Lyme disease

Lyme disease (LB) is the most common tick-borne infection in the Czech Republic and is also the most common anthropozoonosis in Europe, Asia and North America. LB is caused by bacteria of the Borrelia burgdorferi complex sensu lato. The infection is not transmitted only by adult ticks, but also by their younger developmental stages; transmission between humans is not possible. Most infections are asymptomatic, with clinically manifest cases mainly affecting the skin, joints, nervous system and heart. The most common form and typical manifestation is erythema migrans.

Diagnosis of LB is relatively difficult, clinical suspicion can be confirmed by serological examination of anti-Borrelia antibodies by ELISA with confirmation by Western blot in IgM and IgG classes. However, a positive serological finding without clinical manifestations of LB is not an indication for antibiotic treatment.

Early forms of LB usually resolve spontaneously, antibiotics accelerate the disappearance of symptoms and reduce the risk of persistence of Borrelia in the body and other symptoms. LB does not cause death, but its chronic course can reduce the quality of life in the long run. The vaccine is not available for human use.

Epidemiology

LB is transmitted to humans by sucking an infected tick (most commonly Ixodes ricinus in Europe). The reservoir is more than 200 species of mammals, reptiles and birds (especially rodents, squirrels, dogs, cats, sheep, goats, roe deer, wild boars and cattle). Man is only a random host. The vector is ticks of the genus Ixodes and their developmental stages (larva, nymph). Larval → nymph → adult tick transmission is important for Borrelia. Borrelia have also been shown in other insect species, but transmission to humans has not been demonstrated in this way and it is assumed that Borrelia in the bodies of hosts other than ticks do not have optimal conditions and therefore survives only briefly. It is commonly reported that spirochetes live in the gut of a tick and, after sucking, migrate through the intestinal wall into the salivary glands, from where they enter their host. Recent work shows that Borrelia is not excreted in the saliva of the tick, but passes into the wound directly from its digestive tract. However, on the first day after the tick is bitten, Borrelia are not infectious because they are easily recognized by the host's immune system. However, during tick sucking, Borrelia alter the antigens expressed on their surface, gaining the ability to cause persistent infection in another host. Another possible transmission is splashing of the skin with the body's contents in the area of skin microtraumas (squeezing the tick between the fingers), but also with intact skin. Transplacental transmission is also described, but without teratogenic effects.

The disease in the Czech Republic is typically seasonal in nature, which is related to the activity of ticks, ie the maximum incidence is in July. The highest incidence is in children between 5-9 years and in adults between 55-69 years.

The reported incidence of Lyme disease in the Czech Republic in the years 2000–2009 is about 4,000 cases per year, ie. 40 patients per 100,000 inhabitants and year. The probability of clinical manifestation after the infestation of an infected tick is between 2–4%, while the prevalence in the Czech Republic is around 5–10% (sometimes up to 30%).

Originator

The causative agent is the gram-negative spirochete Borrelia burgdorferi sensu lato. Currently, more than 12 Borrelia subtypes are known. Borrelia pathogenic to humans in Europe are most often Borrelia afzelii, Borrelia garinii and least Borrelia burgdorferi sensu stricto. However, other species pathogenic to humans are also known - B. lusitaniae, B. valaisiana, B. spielmanii. In North America there is only one genospecies of this spirochete - Borrelia burgdorferi sensu stricto - causing mainly cardiac disease, in Asia and Europe it is characterized by significant genetic variability, which determines the wide heterogeneity of clinical symptoms and pathogenicity. Individual species have different affinities for tissues (B. burgdorferii sensu stricto → affects mainly the joint and nervous system, B. afzelii → skin manifestations, B. garinii → neurological manifestations).

Spirochetes are generally able to move rapidly with flagella and can pass freely not only through the epithelium but also through the blood-brain barrier, moving well in the viscous environment of the intercellular mass, in connective tissues, in cerebrospinal fluid and in synovial fluid. In the event of adverse external conditions, they can form cysts and then transform back into motile spirochetes.

Pathogenesis

By releasing infected saliva, ticks transmit Borrelia to the host's body during blood sucking 36-48 hours after sucking. After multiplying in the skin, the bacteria are transported by blood and lymph to other organs, especially the reticuloendothelial system or the CNS, where they can survive for a long time without an inflammatory process, but they cause the production of antibodies. The lipopolysaccharide-like component in the cell wall of B. burgdorferi s. Induces the release of interleukin from monocytes, which is directly responsible for tissue damage, leading to clinical symptoms.

Thanks to precise regulation of surface protein (Osp) expression, Borrelia are able to colonize the tick's digestive tract.

Symptomatology

LB has many forms of course and is characterized by a wide range of symptoms that are related to the genetic variability of its causative agent.

Lyme disease is a polysystemic disease that involves:

- skin (65%)
- musculoskeletal (17%)
- nervous (12%) heart and eye disorders.
- Any tissue in the body can be attacked.

Sometimes the disease is asymptomatic, sometimes there may be only some, or so mild that one does not even attach importance to them. Other infectious diseases, when the immune system is weakened, may contribute to their onset. It has a great tendency to self-healing.

