LYME DISEASE

Ivica Urošević (1), Dušan Bastać (2)

(1) INSTITUTE OF PUBLIC HEALTH ZAJEČAR; (2) INTERNAL MEDICAL PRACTICE "DR. BASTAĆ" ZAJEČAR

Summary: Lyme disease (LD) is a multisystem infectious disease caused by bacteria of the Borrelia genus, most commonly Borrelia burgdorferi, and transmitted through the bite of an infected tick (Ixodes ricinus). Rodents (mice, rats) are the primary reservoirs of the bacteria. Transmission occurs most frequently between May and August in temperate climate zones, although the disease can appear outside this period depending on climatic conditions and tick activity. In its early stage, Lyme disease most commonly manifests as a characteristic skin lesion known as erythema migrans, which begins as a red macule or papule and can expand up to 50 cm in diameter, with central clearing and clearly or slightly defined borders. Other symptoms may include headache, fever, fatigue, muscle and joint pain, which can lead to misdiagnosis or delayed treatment. If left untreated, the disease can cause serious systemic complications, including neurological disorders (e.g., meningitis, neuropathies), cardiac problems (atrioventricular block), and arthritis, most often affecting the knees. The late stages of the disease can last for months or years, but with adequate antibiotic therapy, symptoms can often be reduced. Diagnosis is based on the clinical presentation and serological tests such as ELISA and Western blot, which detect the presence of antibodies to the bacteria. It is important to note that serological tests may be negative in the early phase of infection, as antibodies have not yet developed. PCR tests can confirm the presence of bacteria through direct examination of blood, cerebrospinal fluid, or tissue samples. However, in routine diagnosis, the presence of erythema migrans as a clinical finding is considered a sufficient reason to initiate therapy. Prevention focuses on reducing contact with ticks, including wearing appropriate protective clothing, using repellents, and treating clothing with permethrin. Preventive measures also include mowing and maintaining grassy areas, as well as controlling rodent and tick populations in places where people live or spend time.

Keywords: Lyme disease, Borrelia burgdorferi, Ixodes ricinus, vector-borne infection, erythema migrans, bacterial transmission, diagnosis, serological tests, prevention, complications, arthritis, neurological disorders, ticks, and rodents

DEFINITION AND EPIDEMIOLOGY OF LYME DISEASE

Lyme disease (LD), or MORBUS LYME, is a chronic multisystem infectious disease in humans, transmitted through the bite of an infected hard tick, Ixodes ricinus, carrying one of the bacteria such as Borrelia burgdorferi (Bb) (Figure 1), and less commonly other Borrelia species: Borrelia garinii (Bg) and Borrelia afzelii (Ba).

It is a multisystem disease that can affect the skin, joints, heart, and nervous system. Lyme disease is particularly known for its frequent manifestation as the characteristic “erythema migrans”, a bull’s-eye-shaped skin rash [1].

Figure 1. *Borrelia burgdorferi* magnified 400 x

Source: https://upload.wikimedia.org/wikipedia/commons/f/f3/Borrelia_burgdorferi_%28CDC-PHIL_-6631%29_lores.jpg

When discussing the developmental stages of ticks, the starting point is the egg, which the female (adult) lays in early spring. From these eggs, larvae hatch in early summer. The larva takes its first blood meal from the nearest available animal—most often micromammals (forest and field rodents, hedgehogs, and others). Humans can also occasionally be bitten by larvae, although this occurs much less frequently compared to other developmental stages of the tick.

After feeding, the larva molts (matures) into a nymph, which then takes a second blood meal from the nearest host. For nymphs, these hosts typically include hares, birds, deer, and occasionally humans who spend time in tick habitats. Borrelia is transmitted through tick saliva during feeding, usually after 48 hours or longer.

There are three theories regarding the transmission of Borrelia burgdorferi (Bb) from the tick to the next host, with two being most widely accepted. The first suggests that during the tick's intense blood-feeding phase, once it becomes engorged, it regurgitates part of its intestinal contents (Bb resides in the tick's midgut). The second, less common but still recognized in the literature [1,2], proposes that Bb migrates from the midgut to the salivary glands. This theory implies a transmission mechanism similar to that of mosquitoes transmitting Plasmodium. Advocates of this theory often recommend prophylactic antibiotic treatment after every tick bite, which is incorrect.

