

Chronic persistent Lyme Disease (LD) or chronic Borreliosis



Symptoms and treatment recommendations as well as a description of some of the risk factors which can cause a chronic form of Lyme Disease

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For many years, the tick population has increased steadily and so have the number of patients with tick borne Lyme Disease (LD) or Borreliosis. Ticks belong to the family of arachnids, therefore they sting but do not bite to feed on their host's blood.

It is estimated that, at present, there are about 500,000 to 800,000 people who become infected with the spirochete *Borrelia s.l.* (sensu lato i.e. this includes all known subtypes of *Borrelia*) by tick bites in Germany every year, while the infection rate of Tick Borne Encephalitis (TBE), for which a prophylactic vaccination is available, remains at approximately 200-500/year. Several studies have shown that roughly one million people in Germany suffer from chronic Lyme Disease, for which no vaccination is available (see: www.praxis-berghoff.de Wissenschaftliche Beiträge: Häufigkeit der Lyme-Borreliose in der BRD, rev. 2011). These are only estimated figures, as Borreliosis is not a "notifiable disease" in Germany. However, over the last several years there has been a sharp increase of new infections of LD in Germany's Neue Länder (former East Germany), where LD is notifiable. These public health figures are also mirrored in the high numbers of ICD (International classification of diseases) cases for LD, published by the Techniker Krankenkasse (TKK) of Germany. In 2009, they counted nearly 800,000 cases of LD, an increase of 11 % from 2008 to 2009, according to the records of the TKK.

As physicians often find it difficult to identify and treat an infection, many chronic persistent Borreliosis patients remain untreated or are treated insufficiently, causing the number of chronic cases to steadily increase. The degree to which chronic LD affects quality of life, can be judged by looking at the numerous and severe symptoms (see p. 5 ff "**Symptoms**").

This brochure is written to prevent the chronic form of this disease by identifying preventable mistakes which are often made immediately after an infection with spirochetes of the type Borrelia, of which 5 different subtypes are identified as pathogen to humans so far. Furthermore, it will outline a few of the known causes that may lead to chronic systemic inflammation and therefore also to chronic persistent Lyme Disease. When describing the methods of diagnosing Lyme Disease, several new methods of identifying an infection with these spirochetes in question will be presented, as well as the established tests for Antibodies and the Immunoblot. Additionally, it will outline various antibiotic treatments in conjunction with other effective treatments to reduce the symptoms of not only Lyme Disease but other chronic systemic infections as well.

What should be done immediately after a tick bite?

If you find a tick latched onto your skin, you should remove it as soon as possible. This can easily be done by using a pair of tweezers or a “tick creditcard” with a slit in it to carefully lift the tick straight up off the skin. The blood filled body of the tick should not be squeezed during this procedure to avoid the injection of the tick’s saliva with all its pathogens into the deeper layers of the host’s skin. If a camera is available, it is recommended that a photo of the tick is taken before its removal, as well as pictures of the tick bite site itself, if there are changes at or around the bite’s location. This could be important later on, as the aforementioned photos can be used as proof of a previous tick bite to assist in the acknowledgement of a case of LD by medical insurance companies or, also, as an occupational hazard (e.g. for forest rangers, farmers, hunters etc.).

The tighter the tick’s hypostome (stinger) is glued into the host’s skin, the longer the tick has already been drawing blood. Since it takes at least a few hours to become infected (it is estimated that it can take between eight to twelve hours from the time of the initial bite), it is important to estimate how long the tick may have been latched onto its host. If, for example, the tick is discovered in the morning, then the 8 hour limit is surely over and one should seek treatment as if an infection has occurred.

Sending the tick to a special laboratory (see addresses in **Appendix**) to have it checked via PCR (polymerase chain reaction) for the DNA of pathogens like Borr. burgd. (or Ehrlichia, TBE-Virus et al.) is another way to assess the risk of infection. Generally, it only takes two or three days to receive the results. This is a quick and easy way of verifying if the tick in question was carrying Borrelia, TBE-Virus or Ehrlichia (The Medizinische Labor Bremen can even give the number of spirochetes per tick!). Since roughly 30% of ticks in Germany carry Borrelia (although this can vary from 50% to 70%, based on the region), it is particularly important to begin a treatment with antibiotics to reduce the number of pathogens, if the tick was attached long enough to the host and the tick itself contained the bacteria. Under these circumstances, one should not even wait for signs of a round shaped, outwardly expanding rash (known as Erythema migrans (EM or bull`s-eye rash), especially since it only occurs in roughly 50% of all cases of infection.