Lyme disease is a multisystem disease that occurs in 3 stages. The symptoms of the first two stages are given directly by the action of Borrelia on the organism, in the third stage immunopathology is already involved.

Overview of clinical manifestations of Lyme disease[1][2]

Organ system	Stage 1: early localized (days to weeks after infection)	Stage 2: early generalized (weeks to months after infection)	Stage 3: late (months to years after infection)
Skin	Erytema migrans	Lymphocytoma Erythema multiple	Acrodermatitis chronica atrophicans
Nervous system		Facial nerve paresis, aseptic meningitis, encephalitis, myelitis, meningoradiculitis	Chronic encephalomyelitis, peripheral neuropathy
Joints		Arthralgia, oligoarthritis (knee) Myalgia, myositis and fibromyalgia	Chronic arthritis, enthesopathy
Heart		Carditis with heart rhythm disorders (most AV block)	Cardiomyopathy
General manifestations	fatigue, malaise, cephalea, arthralgia		

Early stage

- **Erythema migrans** – red spot and a few centimeters in size, which appears around the place of sucking in 14 days to one month. At the site of the tick's bite, there is a livid stain with centrifugal spread and central fading ("bull's eye"). Sometimes it also disappears and reappears in a different place than the tick. This stain may also not appear at all (stage 1). Or.
  - **Erythema migrans anulare** spreads to the surroundings with a vivid red border with a smooth surface and heals in the center with a central fading.
  - **Erythema migrans maculare** is homogeneous and its center remains reddish throughout, the surface of the macula is smooth.
- **Borrelia lymphocytoma** (lymphocytoma borreliensis, formerly lymphadenosis benigna cutis) is a dark red to purple papule with a smooth glossy surface ranging in size from a few mm to 3-5 cm; it usually occurs only in children, a few weeks after the infection; it is most often on the earlobe, but also on the tip of the nose, the nipples or the scrotum; without treatment it often persists for weeks and months; is rarer than erythema migrans.
- **Fatigue**, and recurrent fever
- **skin burning,**
- **neurological problems**– appear 1 month to 3 months after infection - tics, muscle twitching, paraesthesia, dizziness, irregular heartbeat,
- **back pain**– mainly cervical spine, between shoulder blades, lumbalgia,
- **neuroborreliosis:**
  - ***acute peripheral paresis of the facial nerve*** - Lyme disease is the most common cause of acute peripheral paresis of the facial nerve in children, pleocytosis in cerebrospinal fluid,
  - ***Borrelia meningitis*** - Lyme borreliosis is the third most common demonstrable cause of serous meningitis in childhood,
- **muscle pain**
- **joint pain**
- **visual disturbances** - focusing, double vision,
- **keratitis** - inflammation of the cornea (up to stage 3),
- whistling in the ears, pounding in the ears, various noises,
- **damage to the liver, kidneys, heart, meningitis, various other inflammations and more**. It usually attacks the most damaged organ first (nervous system, liver in an alcoholic, joints in the elderly, etc.).
- **Autoimmune reactions** - recurrent inflammation can trigger an autoimmune reaction. One of them is arthritis. It arises from often repeated mild inflammations. Autoimmune reactions are treated with hormonal drugs.
- Garin-Bujadoux-**Bannwarth** syndrome - lymphocytic meningoradiculitis with a peripheral nervous system, manifested by radicular pain or sensory disorders, typically in adults, rarely in children.

Late stage

- **Acrodermatitis chronica atrophican**s - subcutaneous degeneration, not earlier than one year after infection, but also several years after infection (one of the main symptoms of stage 3), predilection sites are acres and skin areas above large joints These are red or blue-red lesions, initially subcutaneously soaked. The lesions gradually atrophy, the skin is as thin as cigarette paper, wrinkled, the blood vessels are clearly visible. Above the bone protrusions are palpable nodules. Long-term impairment is accompanied by peripheral neuropathy. The causative agent is always B. afzelii.

Diagnostics

Diagnosis of LB is based on epidemiological history, presence of clinical signs, laboratory tests and rapid antibiotic response. In 50% of cases, the history of tick bites and erythema migrans is negative. Due to the frequent asymptomatic course and non-specific clinical symptoms, the diagnosis is based on laboratory methods. These can be direct or indirect.

Direct methods are based on the demonstration of the presence of the agent in the examined biological material (skin biopsy, blood, urine, joint effusion, cerebrospinal fluid, vitreous fluid). These include: cultivation on special soil (very difficult, used more for research purposes), immunohistological examination (not used in practice, risk of confusion with Treponemas), PCR of synovial fluid, cerebrospinal fluid and skin biopsy (detection of nuclear and plasmid DNA), DNA hybridization (older method, uses radioactive isotope labeling), electron microscopy (especially cerebrospinal fluid examination), immunofluorescence. They are highly specific, but their implementation is relatively complicated and time consuming.