Experimental studies on the transmission of Borrelia from infected ticks to mice have shown that infection rarely occurs within the first 24 hours of tick attachment. The likelihood of infection increases with the tick's duration of attachment—particularly after 48 hours, and especially after 72 hours. Therefore, information about the tick's attachment time (less than 24 hours) is extremely important for the prevention of Lyme disease. Prompt and proper removal of the tick within the first few hours can be crucial, especially if the tick is infected with Bb [3].

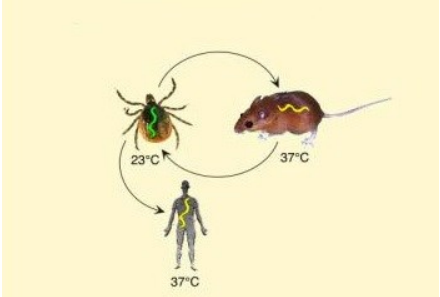
In Lyme disease, the reservoir represents the ecological niche—the place within the host (tick, small rodent, etc.) where the pathogen lives, persists as a species, and/or reproduces, usually without harming its host.

In the case of Lyme disease, the tick can serve both as a reservoir of Bb and as the source of infection (the one that directly transmits Bb to a new host). Once infected, a tick can transmit Bb throughout all its developmental stages—from larva to adult—and even transovarially (from female to offspring). The vector, or carrier of the pathogen, is Ixodes ricinus (Europe), Ixodes pacificus and Ixodes scapularis (America), Ixodes persulcatus (Asia), etc., while the causative agent belongs to the Borrelia burgdorferi genospecies [4,5].

The term "Borrelia cycle" is translated as either the life cycle of Borrelia or the enzootic cycle of Borrelia in English. It refers to the complex life cycle of the Lyme disease bacterium (Borrelia burgdorferi), which alternates between tick vectors and vertebrate hosts. This enzootic cycle involves the transmission of the bacterium from an infected tick to a host, and potentially back to another tick (Figure 2) [6].

Figure 2. life cycle (transmission cycle) of Borrelia, which alternates between the tick vector and the vertebrate host.

Source: https://upload.wikimedia.org/wikipedia/commons/0/08/Borrelia_cycle.jpg



CLINICAL ASPECTS OF LYME DISEASE

Lyme disease is the most common vector-borne infectious disease in Europe and North America. LD is typically a seasonal illness, occurring during periods of tick activity—from early spring and the first warm days (nymphal stage), throughout June (larval and nymphal stages), and up to the late autumn months (adult stage). During the rest of the year, when tick activity ceases, Lyme disease does not occur.

When searching for a diagnosis in patients presenting with symptoms suggestive of LD, serological testing is most commonly used to raise clinical suspicion. The incubation period ranges from 3 to 30 days, from the tick bite to the appearance of signs and symptoms of Lyme disease. It is important to note that not every erythema at the site of a tick bite is Erythema migrans (EM). EM occurs in 60–80% of cases and is often accompanied by flu-like symptoms.

At the site of the tick bite, within 5–7 days or longer, a characteristic skin lesion may appear—Erythema migrans—which begins as a macule or papule and can enlarge to as much as 50 cm in diameter. EM presents as redness expanding from the bite site toward the periphery in the form of irregular concentric rings with serrated, more intensely red edges. The redness is flat, warm to the touch (like surrounding skin), and does not cause pain or itching [7,8,9].

This characteristic skin lesion—EM—is a hallmark sign of Lyme disease. It differs from other skin rashes because it lacks tumor (swelling) and dolor (pain), and the calor (warmth) is the same as in surrounding skin [10]. Alongside the lesion (EM), early symptoms—often flu-like—may include headache, mild fever (rare), chills, shivering (rare), muscle and joint pain, lymphadenopathy, and fatigue, which is profound, persistent, and unrelated to physical activity [10,11]. Symptoms typically last around four weeks [11].