If the following conditions occur:

The tick has been feeding on its host for a long time (over a couple of hours)

and

the tick has been found to contain pathogens,

it is advisable to begin an early antibiotic treatment!

Recommended is **2 x 200 mg of Doxycycline or 2 x 100 mg of Minocycline** for at least 10 days (with a slowly increasing dosage over several days). If clinical signs of early Lyme Disease appear (see p. 3) or the Lymphocyte Transformation Test (LTT) is positive, one should continue medication for a total of 30 days.

Even though it is possible to encounter side effects during the antibiotic treatment such as diarrhea, allergies, sensitivity to light, changes in the ECG or the blood parameter, these are - in my experience with the disease - nevertheless acceptable, because one can treat the disease in a very early stage. Thus one prevents later chronic persistent Lyme Disease which is much more difficult to handle.

For the very same reason, although on average 9 out of 10 people infected with Lyme Disease can effectively fight against the bacteria with their own healthy immune system, I still recommend the above course of antibiotics. This is because at the time of the decision for or against antibiotic treatment, the state of the immune system is unknown. Therefore it is safer to treat with antibiotics as early as possible if there is any risk of infection (see further details below).

Which clinical methods are available to evaluate the risk of an infection after a tick bite?

It is vital to monitor the area around the tick bite and one's own body in general for a period of time after being bitten. One should watch for, during the next several weeks, unusual symptoms such as fever, headaches, insomnia, flu-like symptoms (but without a runny nose) with intense muscle and joint pains as well as general exhaustion without exertion. Additionally there may be a sudden onset of profuse sweating (usually during the night). If these "summer flu" like symptoms appear after a tick bite, they should be regarded as an early and definite sign of infection with the same significance as the appearance of an Erythema migrans (EM), which only occurs - as already mentioned - in about 50 % of all cases of a definite infection.

The development of a so-called **lymphocytoma**, in most cases a lilac coloured swelling, is caused by a build-up of lymphocytes in soft tissue such as the ear lobes, cheeks, around the nipples and the scrotum. This a sure sign of an (early) infection. This skin reaction occurs more often in children, but not exclusively so.

The area of the bite is important in the development of further symptoms, as most appear in close proximity to the initial bite. EM is one of these symptoms as well as painfully swollen lymph nodes close to the bite site (usually at the back of the neck, under the lower jaw, in the groin or under the armpits) and diffuse pain in the bitten extremity and/or itching, numbness or a burning sensation on the skin near the bite site.

Headache and neck pain are common, especially in children who are often bitten at head or shoulder height (adult ticks can crawl up to 120 cm on grass and shrubs, lying in wait to attach themselves to a new host). Children usually suffer from one, or in some cases, two-sided paralysis of their facial nerves; LD infections are the most common underlying cause of facial nerve paralysis in children. Roughly 70% of LD infections, however, are caused by eight-legged adolescent gender-neutral ticks, known as tick nymphs, which are only 1 mm long on average. Tick nymphs can only bite through soft skin and thus prefer warm and moist areas of the body such as the back of the knees, armpits, eyelids, genitals or between the toes and fingers. It may take the tick several hours to make

its way to these sought-out areas, which usually provides the human host enough time to check himself or herself thoroughly for ticks after having been in the outdoors.

The tiny and almost translucent tick nymphs are the most dangerous type of tick for humans, not only because they are barely visible, but because they also carry the most bacteria in comparison to the other tick forms. Besides *Borrelia burgdorferi* other harmful pathogens carried and transmitted by nymphs are *Ehrlichia/Anaplasma phagocytophilum*, TBE-Virus, *Babesia*, *Coxiella* and *Bartonella* as well as some others.

The adult female tick with its characteristic red backside is four times the size of a nymph. It is responsible for the remaining roughly 30% of infections. It has to suck blood for the third time in its lifecycle as an energy reserve in order to lay its thousands of eggs after which it will die immediately. Male ticks, which have completely black bodies, do not transfer pathogens at all. They die after they mate with the adult female tick.

The even tinier six-legged tick larvae very seldom transfer pathogens to human hosts because their bacterial load is minimal and, additionally, they are simply too small to penetrate human skin.

