis, borrelial lymphocytoma [30–32].

Sometimes, obvious signs of the local stage of infection are absent, meaning there is no characteristic erythema migrans (EM). One of the most likely reasons for this is that borreliae relatively quickly leave the site of their initial entry, which prevents local inflammation from developing in the skin. Clinical signs of LB appear only at the second or third stages. In the absence of clear staging or a known duration of illness, the epidemiological link between the disease and a tick bite is often lost. Due to its multisystem involvement, LB frequently remains unrecognized and has thus earned the nickname "the great imitator." At late stages of the disease, when damage to one of the body's systems predominates, patients are seen and treated by specialists in various fields – cardiologists, rheumatologists, neurologists, dermatologists – under "mask diagnoses," unaware of the true nature of the illness [33].

Nervous system involvement usually manifests as a combination of three classic syndromes known as Bannwarth's syndrome – serous meningitis, radiculoneuritis, and cranial neuritis. Bannwarth's syndrome is more common in Europe and less frequent in the United States. Neuroborreliosis (NB) is much more common in Europe, where the causative agent is often B. garinii. In adults, the most common sign of NB is meningo-radiculitis, whereas in children, facial nerve paralysis and/or subacute meningitis are often observed. Headache may be the only symptom of NB in children, especially during the summer months in LB-endemic regions [34]. In the United States, the term "Post-Treatment Lyme Disease Syndrome" (PTLDS) is often used alongside late manifestations of LB in the form of neuroborreliosis to describe those with unexplained subjective complaints, which may or may not be accompanied by positive test results for B. burgdorferi infection in the blood serum [35].

Moreover, in chronic Lyme disease (CLD) with nervous system involvement, all possible concomitant infections should be recognized. For instance, concomitant anaplasmosis may cause demyelinating polyneuropathy and brachial plexopathy. Co-infection with *Mycoplasma pneumoniae* can be the cause of encephalitis, meningitis, myelitis, cranial neuropathy, and cerebellar ataxia. Powassan virus from the Flaviviridae family, which is also transmitted by ticks in North America, causes meningitis, encephalitis, and myelitis. Often asymptomatic infections following *Borrelia burgdorferi* infection can exacerbate and sustain neurological manifestations in patients with the CLD complex; these include *Candida albicans*, cytomegalovirus, Epstein-Barr virus, and human herpesvirus 6 [36].

Nervous system involvement is also accompanied by neurocognitive impairments even after treatment. A challenging aspect for differential diagnosis is that many of the identified psychopathological symptoms of the disease resemble depressive disorders, including irritability, fatigue, emotional lability, difficulty concentrating, memory problems, sleep disturbances, and even the development of depression. Depressive symptoms may result from prolonged dissemination of borrelia or as an emotional reaction to the presence of a serious illness [37].

One of the most characteristic manifestations of LD is the involvement of the musculoskeletal system. The ability of B. burgdorferi to persist long-term in the body and the presence of several cross-reactive antigens of B. burgdorferi with various host cells underlie the participation of an autoimmune component in the clinical signs of Lyme arthritis (LA), Lyme carditis (LC), vasculitis, and chronic atrophic acrodermatitis. The peptidoglycan of Borrelia burgdorferi plays an important role in bacterial physiology and the body's immune response. Synovial fluid from some patients with LA, many of whom had received 1–3 months of antibiotic therapy, showed high levels of detectable peptidoglycans as well as antibodies against peptidoglycan. LA is more common in North America than in Europe. It manifests as intermittent or persistent monoarticular or oligoarticular arthritis, usually affecting one or two joints simultaneously, especially the knees, over several years. Tendons, ligaments, or bursae may also be affected. Since early Lyme disease is usually recognized and effectively treated with antibiotics, LA is now more often observed only in patients with minimal or no early infection symptoms [38–40].

LC is a complication of early disseminated disease that usually appears in the acute and subacute phases of Lyme disease during the second to sixth week of illness. This affects both children and adult patients. LC is a rare but serious complication of untreated LD, typically occurring within the first few weeks after infection. Cardiac involvement in LD occurs in patients in Europe and the USA. Men are more frequently affected. Most cases are accompanied by dermatological symptoms of the disease, about 25–33% of cases are accompanied by neuroborreliosis or Lyme arthritis (especially in late stages), but it is not uncommon for LC symptoms to be the sole manifestation of LD [41].

