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Current guidelines for the management of Lyme borreliosis in European countries

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ABSTRACT:

Introduction and purpose:

Lyme borreliosis, caused by *Borrelia burgdorferi* sensu lato complex, is the most common vector-borne disease in Europe. Transmitted by *Ixodes* ticks, its prevalence is increasing due to climate change, expanded tick habitats, and improved diagnostic awareness. Consequently, unified and evidence-based management guidelines are critical to ensure consistent diagnosis and treatment across European countries. This article provides an overview of current guidelines from 2023 for the management of Lyme borreliosis in Europe.

Materials and methods:

A literature search was conducted by analysing scientific articles published in Google Scholar, PubMed, and UpToDate using keywords included: Lyme disease; guidelines; *Borrelia burgdorferi;* management. We also searched current guidelines of Polish Society of Epidemiology and Infectious Diseases and recommendations from other European countries.

Description of the state of knowledge:

There are 3 stages of Lyme disease: early localized, early disseminated and late. Clinical diagnosis is based on symptoms, history of tick exposure, and observation of erythema migrans. To confirm Lyme disease, laboratory tests must also be performed. Lyme borreliosis is typically treated with antibiotics depending on the character.

Conclusion:

European guidelines for Lyme borreliosis emphasize early diagnosis and appropriate antibiotic therapy based on disease stage. Preventive measures and public health initiatives are essential to reduce the disease burden. While current guidelines ensure effective management, continued harmonization and advancements in diagnostics, treatment, and vaccine development will further enhance Lyme borreliosis care across Europe.

Keywords: Lyme disease; guidelines; *Borrelia burgdorferi;* management.

BACKGROUND:

Lyme borreliosis, multisystem infectious disease, is caused by the species complex *Borrelia burgdorferi* sensu lato [1]. This is the most common tick-borne illness, especially in northern European countries. The number of cases is constantly increasing. The Lyme disease can be associated with severe long-term complications [2].

The prevalence of infected ticks in different parts of Europe ranges from 3 to 34%. In April 2023, an analysis of the epidemiology of Lyme disease on the European continent, was published. It noted the large differences in national reporting standards and systems, which makes it very difficult to determine the true incidence of the disease. Nevertheless, the authors estimated that about 24% of the total European population lives in areas with a high incidence of Lyme disease (43% of countries reporting cases) [3]. Differences in endemicity and *Borrelia* species distribution affect clinical presentations and diagnostic challenges. For instance, *B. garinii* is more neurotropic, whereas *B. afzelii* is associated with dermatological manifestations.

MATERIALS AND METHODS:

A literature search was conducted by analysing scientific articles published in Google Scholar, PubMed, and UpToDate using keywords included: Lyme disease, guidelines, *Borrelia burgdorferi,* management. We also searched current guidelines of Polish Society of Epidemiology and Infectious Diseases and recommendations from other European countries.

DESCRIPTION OF THE STATE OF KNOWLEDGE:

The current version of the Lyme borreliosis management guidelines has expanded the group of co-authors, new issues have been addressed, many of the previous recommendations have been clarified, and new recommendations have been added. The clinical forms of Lyme disease discussed in detail in the guidelines include erythema migrans (EM), Lyme pseudolymphoma of the skin, chronic atrophic dermatitis, neuroborreliosis, arthritis, myocarditis and ocular Lyme disease.

There are 3 stages of Lyme disease:

- early localized – most often occurs in the form of EM. General symptoms, such as malaise, joint pain, muscle pain, may occur from several days to several weeks after *B. burgdorferi* infection [4,5].
- early disseminated – may occur from weeks to months after the tick bite and mainly affects the nervous system, the musculoskeletal system and the heart.
- late – in rare cases, after months or years, a late or chronic manifestation may appear, involving the skin, nervous and musculoskeletal system [6].

Erythema migrans

It is the most common clinical manifestation of Lyme disease. It is an expanding, erythematous, often annular skin lesion. A lesion ≥5 cm in diameter is considered diagnostic. The incubation period of EM is 3 to 30 days. Patients with it may report concomitant systemic

symptoms such as fatigue, joint pain, muscle pain, and headache. Erythema does not cause pain at the site of its occurrence. Redness that appears and disappears within 2 days of the tick bite, especially if it is warm, itchy, or painful, is a nonspecific reaction, not EM [7].

Lyme pseudolymphoma of the skin

It is an inflammatory skin lesion (usually a purple nodule) that appears up to 2 months after infection, most often located on the auricles, scrotum and nipples. It occurs more often in children [8,18].