How can one recognize an infection with *Borr.burgd. bacteriae* when neither a previous tick bite nor a bull`s-eye rash can be recalled?

This question might arise at a certain time in one`s life when a set of unusual and often changing symptoms show up. The standard medical tests and routine physical examination can usually not establish a plausible reason for the condition. Routine lab tests as well as the usual technical methods such as ECG, X-rays, CT-scans, MRI and even the neurological electrophysiology tests will also not give any clarification.

With such a diverse array of symptoms as seen in Lyme Disease ranging from the physical to the psychological and cognitive, it is important to ensure a correct diagnosis. Additionally, the myriad of symptoms, , can vary from patient to patient. Therefore it necessitates a thorough investigation of the physical condition, which should include internal, orthopedic, neurological, psychological and ophthalmological examination techniques in order to identify the origin of the different symptoms (see p.5 ff under “**Symptoms**”).

Unfortunately, due to psychological problems often only caused by LD, a lot of patients are labeled as pure psychological cases. They are told, for example, that their symptoms are “all in their head” or that they are “making them up”. Therefore this leads to the problem of Borreliosis patients often being diagnosed with a psychosomatic disorder, even though this diagnosis was made without the required investigation of possible physical reasons for this condition. This is especially sad because they are therefore steered away from any effective treatment for LD and subjected to - in these cases- mostly inappropriate psychotherapy.

In a true case of a psychosomatic disorder, symptoms usually begin to appear after a psychological trauma. The intensity and type of symptoms normally remain unchanged from the onset and begin mostly between the ages of 16 to 30, more often in women than in men. On the other hand, the symptoms of chronic Lyme Disease fluctuate in intensity and may manifest differently at varied times.

Similarly, misdiagnoses can also occur if the CSF (Cerebrospinal fluid) analysis fails to show *Borrelia* antibodies or inflammation markers. The same applies if the patient has been treated with Cortisone in the past after a tick bite. The lab results are therefore misleading. A case of chronic persistent Borreliosis will not show any signs of inflammation or abnormalities in the CFS after a certain period of time and, also, not if the spirochetes haven't been close enough to the ventricular area or the centre of the brain where the cerebrospinal fluid flows. Nevertheless, CFS is, at the moment, still the standard procedure to rule out the possibility of active Lyme Disease.

Almost all chronic and actively persistent *Borrelia* infections cause neurological, cognitive and psychological impairment and symptoms, therefore it would be more correct to speak of chronic Borreliosis with neuro-psychological symptoms, rather than of Neuroborreliosis, to avoid confusion with the disease pattern of acute Neuroborreliosis.

But even when taking all anamnestic clues/evidence and a thorough physical examination into account, is it often difficult to identify the infectious disease Borreliosis in its chronic state and thus all diagnostic techniques should be consulted.

Which clinical symptoms could be caused by chronic Lyme Disease?

Chronic persistent Borreliosis should be considered as a possible cause whenever several (generally more than 3) of the following symptoms occur. This is especially true in cases when the patient is not aware of ever having been bitten by a tick or having had an EM or when certain symptoms come and go (relapses) even without any treatment.

- Strong and long-lasting **tiredness and exhaustion** without any prior physical strain (for example sleeping several times a day or feeling exhausted half way through the day even after a good night's rest).
- Severe **joint pain** which randomly changes in location and intensity, sometimes seemingly disappearing altogether (without treatment) only to reappear at a later date. Sometimes relatively large joint swelling occurs, especially in the knees and hips (it could even be painless when occurring in the knees).
- Intense **headaches**, mostly throbbing diffused or localized at the frontal, temporal or all around the head, painful combing or brushing of the hair, pain in the throat or tongue as well as the shoulder and neck (often only on one side).
- Chronic **sinus infections** with multiple relapses and slow recovery as well as long-lasting swelling of the mucus membrane.
- **Lymph node swelling** -painless or painful- under the lower jaw and along the cervical spine (neck), under the armpit and in the groin of the leg which was bitten by the tick.
- **Muscle pain and cramps** throughout the whole body without prior physical exertion, usually with an increase of the muscle enzymes (Creatine kinase (CK) and/or Lactate dehydrogenase (LDH)).

