

Lyme Disease (Borreliosis) and Relapsing Fever — Diagnosis and Stages

[See online here](#)

In the following article, we present all the relevant facts, tips and exam questions from the first symptoms to the treatment of the infection with borrelia.



Definition of Lyme Disease



Adult deer tick, *Ixodes scapularis*."

Lyme disease is a disease that is caused by an infection caused by bacteria of the species *Borrelia burgdorferi*, *Borrelia mayonii*, *Borrelia afzelli*, and *Borrelia garinii*. These

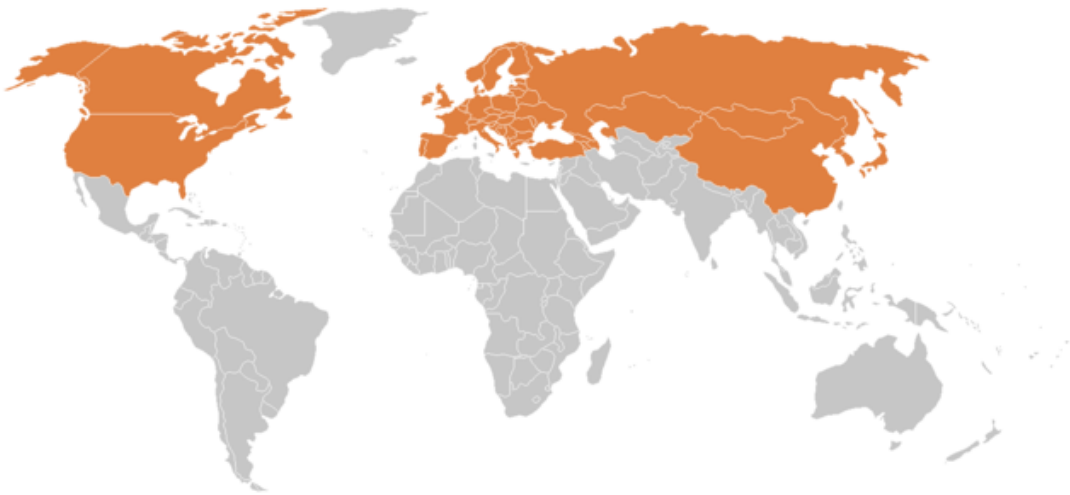
belong to the family of gram-negative spirochetes. The agents are transmitted to humans via bites of infected black-legged ticks known as deer ticks. The ticks are more common in grassy and woody areas of the environment. The disease manifests itself in different organs; particularly affected are the skin, the neuro system, and the joints.

Synonyms: Lyme-Borreliosis, Neuroborreliosis, Lyme disease.

Lyme-Borreliosis is named after the village Lyme (Connecticut, USA). It was in this village, where joint inflammations occurred frequently. W. Burgdorfer discovered the agent in 1981, but the skin manifestations had already been described in Europe before