Chronic atrophic dermatitis

It occurs mainly on the distal parts of the limbs. It appears months or years after infection. It manifests as blue-red lesions, initially with features of inflammatory edema and later skin atrophy. Patients complain of limb pain, which is the main symptom of the often accompanying peripheral neuropathy [6].

Neuroborreliosis

It can be divided into early and late neuroborreliosis. >98% of cases are early neuroborreliosis. Neurological symptoms appear several weeks to several months after the tick bite. Typical clinical forms include meningitis, paralysis of the cranial nerves (most often with unilateral or bilateral facial nerve palsy) and/or spinal nerve roots [19]. Radicular pain is often present. Garin-Bujadoux-Bannwarth syndrome, characterized by the coexistence of meningitis, cranial nerve palsies, and radicular syndrome, is the most common symptom of early Lyme neuroborreliosis in adults in Europe, after EM. In late neuroborreliosis, typical clinical forms are encephalomyelitis with spastic symptoms, gait disturbances and bladder dysfunction [9].

Arthritis

It usually manifests itself as swelling of one or several large joints, most often the knees. The joints are painful. The absence of fever is characteristic. Untreated arthritis may proceed with periodic exacerbations or spontaneously resolve after a few weeks or months [10].

Ocular Lyme disease

It is extremely rare. Ocular lesions most commonly include conjunctivitis, episcleritis, keratitis, uveitis, optic neuritis and retinitis, and cranial nerve palsies. In the course of Lyme disease, retinal arteries or veins may be affected [11].

Myocarditis

It usually presents with first and second degree atrioventricular block, often rapidly progressing to complete heart block. Atrial and ventricular arrhythmias may occur. *B.*

burgdorferi infection may also manifest as pericarditis and acute myocarditis with ventricular dysfunction [12, 21,31].

Diagnosis of Lyme borreliosis

Detailed indication of diagnostic methods based on which Lyme disease can be diagnosed is particularly important in connection with the wide range of different tests offered on the Internet for the diagnosis. Diagnosis is based on information from the history of a tick bite or potential exposure, the clinical symptoms and the results of additional tests. EM is diagnosed clinically without laboratory testing. In cases of atypical rash, antibody testing may be employed. Other manifestations include neuroborreliosis, arthritis, and carditis, often requiring specialist evaluation [22]. Molecular tests include polymerase chain reaction (PCR) which may be used for detecting *Borrelia* DNA in cerebrospinal fluid (CSF) or synovial fluid. Detection of *B. burgdorferi* in blood by PCR is seldom use due to transient spirochetemia and low DNA copy number of spirochetes. Enzyme-linked immunosorbent assay (ELISA) is the first step in serological tests. Also chemiluminescence immunoassay (CLIA), enzyme-linked fluorescent immunoassay (ELFA) can be used (indirect immunofluorescence test method is permissible). The first serological test is followed by a confirmatory Western blot test [30].