- Spontaneous **muscle twitching** (fasciculation), often in the arms or legs. These twitches are usually visible and perceptible.
- Pain in the **ligaments and tendons**, most commonly in the Achilles tendon, but also as in Epicondylitis (also known as tennis or golfers elbow), **Carpal Tunnel Syndrome (CTS)**, “Jumping” fingers (also known as Digitus saltans, caused by a swelling of the tendon inside the tendon sheath) or irritation/inflammation of the Plantar-fascia which causes pain in the sole of foot with the first steps in the morning.
- **Partial or full tendon and muscle tears** without adequate physical exertion, especially applicable to the Achilles tendon, the thigh muscles (M. quadriceps femoris) or the calf muscles (M. triceps surae) and sometimes even the upper arm muscles (M. biceps).
- **Bone pain in the shin and the heel**, especially when lying down or during the night.
- **Deep seated aching pain** in the conjunction of ribs and breast bone or at the lower ribcage, often combined with a feeling of reduced respiratory volume and pressure on the ribcage (can be confused with the feeling of “chest pressure” experienced by patients affected by depression!).
- Often a strong **irritation in the throat with coughing** occurs and shortness of breath after only minor physical activity (like walking upstairs). These symptoms are most commonly encountered when also suffering from a co-infection with Chlamydothrix pneumoniae or Mycoplasma pneumoniae.
- A burning **pain of the skin** and/or a feeling of **numbness**, which can occur all over the body or in certain areas only, or an **itching and crawling** sensation without any visible changes of the skin.
- **“Electrifying” or “water flowing” sensations** under the skin, often under the scalp as well.
- Sudden **stabbing pains** in different groups of muscles, constantly changing location.
- Sudden **racing heart beat**, especially at night, without any previous physical activity, **irregular heart beat** (extrasystoles) or uncomfortably strong heart beat (palpitations).
- In some cases, infestation of the spirochete Borrelia in the heart causes **dysfunction of the regular transmission of heart impulses** which can be the reason for third-degree **AV block** (also known as complete heart block) and arrhythmias. Infection with Borrelia can also cause a fluid build-up around the heart (pericardial effusion) if the patient suffers from myocarditis in conjunction with pericarditis. Angina pectoris on the other hand, is usually not a part of the spectrum of cardiac symptoms of Borreliosis.
- A change from normal to **high blood pressure** (hypertension) mostly with a rise in diastolic values (over 90 mm Hg). Blood pressure will generally normalize after adequate LD therapy and anti-hypertensive medication will not be required anymore.
- **Neurological symptoms** and complaints are numerous and complex. Beside strong pain alongside a peripheral nerve (**polyneuropathy**) and misconceptions of physical sensations

(dysaesthesia), tremors occur in the extremities as well as **(partial) paralysis** of arms or legs. Other clinical symptoms of chronic persistent LD include **paraplegia or hemiplegia** and/or reduced feeling in one half of the body (**hemihyposnesia**). These neurological deficits can all be caused by a borrelia-induced **inflammation in the upper spinal cord** (resembling a stroke). In rare cases, **epileptic seizures** can also be seen in cases of chronic persistent LD.

- **Garin-Bujadoux-Bannwarth-Syndrome (or in short "Bannwarth-Syndrome"):**

This is a typical manifestation of a recent Borr. burgd. infection (although it can also occur in the later stages of the disease). It presents itself as an intense burning and aching, usually in one leg or arm only, **resembling the pain of a slipped (herniated) disc** or – if the upper extremities are affected- a so called shoulder-arm-syndrome.

By the **type of pain one can differentiate between the two conditions**, as the pain caused by the Bannwarth-Syndrome is the **worst at night**, whereas the pain caused by a spinal herniated disc increases with movement through the day. Commonly-prescribed pain relievers or anti-inflammatory drugs will have little impact on the pain if caused by Bannwarth-Syndrome and physical therapy is similarly ineffective. Due to the inflammation of the spinal nerve roots, caused by Bannwarth-Syndrome, a **CFS-analysis can show signs of acute inflammation** such as an increased cell count, an increased Borrelia burgd. antibody index or increased protein. In a case of chronic untreated LD, the symptoms of Bannwarth-Syndrome can occur repeatedly.

- **Dysfunctions of the autonomic nervous system:**

Impaired sense of body temperature with either severe shivering "from deep within" or "hot flashes" as in menopause, but experienced by both women and men. Profuse **sweating** (mostly at night, but also during the day). Often **slight fevers** (sometimes bound to a circadian or monthly rhythm), "**flushed cheeks**" without fever, predominantly in the afternoons, newly-developed **alcohol intolerance** often for only very small amounts of alcohol and the aforementioned **exhaustion and severe fatigue**.