Epidemiology of Lyme Disease

Prevalence of Lyme-Borreliosis

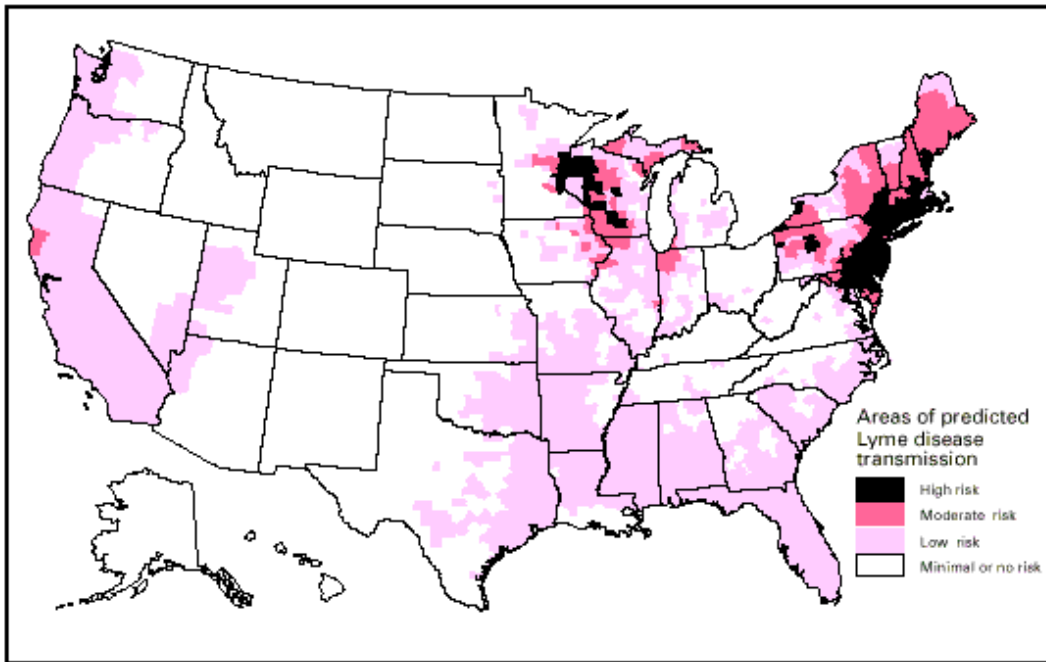


By [Vice regent](#) at en.wikipedia - [Vice regent](#) (talk) ([Uploads](#)). Transferred from en.wikipedia by [SreeBot](#), [GFDL](#), [Link](#)

Lyme Borreliosis represents the most frequently transmitted disease via ticks in Europe.

- 5-35% of the ticks are infected with Borrelia.
- The infection can occur from March to October, the critical period is from June to July.
- The regional spread of the infected ticks applies differently in various locations and should be considered for the diagnosis.

National Lyme disease risk map with four categories of risk



Note: This map demonstrates an approximate distribution of predicted Lyme disease risk in the United States. The true relative risk in any given county compared with other counties might differ from that shown here and might change from year to year. Risk categories are defined in the accompanying text. Information on risk distribution within states and counties is best obtained from state and local public health authorities.

Etiology and Pathogenesis of Lyme Disease

Agents of Lyme-Borreliosis

Lyme-Borreliosis is caused by different species of borrelia, that all belong to the complex *Borrelia burgdorferi sensu lato*. The following 4 human-pathogenic species are most often represented:



- [Image](#): "Using darkfield microscopy technique, this photomicrograph, magnified 400x, reveals the presence of spirochete, or "corkscrew-shaped" bacteria known as *Borrelia burgdorferi*, which is the pathogen responsible for causing Lyme disease. *Borrelia burgdorferi* are helical shaped bacteria, and are about 10 – 25µm long. These bacteria are transmitted to humans by the bite of an infected deer tick, and

caused more than 23,000 cases of Lyme disease in the United States during 2002.” by Centers for Disease Control and Prevention’s Public Health Image Library (PHIL). License: Public Domain.

- *Borrelia burgdorferi sensu stricto*
- *Borrelia garinii*
- *Borrelia afzelii*
- *Borrelia spielmanii*

Reservoir of the Borrelia

- Small rodents and birds.
- Deer and roes are animal hosts for ticks.
- A couple of hundred vertebrate species are potential hosts for the vectors (hard ticks).

Path of infection and pathogenesis of the Lyme Borreliosis



Image: “The black-legged tick (*Ixodes scapularis*), the primary vector for Lyme disease in the central and eastern United States (and elsewhere too. Uploader).” by A New View on Lyme Disease: Rodents Hold the Key to Annual Risk. Gross L, PLoS Biology Vol. 4/6/2006, e182. License: [CC BY 2.5](https://creativecommons.org/licenses/by/2.5/)

In Central Europe, borrelia bacteria are transmitted via the bite of the hard tick *Lxodes (I.) ricinus* and *Lxodes scapularis*. The ticks can move from low vegetation (1.5 m) to humans.

Note: With the attachment period, the risk of disease increases significantly. The attachment period is dangerous from 24 hours on. Certain surface proteins of the Borrelia bacteria ensure that they can attach to the host cells. Also, pro-inflammatory cytokines are released.

More different immune mechanisms are discussed:

- Induction of autoantibodies against neuronal and glial antigens.
- Cross-reactivity of Borrelia antibodies with neuronal antigens.
- T-cell-mediated immune response.

Borrelia bacteria can survive for many years in the host, for example, in phagocytes.

Risk groups are forestry workers, hunters, farmers, and hikers.