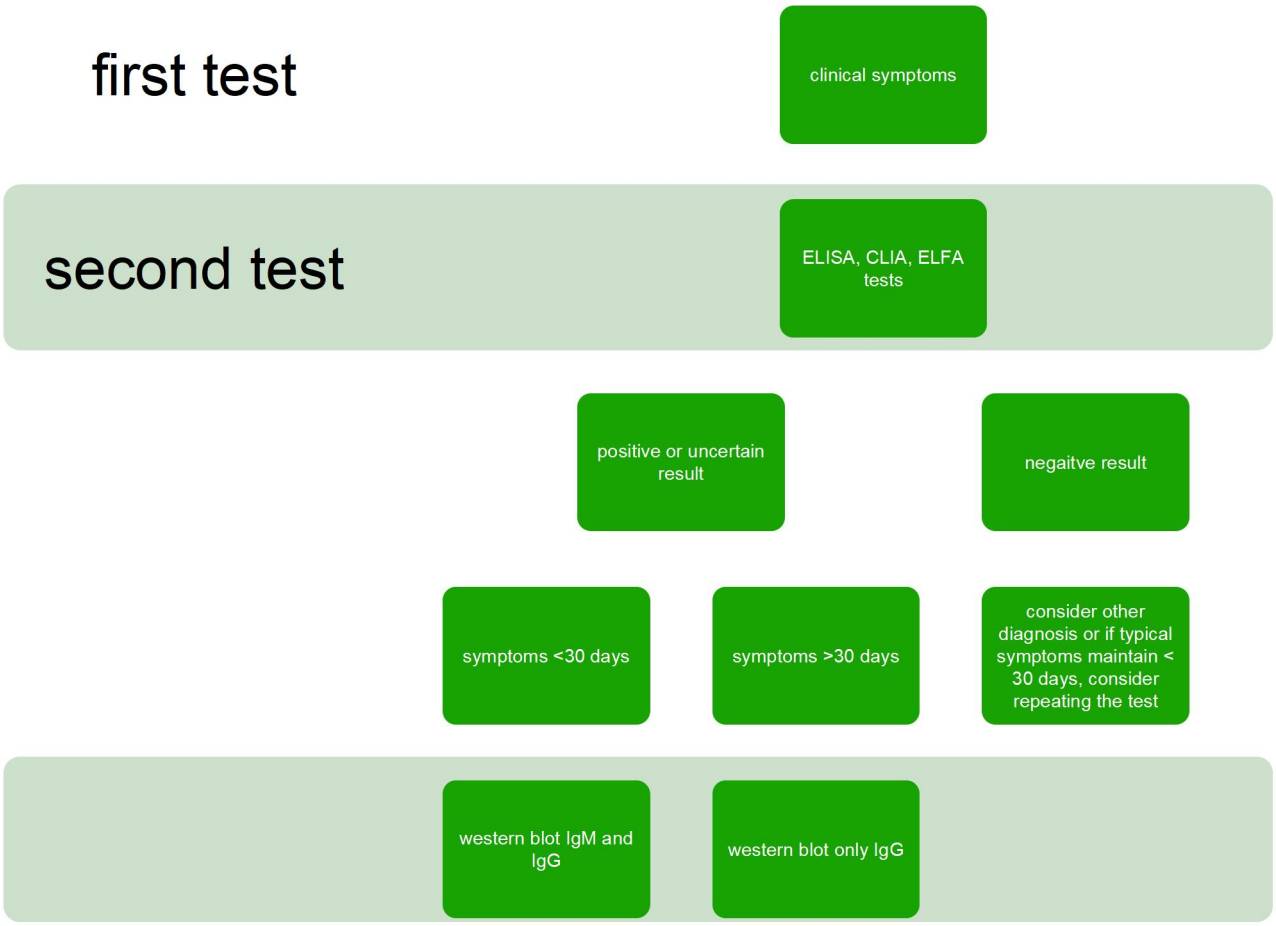

Chart 1. Lyme borreliosis diagnostic algorithm [30].

It is important to pay attention to the persistence of IgM antibodies (without seroconversion to IgG), the so-called persistent IgM antibodies. If a positive result persists for more than a month, it can be assumed with a very high probability that it is a false positive result, because Lyme disease patients should produce specific IgG antibodies within a few weeks [32]. Demonstration of lymphocytic pleocytosis in CSF and intrathecal production of specific antibodies is mandatory in cases of suspected neuroborreliosis [14]. It is important to collect CSF and blood for testing on the same day, preferably at the same time (both samples are tested for albumin concentrations and total and specific antibodies of selected classes) and to report the need for testing of intradural antibody production, so that the tests are performed using appropriate analytical methods, so that the results are reliable. Intradural antibody production is determined using mathematical formulas based on the values of antibody and albumin concentrations determined in CSF and serum. A positive culture result (rarely used due to the long waiting time for results and low sensitivity) or detection of *Borrelia* genetic material by PCR in CSF in a patient with typical clinical symptoms and lymphocytic pleocytosis allows for a certain diagnosis of neuroborreliosis [23]. Serological tests should not be used as screening tests for Lyme disease, but only as an element of diagnostic procedures. It is emphasized that screening tests in the general population are unjustified, but they can be considered in populations occupationally exposed to tick bites [28]. Having Lyme disease does not cause a lasting immune response and recurrence is possible. Confirmation of seroconversion between the acute phase and convalescence, demonstration of spirochetes or their genetic material may be helpful in confirming the diagnosis. A positive culture result is certain evidence of infection, but spirochetes are rarely isolated from lesions associated with Lyme disease, except in EM. *B. burgdorferi* is a very demanding, slow-growing bacterium and must be cultured for up to 12 weeks. Specialized skills and tools are required, and unfortunately most microbiology laboratories do not provide this. The experts also touched on another important topic – tick testing. The public fear of Lyme disease causes many people to spend money unnecessarily on testing ticks removed from their skin. The guidelines emphasize that such testing cannot be used to diagnose Lyme disease [15]. In recent years, the Lyme Detect test has appeared for diagnosing early Lyme disease. The test is based on the detection of antibodies against B. burgdorferi in the IgM and IgG classes and the measurement of interferon γ activity.