Some of the possible cranial nerve dysfunctions:

- **Irritation of some cranial nerves** is common. **Paralysis of the facial nerve** occurs most often during the early stages of the spirochetal infection, while in the later stages of the infection several of the 12 cranial nerves can be affected at the same time.
- **Dysfunction of the eyes:** Pain of the eye muscles during eye movements, slight double vision, light sensitivity, upper eyelid weakness, delayed adjustments to light changes i.e. at dusk (accommodation dysfunctions), pupil dysfunctions (e. g. paradoxical undulating mydriasis when exposed to direct light), burning eye infections (conjunctivitis) and dry eye as well as grittiness of the eye, even scleritis, retinitis and scotoma.
- **Dysfunction of hearing and the labyrinth:** sudden loss of hearing, tinnitus, dizziness (vertigo) and impaired balance.
- **Dysfunction of the sense of smell and taste:**
The ability to smell and taste is impaired as well as the feelings of the face which can be changed by the irritation of the trigeminal nerve (the fifth cranial nerve). This can lead to

too much or too little sensation of the skin (Dysaesthesia and Hyperpathia/Hypaesthesia). These irritations can even imitate toothache or aches of the jaws.

Hormone and metabolic dysfunctions

- **Sexual dysfunctions:** Loss of libido, menstrual irregularities, erectile dysfunction as well as pain in the breasts and mammary glands.
- **Urological dysfunctions:** Burning sensation in the bladder and urethra, pain in the testicles and scrotum without any indications of bacteria in the urine ("Prostatitis" without the presence of bacteria), frequent urination (Pollakisurie) daytime and at night also (nycturia), urinary incontinence, pain in the groin, all of these without urological causes (especially after a tick bite in the genital area).
- **Gastrointestinal complaints:** Stomach ache, flatulence, bloated feeling, stool irregularities with diarrhea alternating with constipation, loss of appetite, newly appearing lactose intolerance/food intolerance and weight gain without changes in diet or eating habits. Elevation of liver enzyme values has also been noticed without any other medical reasons.
- **Changes in metabolism:** Hyperacidity (measurable using the Sander Test with 5 urine samples in one day), newly-appearing increase in cholesterol, thyroid disorders (often hypothyroidism with an increase in the Thyroid-stimulating hormones (TSH basal)) and development of autoantibodies against thyroid tissue (Anti-TPO), causing the so-called Hashimoto-Thyroiditis. The spirochetes could also be responsible for a change in the activity of the enzyme which converts T4 to T3 results in the production of an inactive, inverse form of T3. Even when administering thyroid medication and TSH-values have normalized, the aforementioned change in enzyme activity can still cause symptoms of hypothyroidism (according to Dr. Klinghardt, lecture in Kiel 09/2008).
- **Dysfunction of Serotonin metabolism:** Frequent irritability, panic attacks for the first time after a tick bite, anxiety, underlying (latent) aggression, fits of rage, intensely depressive mood swings and emotional instability caused by low levels of serotonin.
- **Chronic sleep disorders:** Disturbance of sleep patterns with interrupted sleep, trouble falling and staying asleep, light and non refreshing sleep and nightmares. Each of these can be caused by the lack of melatonin (due to a dysfunction of the Tryptophan-Serotonin-metabolism).
- **Attention deficit disorders:** Especially noticeable in children is a lack of the ability to focus and concentrate, as well as a predominantly physical restlessness, so many of them might be wrongly diagnosed as **ADD** or **ADHD**. They may also show changes in social behaviour, newly-developed anxiety about going to school, irritability and aggression with their siblings and friends.