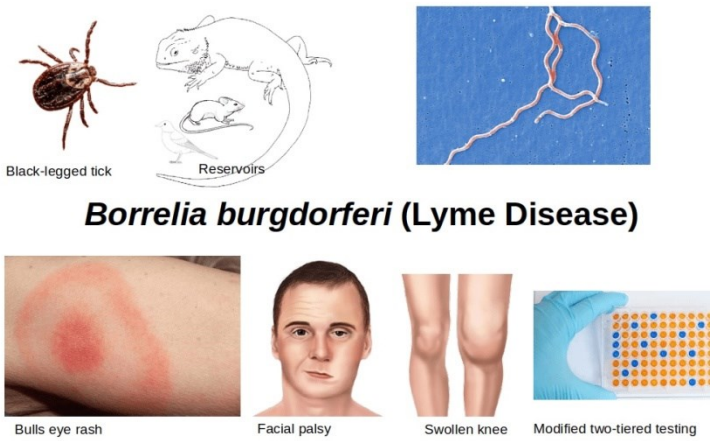
In untreated patients, after several weeks, hematogenous dissemination can occur, leading to systemic manifestations such as fatigue, myalgia, and skin, cardiac, and neurological disorders [10,11]. Arthritis develops in about 60% of patients, usually monoarticular or oligoarticular, predominantly affecting the knee joint—a sign of late-stage LD (third stage) [10,12].

Neurological manifestations occur in about 10–20% of patients, most commonly facial nerve palsy. This belongs to the secondary stage and is less common in Europe. The Centers for Disease Control and Prevention (CDC) identifies this symptom as frequent in the United States [12].

The second stage may also include carditis, occurring in approximately 8% of untreated, infected individuals, presenting with palpitations and atrioventricular (AV) conduction abnormalities, as well as electrocardiographic changes in the S-T segment and T wave [10,12].

The late stage, developing months or even years after untreated Lyme disease, leads to polyarthritis and chronic skin lesions with discoloration, known as acrodermatitis chronica atrophicans [11,13].

Figure 3. Borrelia Burgdorferi - Lyme disease
Source: https://i0.wp.com/microbeonline.com/wp-content/uploads/2021/05/Borrelia-Burgdorferi-Lyme-Disease-min.png?ssl=1



Prolonged attachment of a tick to the skin increases the likelihood of transmitting Borrelia burgdorferi. Therefore, timely removal of the tick is crucial for reducing the risk of infection. The longer the tick remains attached, the higher the probability of pathogen transmission. For this reason, prompt and proper

tick removal is one of the most important steps in preventing the clinical manifestation of Lyme disease [14,15].

If a tick is observed on the body, it is recommended to remove it as soon as possible [16,17]. Ideally, this should be done in a healthcare facility, where a physician can assess the risk of infection and determine further management. If immediate professional removal is not possible, the tick can be removed independently using fine-tipped tweezers. The tweezers should grasp the tick as close to the skin as possible, near its head, and pull it out slowly, steadily, and evenly without sudden movements (Figure 4).

After removal, the bite site should be disinfected with alcohol or iodine [18]. Regardless of successful removal, it is recommended to see a physician promptly to evaluate the risk, monitor for potential symptoms, and decide whether further diagnostic or prophylactic measures are needed [17,19]. The key is not only proper tick removal but also monitoring one's health and seeking medical attention, as infection can occur even after the tick has been removed [16,17].

Figure 4. Removing ticks with tweezers
Source: https://www.bbc.com/serbian/lat/svet-69247310

Routine testing of ticks themselves for the presence of Borrelia burgdorferi or other pathogens is not recommended for clinical purposes, as a positive result does not confirm that infection has been transmitted, nor does it determine therapeutic management. The main criteria for deciding on prophylactic treatment include: the tick species (Ixodes), endemic region, duration of attachment (>36 hours), and time since removal (<72 hours)—as recommended by the IDSA/AAN/ACR Lyme disease guidelines (2020) [20].

LABORATORY DIAGNOSIS OF LYME DISEASE

The laboratory diagnosis of Lyme disease involves a combination of methods applied according to the stage of the disease and its clinical presentation [21,22]. The most accessible and widely used diagnostic approach is serological testing of blood samples (ELISA, confirmed by Western blot) [21,23]. In cases where neuroborreliosis is suspected, both serological testing and PCR analysis of cerebrospinal fluid (CSF) are performed [22,24].

The PCR method enables the direct detection of Borrelia burgdorferi DNA in blood, CSF, or specific tissue samples; however, a negative result does not exclude infection. Although removed ticks can also be tested by PCR for pathogen detection, such testing has epidemiological significance only and does not guide therapeutic decisions [21,25].

Proper interpretation of laboratory findings requires integration of test results with the clinical picture and epidemiological factors, since serological tests may yield false-positive or false-negative results, particularly in the early stages of the disease.

