Laboratory diagnostics and therapy for Lyme disease

Epidemiology

The Lyme borreliosis is the most prevalent infection transmitted by ticks in Europe and the USA. It man-ifests in different organs such as the skin, nervous system, heart, lymphatic system and the joints. The pathogen is the spirochete Borrelia burgdorferi which is transmitted in Europe by the hard-bodied tick Ixodes ricinus. The infection rate of the ticks is about 10–35 %. Rodents, hedgehogs and wild game are natural reservoirs. If you are bitten, the infection risk is generally relatively low providing that you mechanically remove the tick in full within 24 hours (preferably with tweezers, do no use oil or ointments). In endemic areas ticks also transmit tick-borne encephalitis (TBE).

Clinical manifestations

Early phase: Erythema (chronicum) migrans (EM), borreliosis lymphocytoma, early neuroborreliosis (in children often facial palsy).
Late phase: Lyme arthritis, Acrodermatitis chronica atrophicans, very rarely chronic neuroborreliosis.

Therapy

A therapy is indicated for all cases involving a symptomatic infection. Doxycycline is generally rec-ommended in the early stages and with skin manifestations. Amoxicillin has proven effective in the treatment of children. Advanced stages should be treated parenterally. The best success has been obtained with cephalospori-

Therapy recommendations for Lyme disease

Antibiotic oral (p.o.) / intravenous (i.v.)	Adults (dose/day)	Children (dose/kg body weight)	Duration
Erythema migrans and Borreliosis lymphocytoma			
Doxycyclin p.o.	2 x 100 mg	≥ 8 years: 1st day 4 mg/kg, from 2nd day 2 mg/kg in 1 dose	14 (10-21) days
Amoxicillin p.o.	3 x 500 mg-1 g	25-50 mg/kg in 2-3 doses	14 (10-21) days
Cefuroxim p.o.	2 x 500 mg	30-40 mg/kg in 2-3 doses	14 (10-21) days
Penicillin V p.o.	2 x 1,0-1,5 million I.U.	0,1-0,15 million I.U./kg in 2-3 doses	14 (10-21) days
Azithromycin p.o.	1st day 2 x 500 mg, from 2nd day 1 x 500 mg	1st day 20 mg/kg, from 2nd day 10 mg/kg in 1 dose	5 days
Neuroborreliosis			
Ceftriaxon i.v.	1 x 2 g	50-100 mg/kg in 1-2 doses	14 (10-30) days
Penicillin G i.v.	20 Mio. I.E.	0,25-0,5 million I.U./kg	14 (10-30) days
Doxycyclin p.o. (early Neuroborreliosis)	2 x 100 mg	≥ 8 years: 1st day 4 mg/kg, from 2nd day 2 mg/kg in 1 dose	21 (14-30) days
Lyme-Arthritis and Cardio-Borreliosis			
Doxycyclin p.o.	2 x 100 mg	≥ 8 years: 1st day 4 mg/kg, from 2nd day 2 mg/kg in 1 dose	21 (14-30) days
Amoxicillin p.o.	3 x 500 mg-1 g	25-50 mg/kg	21 (14-30) days
Deftriaxon i.v.	1 x 2 g	50-100 mg/kg	21 (14-30) days
Acrodermatitis chronica atrophicans			
Deftriaxon i.v.	1 x 2 g	50-100 mg/kg	21 (14-30) days
Doxycyclin p.o.	2 x 100 mg	≥ 8 years: 1st day 4 mg/kg, from 2nd day 2 mg/kg in 1 dose	21 (14-30) days
Amoxicillin p.o.	3 x 500 mg-1 g	25-50 mg/kg	21 (14-30) days

Reference: modified according to recommendations of EUCALB, cited: 2nd June 2014; doses of Doxycyclin for children according to DGPI-handbook, 2013.

MVZ Labor Ravensburg
Labor Dr. Gärtner

MVZ Labor Ravensburg GbR
Elisabethenstrasse 11 | D - 88212 Ravensburg
Phone: +49 751 502-0
www.labor-gaertner.com

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nes such as ceftriaxon as they penetrate the blood cerebrospinal fluid barrier better than, for example, penicillin G. A temporary improvement from doxycycline in treating suspected Lyme disease may also be due to an anti-inflammatory effect of this medicine.

The IgG and IgM antibody titres against borrelia only change slightly or do not change at all with antibiotic treatment and after a clinically successful therapy or spontaneous healing, they can also be retained at an elevated level for years. First and foremost an improvement in the clinical picture is key to evaluating the success of treatment.

Laboratory diagnostics

The IgG and IgM antibodies against borrelia are determined using enzymeimmunoassay as a screening test and are confirmed by an immunoblot if the screening test is positive. The antibody reactions or pattern in this test are a hint for early or late phases of the infection.

IgM antibodies can occur approx. three weeks after the tick bite, and even endure for many years. In addition, IgG antibodies can also often be detected in the early phase, but may not be found. The immunoblot mainly finds antibodies against the very specific OspC (25 kDa) and the unspecific flagellin (41 kDa) in addition to antibodies against the surface protein VlsE (Variable major protein like sequence, Expressed). The EM can be seronegative, as also the early phase of neuroborreliosis and facial palsy in children. Isolated positive IgM reactions in the serum can be also false positive, e.g. in patients with syphilis, autoimmune diseases or if a rheumatoid factor is present.

When infections persist for longer and there are late manifestations, **IgG antibody** detection is generally positive. In the immunoblot IgG antibodies against various specific borreliosis antigens such as OspB (34 kDa), p58 (58 kDa) and p83/100 (83 kDa) can occur as late markers, but also persist for long time. This does not permit any conclusion on the activity of an infection or treatment outcome. Another infection is always possible even if there are pre-existing antibodies from prior infections. Due to a lack of standardisation, mainly from using differing antigen preparations, there can occur divergent results between the tests of different manufacturers especially in the borderline/weakly positive range.

The laboratory diagnosis of a neuroborreliosis is not possible solely from determining antibodies in the serum. It requires detection of a specific intrathecal antibody synthesis in the central nervous system by testing a cerebrospinal fluid-/serum pair. As the serological results depend on the stage of the infection, the duration and severity of the symptoms and any prior antibiotic therapy, the following clinical and anamnestic details are key to a conclusive interpretation:

1. The time the tick bite occurred (if noticed)
2. The onset of disease and symptoms
3. Previous therapy/earlier infections

Borrelia, like other spirochetes, are hard to cultivate. Therefore the PCR is more suitable for detecting borrelia DNA from a skin punch in EM, in joint punctates in arthritis and at low sensitivity in the cerebrospinal fluid in neurological diagnoses. Testing the tick for borrelia infestation using PCR is not generally recommended as borrelia are not transmitted until the end of the blood meal. At present it is not advisable to detect borrelia DNA in urine or EDTA blood.

Author:
Dr. med. Dr. rer. nat. Dipl.-Chem. Ebbo Michael Schnaith,
Dr. med. Frauke Albert, Limbach Gruppe

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Your contact:
Prof. Dr. med. Nele Wellinghausen
Head of Department of Infection immunology
e-mail: info@labor-gaertner.com
phone: +49 751 502-220