- **Serious psychological changes:** In adults even more serious psychological conditions may occur in some cases like **psychosis, manic-depressive mood swings, obsessive compulsive disorder (OCD)**, irritability and uncontrollable aggression.
- **Cognitive dysfunctions:** Almost every patient with chronic LD will suffer from some form of cognitive dysfunction, though with varying degrees of manifestation. Often patients complain of **short-term memory loss, lack of concentration and easy distraction**. Difficulties in **planning and organizing** every day activities and thinking in the abstract are frequently reported. There are frequent difficulties in academic and job- related **learning** and, in general, absorbing new information. Patients complain also about **reading, calculating and writing difficulties** (mixing up letters especially when using the computer keyboard) as well as in **speaking** (e.g. mispronouncing words, having trouble finding the correct words) and in **thinking** (“mental fog”). There is a constant feeling of not being quite right within oneself.
- **Pseudo-Dementia:** In rare but severe cases of chronic LD, symptoms similar to those of an organic brain syndrome can be observed. This includes disorientation, severe short-term memory problems and even hallucinations and delusions.

Skin changes

- **Skin conditions:** A rare but typical (pathognomonic) skin change, which only occurs in 2% of all chronic LD patients, is the so-called cigarette paper skin, which normally occurs in only one extremity. This is stage III of ACA (**Acrodermatitis chronica atrophicans**). Stages I and II of ACA are much more common and show subcutaneous swelling and lilac color. Often you will see bluish and white blotchy skin in combination with cold extremities.

Recently, **Focus Floating Microscopy** (FFM see below) has been developed to research rare skin conditions such as **Morphaea** (Scleroderma circumscripta), fibrotic-like **nodules** in close proximity to joints as well as **Granuloma anulare**. These skin conditions could, by this histological method, be proven to be a result of an earlier infection with Borr.burged. Additionally, in 30% of all of these patients Borrelia antibodies were found

- **Erythema migrans** (or **Erythema chronicum migrans**, if it is present for more than 4 weeks) has already been mentioned earlier as a typical LD skin symptom (commonly known as a bull`s-eye rash). Not as well known might be that EM can appear in multiple forms and at various locations at the same time. It can also reappear as long as the spirochetal infection is ongoing, particularly during antibiotic therapy. This means, on the other hand, that not every EM is a sign of a recent Borrelia infection, but can also indicate a reactivation of an already existing LD infection.
- **Lymphocytoma** is another typical skin reaction to the Borr. burged. infection as already described above.
- **Skin Rashes** of various types like papules, urticaria, blotches, flakes etc. are seen. Atrophy of the follicles of the skin and hair (Anetoderma), hair loss (Alopecia areata) as well as inflammation of the subcutaneous tissue (Panniculitis) which causes painful skin nodules.
- **Problems of nails or hair: Nail growth anomalies** like brittleness or nail grooves develop as well as **profuse hair loss** (mostly in women).

- Another symptom, not specific to but often found in Borreliosis patients, is a much stronger reaction to **anaesthetics and vaccinations** than previous to the Borrelia infection. In particular, a vaccination for Tick borne encephalitis (TBE) can exacerbate LD symptoms. However, it is not uncommon that other infections, especially those caused by viruses, do result in relapses.

Using lab tests to identify persistent Lyme Disease infection

While the above named symptoms could evoke suspicion of a possible case of Lyme Disease, this should always be **confirmed by supporting laboratory results** such as, for example, increased antibodies of Borrelia burgd. or some (highly) specific bands in the Immunoblot test.

However, even without positive laboratory results, the possibility of a Borreliosis shouldn't be excluded, as **seronegative test results are possible** in some cases. Thus, tests to prove Borrelia burgd. directly should always be preferred to indirect serological laboratory tests.

The following laboratory tests should at least be done to prove an infection with the spirochete Borrelia s.l.:

- 1.) **Increased Borrelia antibodies (AB)** (which can be identified using the ELISA or EIA testing method) are evidence that the immune system has had to deal with the spirochete Borrelia at some time in the past. It is not, however, confirmation of a still active Borreliosis. It has also been described in retrospective studies that in roughly 20% of patients infected by Borrelia, hardly any antibodies were developed. Various different reasons for seronegativity are known so far, e.g. previous use of cortisone or other immunosuppressants or an early antibiotic therapy immediately after the spirochetal infection or a weakening of the immune system due to other diseases or a lack of immunoglobulin or a hypogammaglobulinemia.
- 2.) A more accurate test for identifying LD is the **Protein Immunoblot test** (also known as the **Western Blot test**). This test is particularly useful for determining the necessary course of treatment for an LD infection as it gives an idea if the infection occurred recently or long ago. Typical "**old bands**" which are highly specific are for example **VlsE, p 18, p 28/29, Osp A/p31, OspB/p 34, BmpA/p 39, p 83, p 100**.