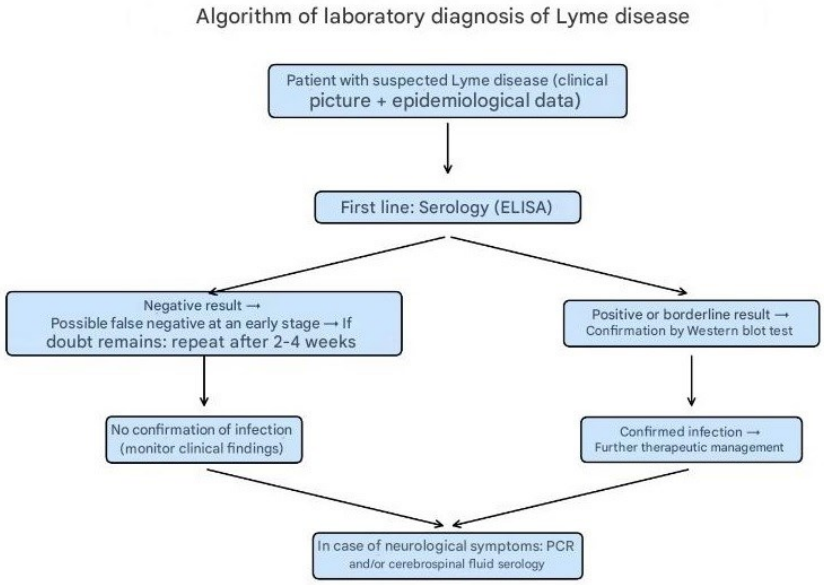


Table 1. Laboratory diagnostics

Sample	Method	Advantages	Limitations / Notes
Blood	Serology (ELISA → Western blot)	The most affordable method, widely available	Antibodies appear slowly (3–6 weeks); false positive and negative results can be >20%; requires clinical correlation
Blood	PCR	The possibility of DNA detection in the early stages of the disease	A negative result does not rule out infection; sensitivity varies in different stages of the disease
CSF	Serology / PCR	Useful in suspected neuroborreliosis	Invasive procedure; results depend on the stage of the disease
Synovial fluid / tissue	PCR	Specifically for arthritis or local infections	It is used only in selected cases; laboratory required process
Tick	PCR	Determination of the presence of Borrelia burgdorferi (epidemiological significance)	It is not used for clinical diagnostics; the finding does not determine the therapy

Ticks are not used for serological diagnosis in clinical practice. Their testing serves exclusively epidemiological purposes or research on the distribution of pathogens. Serological tests of blood and cerebrospinal fluid remain the cornerstone of routine laboratory diagnosis of Lyme disease.

Serological testing is the most accessible diagnostic approach (performed by almost all public health institutes) and represents the first step in the serological diagnosis of Lyme disease. However, these tests are neither highly specific nor highly sensitive, yielding more than 20% false-positive and false-negative results. It is also important to emphasize that antibodies to Borrelia burgdorferi develop slowly, and blood sampling should not be performed before the end of the third or fourth week after the onset of symptoms. Therefore, caution is required when interpreting serological results in Lyme disease.

The main serological tests used for diagnosis are ELISA and immunofluorescence assays (IFA). The ELISA test (Figure 5) for Borrelia burgdorferi identifies the presence of IgM and IgG antibodies, indicating whether it is an acute infection (IgM) or a past infection (IgG)—although it is important to note that the presence of IgG antibodies in Lyme disease does not always confirm a past infection, as it might in other diseases [26,15].

IgM antibodies usually appear 2–4 weeks after the onset of the erythema migrans lesion but are not always detectable at sufficient levels for serological identification and typically disappear after 4–6 months. In some cases, IgM antibodies may persist for several months after initial detection. IgG antibodies typically appear 8–12 weeks after the onset of illness and reach their peak within 4–6 months.

In the serological diagnosis of Lyme disease, the initial tests include ELISA, EIA (enzyme immunoassay), or IFA (immunofluorescence antibody assay). Negative results in the early phase of the

disease do not exclude the diagnosis, as antibodies may still be insufficiently developed—particularly if antibiotic therapy was initiated early or if erythema migrans is still present. Positive or borderline results should be confirmed using the Western immunoblot test (Figure 6).

If serological results are negative, but clinical symptoms of Lyme disease persist, it is recommended to repeat testing after 2–4 weeks [27,28].

