

### **Neuroborreliosis (Lyme disease)**

Lyme disease is an infectious disease contracted through a tick bite. The disease exists worldwide, except in areas with very extremely climates. While many infected patients recover with or without treatment with antibiotics, Neuroborreliosis represents a frequent complication of Lyme disease. The causes of the disease are Borrelia, named after Borrel, the French researcher who discovered the cause of this disease. Preferred tissues of Borrelia are synovia tendons and the central nervous system. Therefore Arthritis (mostly not swollen) and Fibromyalgia are often caused by Borrelia.

Borrelia are long, spiral organisms are capable of moving freely through cells and tissues. This allows the bacteria to spread throughout the body and even enter brain cells and infect the central nervous system.

Additional information about the cause of Neuroborreliosis and suggested courses of treatment can be found on this web site.

Best regards,

Prof. Dr. Friedrich W. Schardt

## Information

During Stage I of the disease (2-3 weeks after the tick bite) the most common symptom is erythema migrans, headaches and joint pain, as well as fever. During stage II, which lasts up to six months, the primary symptoms are spinal and cranial meningoradikulitis, isolated meningitis and mono- or polyneuritis (recurring and wandering head and nerve pain), together with chronic erythema migrans (mostly on the torso).

During stage III (lasting 6 months to many years), acrodermatitis chronic atrophicans (blue to black skin changes on the fingers and tip of the toes) together with mono- or polyneuritis or chronic progressing encephalomyelitis. Typical for neuroborreliosis are also constantly wandering pain and paralysis in all part of the body. Cerebrovascular Neuroborreliosis can occur during both stages.

In addition, rheumatic joint pain, cardiac arrhythmia and liver parenchyma (elevated liver specific transeminase), as well as panic attacks, depression, and apoplexy may be related symptoms. While during stage I, a high cure rate is seen in children with the use of Penicillin G. In adults, a successful treatment with permanent healing of Neuroborreliosis (stage II and III) with Doxycycline, Penicillin or Ceftriaxon-Infusionen is rarely seen.

Lasting treatment success is achieved only through a combination therapy with antibiotics (Macrolides and Tetracyclines) and antimalaria medications (see suggested Therapy).

Laboratory tests used to confirm borreliosis include the ELISA test (IgG and IgM) and Immunoblot or Westernblot (IgG and IgM), whereas the Immunoblot tends to be more sensitive.

## **Borreliosis**

The cause are bacteria, called borrelia, named after the french bacteriologist, Borrel, who discovered the bacterium. Borrelia belong to the subgroup of spirochetes. These are elongated corkscrew-like organism that, according to recent findings, are able to actively move through body tissues and can spread without hindrance throughout the body. They are even able to cross the blood-brain barrier and take hold in the central nervous system.

Research also shows that due to their intercellular existence, borrelia can enter cells and resist any type of antibiotic treatment. This explains why symptoms continue to recur and even fail to respond to multiple courses of antibiotics even if administered over a period of several months using different types of antibiotics. (For additional information please refer to the “Symptoms” section).

Borrelia typically are transmitted by ticks, which transmit the pathogen during the act of sucking about 6 to 24 hours after the initial bite. Only after contact with human blood in the intestinal track of the tick, the borrelia become active and infectious. During that time frame, the tick transmits the borrelia into the human body either on its own or during manipulation (i.e., during the removal or pinching).

Additional potential transmitters currently considered by researchers are horseflies and mosquitoes. There are no known cases of direct transmission between individuals; i.e., the disease is not contagious. During pregnancy, infection with borrelia bacterium increases the risk of stillbirth and birth defects.

## Symptoms

ased on most current findings, the symptoms shown in the following table typically are associated with Lyme disease.

	<b>Incubation Period</b>	<b>Skin</b>	<b>Nervous System</b>	<b>Skeletal and Orthopedic</b>	<b>Other</b>
<b>Stadium I</b>	1-3 weeks after tick bite	Erythema migrans	Headaches	Painful limbs	Sub-febrile Temperatures
<b>Stadium II</b>	Weeks or Months	Lymphozytom (soft-tissue inflammation)	Meningo-Polyneuritis (nerve pain)	Arthralgien, Myalgien, Arthritis (muscle – and joint pain)	Carditis (inflammation of the heart muscle), Cardiac arrhythmia, Lymphome (swelling of the lymph knotes), Chorioiditis (inflammation of the choroid)
<b>Stadium III</b>	Months or Years	Acrodermatitis Chronica Atrophicans (various inflammatory skin diseases of the hands and feet)	Enzephalomyelitis (Encephalitis), Radiculitis, Polyneuropathy (nerve pain), forgetfulness, depression, Panic attacks	Arthritis, Bursitis, Tendonitis, Myositis (Muscle inflammation)	Cardiomyopathy, Vasculitis (vascular inflammation)

## Suggested Therapy

The following therapy suggestions are based on the results of bacteriological research. Refer to the “Symptoms” link for information regarding the timing of each stage.