There are, however, so-called "**seronegative**" patients who show neither antibodies in the ELISA-test, nor have specific immunoblot bands. This applies mostly to patients with a weakened immune system or a lack of immunoglobulin. The Borrelia's ability to "hide" itself (Borrelia spirochetes can, for example, appear as **cysts, blebs or granula or as a biofilm or immunocomplex**) can result in the immune system's inability to recognize it. Or, the Borrelia spirochete in all its forms are located in host tissue with few blood vessels like ligaments or tendons, so that no antigens can be presented to the immune system. Therefore, no humoral defense strategies, like antibodies, can be implemented by the immune system. The same applies to the ability of the bacteria to **disguise themselves as**

“human cells” by using **Factor H**, a specific cell adhesion protein, which was fully chemically deciphered in 2005. Thus the immune system fails to recognize them as foreign antigens.

It should be noted that not all laboratories have the ability to diagnose LD and that some LD test kits do not contain the latest highly-specific recombinant *Borrelia* antigens and thus do not always give reliable results. (If in doubt of the validity of the test result, one should consider using a more specialized laboratory for retesting).

Even though seronegative LD patients show a lack of antibodies, a *Borrelia* infection can still be detected by using either the **Melisa test** (offered by Laborzentrum Bremen) or the quite similar **Lymphocyte transformation test (LTT)**. Another similar method is called **EliSpot**. (For laboratory addresses see **Appendix**).

- 3.) The Lymphocytes transformation test (LTT) measures cellular (rather than humoral) antigen specific reactions of the immune system and has, in all performed studies, provided a more sensitive result than tests which measure humoral antibody production. This cellular immunological reaction of the Memory-T-cells is the **first positive immune system reaction**, and occurs within 10 days after infection (i.e. long before the humoral IgM- or IgG anti-body production has started, which usually occurs 4 to 6 weeks after infection). The LTT remains positive as long as cellular immunological action takes place between the immune system and the *Borrelia*. The LTT is currently the only test to prove the **ongoing activity of *Borrelia* bacteria**. These test are all called indirect, as they all can only show the immune system's reaction towards the intruding bacteria rather than being able to detect the presence of the pathogen itself. Some causes for a failure of the immune system's reaction were mentioned above.
- 4.) The T-cellspot or “**EliSpot-Test**” for *Borrelia*, now offered by some laboratories, measures the release of cytokines (Interferon gamma) by T-Lymphocytes after stimulation by *Borrelia* specific antigens. The EliSpot-Test detects with a high sensitivity those infected with *Borrelia*, but cannot indicate the activity of the *borrelia* bacteriae. Nevertheless, one advantage is the results of the EliSpot are more quickly available than those of an LTT (6 days versus 14 days for the LTT).
- 5.) **Analyzing the Cerebrospinal fluid (CSF) in the later stages of a *Borrelia* infection** does not often yield any new results as to “*Borrelia*-Antibody-Index” and cell count because they are **normalized** after being increased in the acute stage of the infection. At the most, one would, perhaps, find signs of a slight dysfunction of the blood-brain barrier with an increased protein and albumin concentration in the CSF. Therefore, the activity of LD cannot be determined by these lab tests as **not all *Borrelia* infections cause an infectious response in the CFS**. If, after a *Borrelia* infection, neither *Borrelia* antibodies nor *Borrelia* specific immunoblot bands are found in the CFS, it does **not prove the absence of chronic (Neuro-)Borreliosis** (or to put it better, a chronic Borreliosis with neuro-psychological symptoms). Rather, it only shows that, in a cerebral *Borrelia* infection, there is no involvement of meninges and brain tissue located within the proximity of the dural membranes, which contain the CFS. A medical history showing an array of certain symptoms and complaints (see **Symptoms** above) and the current clinical state are decisive in determining whether the patient needs therapy at all and if so, which treatment should be administered.

Besides all these indirect methods to prove the presence of Borreliae, there are also **direct methods**. These would, however, only be preferable if these tests were highly sensitive. Unfortunately, this is not yet the case with the presently available methods.