Figure 5. How to choose the right propeller kit

Source: https://www.bmgrp.com/how-to-choose-the-right-elisa-kit/

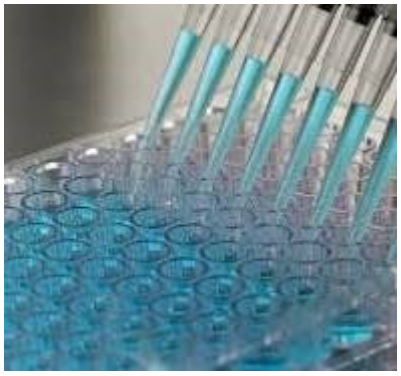
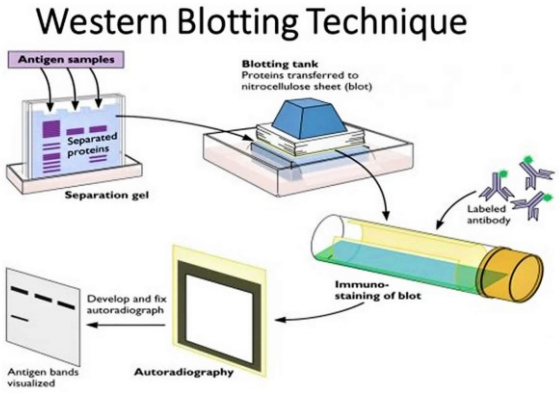


Figure 6. Western blotting technique, used to detect specific proteins in samples

Source: https://healthjade.net/western-blot/



In addition to these tests, PCR is less commonly used in diagnostics and is recommended for testing the tick itself for the presence of Lyme disease pathogens (primarily for research purposes, not routine diagnostics). PCR is also the only method used in everyday diagnostics, apart from the cultivation of Borrelia on BSK II medium, which is performed only in research settings.

False-positive serological results for Lyme disease can occur in patients with syphilis. Early diagnosis and timely administration of antimicrobial therapy play a key role in preventing cardiac, neurological, and musculoskeletal complications. It is important to note that antibiotics in the initial stage of Lyme disease do not prevent the development of symptoms in later stages but serve as prophylactic treatment to reduce the risk of disease progression..

TREATMENT OF LYME DISEASE

In the treatment of early Lyme disease, oral antibiotics such as amoxicillin, doxycycline, or cefuroxime are used. The choice of antibiotic and duration of therapy depend on the patient's age and the clinical stage of the disease. Doxycycline is generally avoided in children under 8 years due to potential effects on teeth and bones, while amoxicillin is preferred in pregnant women.

For patients with recurrent arthritis or involvement of the central or peripheral nervous system, parenteral therapy with intravenous antibiotics—most commonly ceftriaxone, cefotaxime, or penicillin G—is administered. IV therapy is reserved for severe or chronic forms of the disease, with dose, duration, and patient age being crucial factors for treatment effectiveness and complication prevention.

Lyme disease therapy is guided by the clinical form, disease severity, and patient age. In early localized forms, oral antibiotics—doxycycline, amoxicillin, or cefuroxime—are prescribed, with restrictions for children under 8 years and pregnant women. Treatment duration ranges from 10 to 21 days, depending on the antibiotic and clinical presentation. For more severe or chronic forms, including neuroborreliosis and recurrent arthritis, parenteral therapy with intravenous ceftriaxone, cefotaxime, or penicillin G is used, typically for 14–28 days. Treatment efficacy depends on timely administration, appropriate dosage, therapy duration, and patient age. [29,30].

Table 2. Lyme Disease Therapy: Antibiotics, Dosages, and Duration

Form of Lyme disease	Antibiotic	Dose (adult)	Duration of therapy	Notes / age
Early localized (erythema migrans)	Doxycycline	100 mg orally 2× daily	10–21 days	Not recommended for children <8 years; not for pregnant women
	Amoxicillin	500 mg orally 3× daily	14–21 days	Suitable for children and pregnant women
	Cefuroxime axetil	500 mg orally 2× daily	14–21 days	Alternative for children and adults
Early disseminated / neuroborreliosis	Ceftriaxone i.v.	2 g daily	14–28 days	Application in severe and chronic forms
	Cefotaxime i.v.	2 g every 8 hours	14–28 days	-
	Penicillin G i.v.	18–24 million IU per day in 4–6 doses	14–28 days	-
Recurrent arthritis / central and peripheral nervous system	Ceftriaxone i.v.	2 g daily	14–28 days	More severe forms of the disease, the age of the patient affects the dose
	Cefotaxime i.v.	2 g every 8 h	14–28 days	-
	Penicillin G i.v.	18–24 miliona IU per day in 4–6 doses	14–28 days	-

Notes: Doxycycline is not used in children under 8 years of age and in pregnant women due to the risk to teeth and bones. Oral therapy is applied in early localized forms. I.V. therapy is used in severe, disseminated, or chronic forms, in cases of neuroborreliosis and recurrent arthritis. The duration of therapy can be adjusted according to the patient's clinical response..