### Stage I

Medication	Treatment Dosage / per day	Duration of Treatment
Penicillin G or V	2 to 4 x 1.5 Mega	2-3 weeks
Cefuroxim	2 x 1 x 500 mg (250 mg children)	2-3 weeks
Amoxicillin	3 x 1000 mg (50 mg/ kg body weight)	2-3 weeks

Doxycycline should not be used during stage I because it is only effective during the reduplication period (occurring every 18-20 hours) and this would allow the borrelia to infiltrate every type of tissue. Basically in stage I, a therapy should be sustained till the symptoms (fever, headache, weakness, erythema migrans ) have completely disappeared. Even though Doxycycline is used, it should be always combined with Hydroxychloroquine (2x200mg).

**Stages II & III\***

<b>Medication</b>	<b>Treatment Dose/per day</b>	<b>Duration of Treatment</b>
First course of treatment Azithromycin or Telithromycin (2x400mg) and Riamet or 2 x 4 (should be taken with vegetable oil, i.e. oliv oil) Malarone 4 x 1	1 x 500 mg (administer for three days followed by a three day pause)	6-12 days
Followed by...		
Second course of treatment Minocycline and Hydroxychloroquine (or Cotrimoxazol 2x960mg) or Roxithromycin and Hydroxychloroquine or Clindamycin and Hydroxychloroquine	2 x 100mg 2 x 200mg  1 x 300 mg 2 x 200 mg  2 x 600 mg 2 x 200 mg	50-100 days  50 days  20-25 days
Followed by....		
Third course of treatment Fluconazole*	200 – 400 mg (Children up to 40 kg weight: 100 mg)	20-50 days

\* With organ involvement and neurological symptoms (arthritis, fibromyalgia, polyneuritis, radiculitis, encephalomyelitis, depression, panic Attacks and amnesic aphasia).

Basically, in stage II and III the combination of an antibiotic and an antimalarial should be strictly performed.

If joint pain intensifies during the course of treatment with fluconazole, fluconazole therapy should be limited to 20 days and the entire treatment started from the beginning.

All stages of Lyme disease (borreliosis) must be treated with antibiotics therapy, including stage I, erythema migrans. Only a rigorous adherence to the therapy can prevent the development of neuroborreliosis. Bactericidal antibiotics (penicillin, cefalosporine, makrolide) generally are more effective than doxycycline. Doxycycline should not be the first choice of antibiotics because it only acts bacteriostatic (preventing the growth and multiplication of borreliosis). Moreover, bioavailability of minocycline in the tissues is better and also works against ehrlichia, babesia and bartonella in stages II and III.

**It is important to note that because of its effectiveness on the neurological system, Fluconazole should only be utilized when neurological symptoms are present.**

The diagnosis of neuroborreliosis is determined utilizing the following criteria.

- Positive ELISA or/and Westernblot and
- Typical symptoms, such as unspecified, wandering nerve pain (especially at night), alternating paralysis in the lower extremities, depression, forgetfulness and panic attacks.

**Important:** Other possible causes for these symptoms must be eliminated through laboratory tests (blood tests) and MRI.

Since fluconazole does not appear to eliminate borrelia from the central nervous system but instead prevents their growth and reproduction, the therapy must be continued for at least 20-50 days in order to be effective. If after that period symptoms persist, the therapy (antibiotics, followed by fluconazole) can be repeated consecutively up to three times.

The following schematic presentation summarizes and reemphasizes the suggested therapy:

Treatment Protocol: Neuroborreliosis		
Azithromycin 1 x 1 500 mg + Riamet 2 x 4 (3x3 days, with 2-day break in between)	Minocycline 2 x 100 mg + Hydroxychloroquin 2 x 200 mg (50 days)	Fluconazole 1 x 200-400 mg + Chinin 200mg
<p>Repeat this cycle 2 to 3 times</p> <p>The treatment for Neuroborreliose always should be concluded with Fluconazole. During the antibiotics treatment, sweets should be avoided! Probiotics (Lactobacillus, Coli and Saccharomyces bacteria) should be provided.</p>		

Riamet should be taken with a big spoon filled with oil or fatty cream. Instead of Riamet also Malarone can be taken. Fluconazole is well tolerated; however, a number of interactions with other medications have been reported. **Because of potential interactions, fluconazole should be alternated with antibiotics therapy and not be taken at the same time.**