Incubation period: 4-18 days

Symptoms and Clinic of Lyme Disease

Staging for Borreliosis

There are three stages to the symptomatology of a Borreliosis:

Stage I Week 1 - 5

Incubation period: Weeks to months



Erythema migrans - erythematous rash in Lyme

The creation of *Erythema chronicum migrans*, a bull's eye rash that appears about 2 weeks after a tick bite. This skin reaction corresponds to the local spread of the agent in the dermis. Just half of the patients, that are experiencing stage 2, have *Erythema chronicum migrans*. Furthermore, symptoms, such as fever, myalgia, arthralgia, and weariness can occur. Typically, the patients without the symptoms have issues in the respiratory tract (flu without a cough, sputum or rhinitis).

Note: *Erythema chronicum migrans* may not occur!

Stage II

Incubation period: Weeks to months

Meningoradiculitis: Radicular pains (**Bannwarth-syndrome**), partly radicular paresis, peripheral facial palsy (often on both sides). Also joint involvement, myocarditis, pericarditis or *Lymphadenosis cutis benigna*. The latter describes reactive hyperplasia of the lymphatic cells. The Lymphadenosis cutis benigna manifests itself mainly in terms of bluish-red nodes in the skin, for example, near the earlobe.

Stage III

Incubation period: Months to years

The patients suffer from *Acrodermatitis chronica atrophicans herxheimer*. This dermatologic manifestation of the Borreliosis has chronic-progressive stages; the extensor sides of the extremities are the most affected. At first, there is edema. Next, atrophy of the subcutis develops resulting in the subcutaneous fat whereby the thickness of the skin becomes reduced and the vessels beneath the skin can shine through. Finally, the affected parts of the skin become sclerotic and develop a significant thickening that is hairless.

Other symptoms include Lyme arthritis with a 90% manifestation in the knee joint. The **symptoms appearing in the stage 3 of a chronic neuroborreliosis** are:

- Encephalomyelitis: Paraparesis and tetraparesis
- Distal-symmetric Polyneuropathy
- Ataxia
- Bladder dysfunction
- Dysesthesias and asymmetric radicular signs of paralysis
- Heart problems such as irregular heartbeats
- Hepatitis
- Severe fatigue

There is also a possibility of an eye involvement with uveitis, keratitis, episcleritis, and retinal vasculitis.

Note: The staging for Borreliosis should be considered as a theoretical construct, as it is too artificial.

For the clinical classification, the categorization is considered in an early and late manifestation of the disease:

- **Early manifestation (located: *Erythema migrans*; disseminated: e.g. acute neuroborreliosis)**
- **Late manifestation (arthritis, acrodermatitis and chronic neuroborreliosis)**

Diagnostic and Therapy of Lyme Disease

The Lyme-Borreliosis is primarily a **presumptive clinical diagnosis**. This is supported by the medical history and laboratory diagnostics. 80–90% of the patients with clinical neuroborreliosis will have the suspicion confirmed by a **specific intrathecal antibody synthesis**.

Pathogen detection: Serology-Step-by-Step diagnosis

1. **ELISA (or immunofluorescence test):** Verification of antibodies (IgM/IgG) against *B. burgdorferi* in the **enzyme-linked immuno-absorbent assay tests**. Warning: the increase of the borrelia antibodies doesn't have to be always detectable, or can also happen to be detectable a couple of days after the tick bite. The antibodies are not appropriate for the evaluation of the therapeutic process! After a successful antibiotherapy, the antibodies can also, over months to years, circulate in the cerebrospinal fluid. If the test for the first stage is positive, follow 2.
2. **Immunoblot (Western Blot):** As confirmation test.

A positive antibody finding and corresponding clinical findings suggest Lyme-Borreliosis.

Note: If there is at the same time infection with syphilis, it may happen that false positive findings occur because of cross-reactions (TPHA test!).

Overview of the Diagnostic and Therapy of the 3 Stages of Borrelia

Stage	Diagnostic	Therapy
Stage I	Medical history of tick bites (50% of the patients don't remember). Antibody detection in the blood (successful in just 40% of the patients).	Doxycyclin or erythromycin p.o. for 2 weeks; for children and pregnant women: amoxicillin and cefuroxime; in case of intolerance: azithromycin
Stage II	IgG-antibody detection in blood, confirmation test with Western Blot. For Lyme arthritis: agent detection in punctate.	Cephalosporin of the 3rd generation (e.g., ceftriaxone) Penicillin G intravenous for 2-3 weeks if symptoms are particularly severe.
Stage III	Antibody detection in blood and liquor examination: lymphocytic pleocytosis, increased the percentage of protein, intrathecal Borrelia-specific IgG/IgM antibodies, and occasionally direct pathogen tests (Borrelia-DNA).	Cephalosporin of the 3rd generation intravenous for 2-3 weeks