In practice, **indirect methods** are more often used, aimed at the detection of specific IgM and IgG antibodies in serum or other biological material (cerebrospinal fluid, joint puncture). Indirect methods include: ELISA - enzyme immunoassay, IFA - indirect immunofluorescence (allows to detect differences in antibody titers of acute and convalescent sera, performed when acute infection is suspected before and after treatment), western blot hybridization, indirect hemagglutination, complement fixation test, blast transformation of T lymphocytes. These tests are only of supportive, not confirmatory, in determining the diagnosis because they do not distinguish the antibodies of the current infection from the antibodies of the old infection.

Further examination:

- examination of cerebrospinal fluid for intrathecal immunoglobulin synthesis in suspected neuroborreliosis; serum and IgG albumin and IgG levels are compared;
- electrocardiographic examination in case of suspected Borrelia carditis.

Most used serological diagnostics:

- ELISA or EIA (enzyme immunoassay);
  - detection of antibodies against B. afzelii, garinii, burgdorferi sensu stricto using single or mixed (recombinant) antigens;
- western blot (immunoblot) - more accurate, sensitive and more expensive than ELISA, so it is used to confirm ELISA results; detection of antibodies against individual parts of the Borrelia body.

Most patients respond in the early stages of the disease by producing IgM antibodies, which begin to form at weeks 3 to 6 after infection and reach a maximum around week 8, when IgG antibodies begin to form. Therefore, a laboratory examination does not make sense until about 4 weeks after the tick has been sucked in. Both clinical and laboratory findings should be considered for the definitive diagnosis of Lyme disease and the initiation of antibiotic treatment. This is because the presence of specific antibodies is common in people without clinical manifestations of the disease, as is the absence of specific antibodies in patients with clinical problems. Thus, the finding of specific antibodies alone should not be an indication for antibiotic treatment.

Differntial diagnostics

- Skin form - rose, phlegmon, cellulite,
- lymphocytoma - tumors
- acrodermatitis - trophic changes
- CNS involvement - other aseptic neuroinfections.
- Tick-borne diseases in Europe: tick-borne encephalitis (flaviviruses), Marseilles fever, Q fever, TIBOLA (tick-borne lymphadenopathy) and human granulocyte anaplasmosis (Anaplasma, Ehrlichia), Cat scratch disease (Bartonella henselae), tular , Babesiosis.

Treatment

Beta-lactam antibiotics and tetracyclines are the drugs of choice (only in children over 8 years of age); in case of penicillin allergy and tetracycline intolerance macrolides (azithromycin). The choice of antibiotic depends on age, clinical manifestations and the duration of clinical manifestations. The therapeutic effect of antibiotic treatment is evaluated by alleviation or disappearance of clinical manifestations.

A significant decrease in antibody response can be expected in a few months, sometimes years. In disseminated and late forms of LB, antibodies decline very slowly and persist after antibiotic treatment. On the contrary, despite the decrease in antibodies, Borrelia rarely persists in the body.

Erythema migrans and lymphocytes

Treatment is initiated on the basis of clinical evaluation and without undue delay. The following is served for 14 days:

- in young children amoxicillin (after food)
- doxycycline over 9 years of age. The duration of doxycycline administration can be shortened to 10 days.

the lymphocytoma usually disappears after treatment, usually within one month.

Early neuroborreliosis, Lyme carditis, ocular forms of LB

ceftriaxone, cefotaxime, penicillin G i.v. 14-21 days. :Late Lyme arthritis
doxycycline, amoxycillin (after food for 28 days)

Late neuroborreliosis

ceftriaxone, cefotaxime, penicillin G i.v. 14-28 days.

Acrodermatitis chronica atrophicans

doxycycline, amoxycillin (after food for 21 days).

Another part is symptomatic treatment - anti-inflammatory, anti-edematous, analgesic,...

⚠**Initiation of antibiotic therapy only on the basis of a positive serological finding without signs of disease is not indicated.**

Prevention

Prevention is focused on protection against ticks.

History

The disease was named after the American town of Old Lyme (Connecticut), where there was a high incidence of joint disease in children. An epidemiological survey in 1975 found that most patients lived in forest areas, the first symptoms appeared in the summer, preceded by skin manifestations (widening red spots), and that the disease did not appear to be transmissible from person to person. The causative agent was discovered in 1982 by Dr. Burgdorferem.

Links

Related articles

- Klíšťová encefalitida

External links

- SZÚ: Lymeská borrelióza – epidemiologická data za rok 2014 (http://www.szu.cz/uploads/Epidemiologie/Lymeska_borrelioza/Lymeska_borelioza_CR_data_do_roku_2014.pdf)
- Lymeská borrelióza: Doporučený postup ČLS JEP v diagnostice, léčbě a prevenci (2011) (https://www.infekce.cz/DoporLB11.htm)
- Diagnostika lymeské borreliózy v NRL LB (2008) (http://www.szu.cz/tema/prevence/diagnostika-lymeske-borreliozy-v-nrl-lb)
- Template:Mefanet
- Lze léčit přetrvávající potíže po lymské borelióze? (https://www.osel.cz/11566-lze-lecit-pretrvavajici-potize-po-lymske-borelioze.html)

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