The dominant form of cardiac pathology is conduction disturbances at various levels of the heart's conduction system, leading to blocks of varying degrees of severity. Atrioventricular (AV) block of varying

severity is the most common conduction disorder in LC. Although it is usually mild, AV block can rapidly change and progress from a prolonged PR interval to a His-Purkinje block within minutes, hours, or days. Rarely, LD can cause endocarditis, while some studies and reports based on serological and/or molecular research suggest a possible influence of *Borrelia burgdorferi* on the development of degenerative heart valve diseases. Myocarditis, pericarditis, pancarditis, dilated cardiomyopathy, and heart failure have also been described as possible manifestations of LD. The clinical course of carditis is generally mild, short-term, and in most cases fully reversible after adequate antibiotic treatment. Cardiac rhythm disturbances occur in 10–20% of patients. The most severe complication is complete heart block, accompanied by syncope and even fatal outcomes, which requires the use of artificial pacemakers; however, with timely diagnosis and treatment, this procedure can be avoided [42–44]. Cardiac arrest associated with malignant arrhythmia due to LD is rare. Nevertheless, in clinical scenarios of unexplained conduction disturbances or arrhythmias, to identify key risk factors – especially considering the limitations of serological tests in emergency settings – the Suspicious Index in Lyme Carditis (SILC) score should be used [45].

In children, myocarditis in LD initially presents with chest pain, later manifested by a weakening of the intensity of heart sounds, shortness of breath, and the development of conduction block. The course of myocarditis is generally favorable, with a tendency toward regression over several weeks of treatment [46].

Considering the polymorphism of clinical signs of LD, modern diagnostics in most countries are based on two-tier serological testing at all stages of infection, except for the early localized dermatological manifestations known as erythema migrans [47].

Evidence-based clinical guidelines for the prevention, diagnosis, and treatment of Lyme disease have been developed by an interdisciplinary group (the Infectious Diseases Society of America (IDSA), the American Academy of Neurology (AAN), and the American College of Rheumatology (ACR)). These guidelines address prevention, diagnosis, treatment of Lyme disease, and complications from coinfection with other tick-borne pathogens [9]. In Ukraine, the medical care standard for “Lyme Disease” and the evidence-based clinical guideline “Lyme Disease” were approved and enacted in September 2024 [48, 49].

CONCLUSIONS

Surveillance of Lyme disease in Europe is conducted in only 25 out of 52 countries (48.1%), and it is hindered by differences in national standards and reporting agreements.

The implementation of standardized case definitions in surveillance systems across Europe will be important for establishing the true incidence of Lyme disease and tracking its burden in relation to future interventions, including vaccination. To this end, a revision of national surveillance strategies and wider adoption of standardized case definitions are urgently needed to optimize their usefulness before a vaccine becomes available.

The development of new methods for disease control and risk prediction to enable better targeted interventions requires an understanding of the dynamics of pathogens and diseases; therefore, it is desirable to create distribution maps of Ixodes ticks and assess their infection rates.

For confirmation of Lyme disease diagnosis in patients with peripheral or central nervous system involvement, it is recommended to detect antibodies in serum rather than perform PCR.

When diagnosing cardiac rhythm disturbances in endemic areas, patients should be examined to exclude or confirm Lyme disease as the cause of carditis.

In patients with Lyme disease who present with high fever or characteristic laboratory abnormalities, co-infection with *Anaplasma phagocytophilum* and/or *Babesia microti* should be ruled out in endemic regions, and other infectious agents should be considered.

PROSPECTS FOR FUTURE RESEARCH

Studies related to LD may be aimed at supporting the achievement of United Nations Sustainable Development Goal 3 – "Good Health and Well-being," which focuses on ensuring access to quality healthcare for all [50].

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1. Significant contribution to the development or preparation of the manuscript; acquisition, analysis, or interpretation of data for the manuscript;
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3. Final approval of the version to be published;
4. Agreement to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are properly investigated and resolved.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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