PREVENTION

Control of ticks in areas frequently visited by people (parks, forested parks, recreational areas) represents a fundamental measure for preventing tick bites and, consequently, reducing the risk of Lyme disease transmission. Preventive activities can be divided into ecological control measures, personal protective measures, and public health interventions:

Ecological control measures include the application of appropriate acaricides on limited areas with high tick populations, mowing and maintenance of grassy areas—especially in places used for recreation and play—removal of leaves, low vegetation, and branches in parks and yards to reduce suitable tick habitats, control of rodent populations that are natural reservoirs of Borrelia burgdorferi, and minimizing human-rodent contact.

Personal protective measures involve wearing appropriate clothing when in nature: long sleeves, long pants tucked into socks, closed shoes, and light-colored clothing to facilitate tick detection; using repellents based on DEET, icaridin, or permethrin (on clothing), especially for individuals spending extended time outdoors in endemic areas; and performing a full-body tick check after outdoor activities, including hair, skin folds, and areas where ticks commonly attach.

Public health interventions include educating the population about the risks of tick bites, protection methods, and the importance of early tick removal; organizing tick control campaigns in public areas during peak activity seasons (spring and summer); monitoring and surveillance of tick populations in endemic regions; and risk mapping for the local population. [31-33].

CONCLUSION

Lyme disease represents a significant public health problem in endemic areas of Europe and North America. Prevention is based on reducing contact with ticks, wearing protective clothing, using repellents, and implementing ecological measures to control tick and rodent populations. Diagnosis is primarily clinical, supported by serological testing, while molecular methods serve as supplementary diagnostic tools. Timely and appropriate antibiotic therapy in the early stage of the disease is crucial for preventing systemic complications. Educating the public and healthcare personnel, as well as proper tick removal, are the most effective strategies for controlling and preventing Lyme disease.

LITERATURE:

1. Connie R. Mahon I Donald C. Lehman TEXTBOOK OF DIAGNOSTIC MICROBIOLOGY. ELSEVIER. 2019.
2. Savić B, Mitrović S, Jovanović T. MEDICINSKA MIKROBIOLOGIJA. Medicinski fakultet Beograd. 2022.
3. Nikolić S., Stojanović D. INFEKTIVNE BOLESTI SA EPIDEMIOLOGIJOM – priručnik za zdravstvene radnike, Nota, Knjaževac, 1998 (ISBN 86.357.0437.1).
4. Barbour, A. G., and G. R. Johnson. 1988. "The Borrelia burgdorferi sensu lato: the Lyme disease spirochete." Annual Review of Microbiology 42: 345-372.
5. Stanek, G., et al. 2011. "Lyme borreliosis." The Lancet 379(9714): 461-473.
6. Estrada-Peña A, de la Fuente J. The ecology of ticks and epidemiology of tick-borne viral diseases. Antiviral Res. 2014;108:104-128. doi:10.1016/j.antiviral.2014.05.016.
7. Stanek G, Wormser GP, Gray J, Strle F. Lyme borreliosis. *Lancet*. 2012;379(9814):461-473. doi:10.1016/S0140-6736(11)60103-7.
8. Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al. Lyme borreliosis. *Nat Rev Dis Primers*. 2016;2:16090. doi:10.1038/nrdp.2016.90.
9. Rizzoli A, Hauffe HC, Carpi G, Vourc'h GI, Neteler M, Rosa R. Lyme borreliosis in Europe. *Euro Surveill*. 2011;16(27):19906.
10. Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JW, et al. Lyme borreliosis. *Nat Rev Dis Primers*. 2016;2:16090. doi:10.1038/nrdp.2016.90.
11. Stanek G, Wormser GP, Gray J, Strle F. Lyme borreliosis. *Lancet*. 2012;379(9814):461-473. doi:10.1016/S0140-6736(11)60103-7.
12. Centers for Disease Control and Prevention (CDC). Lyme Disease [Internet]. CDC; 2023. Available from: https://www.cdc.gov/lyme
13. Hu LT. Lyme disease. *Ann Intern Med*. 2016;164(9):ITC65-ITC80. doi:10.7326/AITC201605030
14. Centers for Disease Control and Prevention (CDC). Lyme Disease: Transmission [Internet]. Atlanta: CDC; 2024 [cited 2025 Oct 1]. Available from: https://www.cdc.gov/lyme/causes/index.html
15. European Centre for Disease Prevention and Control (ECDC). Factsheet about Lyme borreliosis [Internet]. Stockholm: ECDC; 2025 [cited 2025 Oct 1]. Available from: https://www.ecdc.europa.eu/en/lyme-borreliosis/facts
16. Centers for Disease Control and Prevention (CDC). Tick Removal and Testing [Internet]. CDC; 2023. Available from: https://www.cdc.gov/ticks/removing_a_tick.html
17. Stanek G, Strle F. Lyme borreliosis–from tick bite to diagnosis and treatment. *FEMS Microbiol Rev*. 2018;42(3):233-258. doi:10.1093/femsre/fux047.
18. World Health Organization (WHO). Vector-borne diseases – Ticks [Internet]. WHO; 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases
19. Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2006;43(9):1089-1134. doi:10.1086/508667.
20. Lantos PM, Rumbaugh J, Bockenstedt LK, Falck-Ytter YT, Aguero-Rosenfeld ME, Auwaerter PG, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. Clin Infect Dis. 2021;72(1):e1-e48.
21. Centers for Disease Control and Prevention (CDC). Lyme Disease: Laboratory Testing [Internet]. CDC; 2023. Available from: https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/index.html
22. Stanek G, Strle F. Lyme borreliosis–from tick bite to diagnosis and treatment. *FEMS Microbiol Rev*. 2018;42(3):233-258. doi:10.1093/femsre/fux047.
23. Hu LT. Lyme disease. *Ann Intern Med*. 2016;164(9):ITC65-ITC80. doi:10.7326/AITC201605030.
24. Mygland Å, Ljøstad U, Fingerle V, Rupprecht T, Schmutzhard E, Steiner I. EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis. *Eur J Neurol*. 2010;17(1):8-16. doi:10.1111/j.1468-1331.2009.02862.x.
25. Dessau RB, van Dam AP, Fingerle V, Gray J, Hunfeld KP, Jaulhac B, et al. To test or not to test? Laboratory support for the diagnosis of Lyme borreliosis: a position paper of ESGBOR, ESCMID Study Group for Lyme Borreliosis. *Clin Microbiol Infect*. 2018;24(2):118-124. doi:10.1016/j.cmi.2017.08.025.
26. Infectious Diseases Society of America; American Academy of Neurology; American College of Rheumatology. Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease. Clin Infect Dis. 2020;72(1):e1-e48. OUP Academic
27. European Centre for Disease Prevention and Control (ECDC). Factsheet about Borreliosis (Lyme disease) [Internet]. Stockholm: ECDC; 2025 [cited 2025 Oct 1]. Available from: https://www.ecdc.europa.eu/en/borreliosis/facts/factsheet Evropski centar za prevenciju bolesti
28. Centers for Disease Control and Prevention (CDC). Clinical Care of Lyme Disease [Internet]. Atlanta: CDC; 2024 [cited 2025 Oct 1]. Available from: https://www.cdc.gov/lyme/hcp/clinical-care/index.html cdc.gov
29. Lantos PM, et al. 2020 guidelines for the prevention, diagnosis, and treatment of Lyme disease. *Arthritis Care Res (Hoboken)*. 2021 Jan;73(1):1-9. doi: 10.1002/acr.24495.
30. Centers for Disease Control and Prevention (CDC). Lyme disease treatment. Available from: https://www.cdc.gov/lyme/treatment/index.html
31. European Centre for Disease Prevention and Control (ECDC). *Personal protective measures against tick bites*. Available from: https://www.ecdc.europa.eu/en/disease-vectors/prevention-and-control/protective-measures-ticks
32. National Park Service (NPS). *Ticks and tickborne diseases*. Available from: https://www.nps.gov/articles/000/ticks-and-tickborne-diseases.htm
33. National Institute for Occupational Safety and Health (NIOSH). *Tickborne diseases in workers*. Available from: https://www.cdc.gov/niosh/outdoor-workers/about/tick-borne-diseases.html