Differential diagnosis of Lyme Disease

Dependent on the stage of the disease, there are many possibilities that can be considered for a differential diagnosis:

- Disease with infection via ticks: FSME, anaplasmosis, and rickettsiosis
- Neurological symptoms: multiple sclerosis
- Joint inflammations: activated arthrosis and rheumatoid arthritis
- If therapy is unsuccessful: search for tumors

Prophylaxis and Prevention of Lyme Disease

If the tick is removed within the first 12 hours, the risk to be infected with Borrelia is very low. For the removal, a tick tweezer should be used. For persons from non-endemic areas, there is no need for prophylactic antibiotics, but the side of injection should be observed.

Precautions against ticks:

- Adequate clothing
- Repellents
- Scanning the body for ticks after being outside (focus on the axillary and inguinal regions!).
- Create a tick-proof yard by clearing brush and leaves where ticks live and keeping wood piles in sunny areas.
- Remove ticks from bite site as soon as possible and do not assume immunity is developed after the initial infection.

Note: There is no vaccine against Borreliosis yet. A person who already suffered from Borreliosis is not immune to a re-infection.

Complications of Lyme disease

- Chronic joint inflammation (Lyme arthritis).
- Neurological symptoms such as facial palsies and neuropathies.
- Impaired memory.
- Irregular heart rhythm.

Epidemic and Endemic Relapsing Fever

Facts to the relapsing fever in an overview.

	Epidemic relapsing fever	Endemic relapsing fever
Agents	<i>Borrelia recurrentis.</i>	<i>Borrelia duttoni</i>
Transmission	Lice (<i>Pediculus humanus</i>), "Relapsing fever due to lice," mainly in the cold season; lack of hygiene	Lederzecken (<i>Ornithodoros</i>), "Recurrent fever" in Germany is known as imported travel disease.
Pathogenesis	Pyrogenic effects by cell wall antigens	
Symptoms	Recurrent fever for 3-6 days, symptom-free intervals, chills, arthralgias, myalgias, stomach aches, hepatosplenomegaly, diffuse petechial hemorrhages, and pinpoint large macular exanthema.	
Complications	30% of the patients develop seizures, coma, hemiplegia, CNS-bleedings, myocarditis with arrhythmia, and liver failure.	
Diagnostic	Serological diagnostics is unreliable! Detection of the pathogens in peripheral blood via dark-field microscopy.	
Therapy	Erythromycin, alternatively tetracycline	
Lethality	2 - 5%	Up to 40%

Review Questions

The correct answers can be found below the references.

1. If drug therapy for Borreliosis is indicated, which antibiotic should be prescribed for pregnant women?

- A. Doxycyclin
- B. Amoxicillin
- C. Ciprofloxacin
- D. Vancomycin
- E. Erythromycin

2. A 21-year-old teacher, who until now was never seriously sick, shows the following symptoms (in March): slight fever, flushing of the face and symptoms of a cold. She goes to the Doctor's surgery. The physical examination shows exanthemas in the extremities. Which diagnosis does she fit the most?

- A. Exanthema subitum
- B. Lyme-Borreliosis
- C. Erythema infectiosum
- D. Rheumatic nodules
- E. Measles

3. The initial manifestation of the borreliosis consists probably of an ...

- A. ...*Erythema anulare centrifugum*
- B. ...*Erythema (exsudativum) multiforme*
- C. ...*Erythema infectiosum*
- D. ...*Erythema nodosum*
- E. ...*Erythema (chronicum) migrans*

References

Berger, S. (2018). *Relapsing fever*. Los Angeles, CA: GIDEON Informatics Inc.

Halperin, J. J., & García-Monco, J. C. (2014). The Human Borreliosis: Lyme Neuroborreliosis and Relapsing Fever. *CNS Infections*, 211-226. doi:10.1007/978-1-4471-6401-2_11

Peterson, J. M. (2001). *Lyme disease*. Mankato, MN: LifeMatters.

Rath, P. -, Fehrenbach, F. -, Rögler, G., Pohle, H. D., & Schönberg, A. (1992). Relapsing fever and its serological discrimination from Lyme borreliosis. *Infection*, 20(5), 283-286. doi:10.1007/bf01710797

Correct answers: 1B, 2C, 3E

Legal Note: Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).