Treatment Guidelines

Treatment of Lyme borreliosis in Europe is guided by European Society of Clinical Microbiology and Infectious Diseases and national protocols. The choice of antibiotic and duration of treatment varies depending on the form of Lyme disease. For EM oral antibiotics such as doxycycline, only over 8 years of age, (100 mg twice daily) or amoxicillin (500 mg three times daily) are recommended for 7–21 days [16]. Also cefuroxime axetil (500 mg twice daily) can be used for 14–21 days. In case of allergy to semisynthetic penicillins, azithromycin is used as a second line for 5-10 days. Neuroborreliosis requires prolonged treatment, often with intravenous ceftriaxone or cefotaxime (2 g daily) for 14–21 days or oral doxycycline for early-stage manifestations of meningitis and cranial nerve palsy also for 14-21 days. Penicillin G has been added to the list of drugs that can be used to treat neuroborreliosis. For Lyme arthritis, oral doxycycline, amoxicillin or cefuroxime axetil for 21–28 days is the standard. Persistent arthritis may require additional antibiotic courses or synovectomy in resistant cases. Carditis or severe systemic disease may necessitate hospitalization and intravenous ceftriaxone for 14–21 days [27]. Symptoms like fatigue, musculoskeletal pain, or cognitive dysfunction may persist despite successful antibiotic therapy. It is called Post-Treatment Lyme Disease Syndrome (PTLDS). European guidelines emphasize supportive care and discourage prolonged antibiotic courses due to the lack of evidence for efficacy and risks of resistance or adverse effects [17,26].

Clinical form	Antibiotic	Duration of therapy (days)
Erythema migrans	1.choice doxycycline	7-21
	amoxicillin	14-21
	cefuroxime axetil	14-21
	2.choice azithromycin	5-10
Lyme pseudolymphoma of the skin	doxycycline	14-21
	amoxicillin	14-21
	cefuroxime axetil	14-21
Arthritis	1.episode doxycycline	28
	amoxicillin	28
	cefuroxime axetil	28

	recurrence- ceftriaxone	14-21
Neuroborreliosis – meningitis or radiculopathy	1.choice doxycycline	14-21
	ceftriaxone	14-21
	cefuroxime axetil	14-21
	2.choice penicillin G	14-21
Neuroborreliosis – paralysis of the cranial nerves	doxycycline	14-21
Myocarditis	1.choice doxycycline	14-21
	amoxicillin	14-21
	cefuroxime axetil	14-21
	ceftriaxone	14-21
	2.choice cefotaxime	14-21
	penicillin G	14-21
Chronic atrophic dermatitis	doxycycline	21-28
	amoxicillin	21-28
	cefuroxime axetil	21-28

Tab. 1. Duration of antibiotic therapy in individual clinical forms of Lyme borreliosis in adults [27].

Prevention and Public Health Recommendations

Preventive measures play a critical role in reducing Lyme borreliosis incidence. Early and proper removal of ticks reduces the likelihood of infection. Using insect repellents, wearing protective clothing, and performing tick checks after outdoor activities are an important part of personal protection. Local governments collaborate on reducing tick habitats through landscaping measures. While human vaccines against Lyme borreliosis are not yet widely available, research is ongoing, with promising candidates in clinical trials. Variations in awareness campaigns, access to healthcare, and training of general practitioners influence early detection and treatment outcomes [25,29]. Routine prophylactic antibiotics are not generally recommended after tick bites unless specific conditions are met: high-risk exposure (tick bites occurred in areas highly endemic for Lyme borreliosis), bites are from *Ixodes* ticks known to transmit *Borrelia burgdorferi* and multiple bites in an endemic area in a person

from outside that area. A single dose of doxycycline (200 mg for adults and 4 mg/kg, up to 200 mg, for children aged ≥8 years) is recommended within 72 hours of removing a high-risk tick bite (e.g., prolonged attachment, species in endemic areas) to prevent Lyme disease [10,23].

CONCLUSIONS:

Current guidelines for managing Lyme borreliosis in Europe emphasize early recognition, accurate diagnosis, and timely antibiotic treatment to prevent complications. While significant progress has been made in standardizing care, continued efforts to harmonize guidelines and address regional challenges are essential. Collaborative public health strategies and advancements in diagnostics and prevention will play a vital role in mitigating the growing burden of Lyme borreliosis in Europe.

DISCLOSURE:

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Writing -review and editing: Wiktoria Zamachowska

Visualization: Zuzanna Wyleciał

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