- 6.) After an infection, the **direct proof of the presence of viable Borrelia bacteria** can be obtained by culturing, in a special growth medium for Borrelia, biopsy material from a patient's skin or synovial fluid or CFS. The growing of Borrelia in the culture medium, however, can take several weeks and is, nevertheless, often not successful due to the very slow replication time of 12 to 24 hours of the spirochetes. Lastly, this culturing method is currently only done by a few specialized laboratories in Germany.
- 7.) Another possible way of verifying the presence of Borrelia is the **Polymerase chain reaction (PCR) method** by which the genetic material (DNA) of Borrelia can be found. The PCR method can be performed using various bodily fluids, in the order indicated as follows, with decreasing likelihood for a positive result (synovia > synovial fluid > CFS > urine > blood). The PCR method can also be used taking biopsy material from infected tissue (for example from a biopsy of an EM, ACA, the inner lining of the bladder, mucous membranes of the sinuses, muscle fibers or tendon tissue).

If a PCR result is positive for Borrelia DNA, one can assume a recent or still active Borrelia infection. As the PCR-method does not differentiate between live and dead Borrelia it is scientifically not quite clear if a positive PCR indicates an still ongoing infection. However, through phagocytosis, dead Borrelia material including its DNA will be removed usually in about 4 weeks. IGeneX laboratory in California, USA, developed and patented a new PCR method, the so-called Multiplex PCR, which besides genome-sequence analysis, can also determine the plasmid-sequences of Borrelia and can thus prove the presence of Borrelia persister forms, even if they are hidden in blebs and cysts.

As such, Multiplex PCR seems to be much more sensitive than the "nested PCR" in the attempt to identify the "genetic fingerprint" of Borrelia. When this method is used, Borrelia DNA can be found in blood and blood smears, skin samples, CFS and sediments (eluats) obtained by apheresis.

The same method can be used to analyse the ticks themselves for Borrelia DNA or DNA of other pathogens. This helps to verify whether, through a tick bite, Borrelia and/or TBE-Virus, Babesia, Bartonella, Rickettsiae or Ehrlichia/Anaplasma could have been transmitted at all. (For laboratory addresses see **Appendix**)

Even when there is a negative result of the DNA analysis of the tick, one should be cautious. Even though immediate antibiotic treatment is not necessary, great attention should still be paid to physical symptoms/complaints for a longer period of time after the tick bite as one can never be sure if any other tick latched onto the body as well.

- 8.) Another **direct method** of proving a Borrelia infection is the almost forgotten **Dark Field Microscopy (DFM)** which analyses fresh (that is, unstained and not centrifuged) blood. One can use a small drop of capillary or vein blood, taken without prior skin disinfection, and prepare a blood smear. A small vial of blood, without being centrifuged, can also be sent by mail as even after one or two days, liquid parts of the blood sample are still available for analysis.

The blood sample is then observed over a period of several days using the Dark Field Microscope to monitor changes in the blood sample. When the positive surface tension of the blood cells is no longer present, i.e. the cells no longer repel each other, then the previously-intracellular spirochetes will show up.

In a fresh Borrelia infection, the spirochetes are still moving around freely in the blood and, characteristically, spin around their own axis, making it easy to identify them. In case of a chronic infection, it can take several hours or even days until they are visible under the microscope, as they “slip out” of the cells (erythrocytes and macrophages). It is known that Borrelia can penetrate various tissue cells as well as endothelial and blood cells within hours after infection. In standard medical literature for microbiology Dark Field Microscopy is, still today, considered to be a suitable direct method of proving the presence of leptospira and spirochetes. Nonetheless, it is mainly used for samples of fresh skin lesions to directly prove the presence of Treponema pallidum, the spirochete of the Syphilis infection. This method of analysis can, however, also be applied to Borrelia recurrentis, the pathogen causing relapse fever, as well as to all sorts of Borrelia subtypes (i.e. Borr. burgdorferi s.l. = sensu lato).

Besides Borrelia, the Dark Field Microscopy can show other intracellular pathogens such as Chlamydia or Yersinia. Extracellular pathogens can also be seen, for example, Candida, Streptococcus, Diplococcus, Staphylococcus and parasites such as Giardia/Lambia. For the latter this may be quite helpful because the serological detection of antibodies or LTT for Giardia/Lambia is not always conclusive.

With Dark Field Microscopy, hyperacidity can also be identified by the presence of crystalline structures in the patient’s blood and, furthermore, it can also show exposure to heavy metals (i.e. mercury, palladium, cadmium and lead). Unfortunately, this helpful method of analysis is now used mostly by naturopaths following the teachings of Professor Enderlein and no longer by laboratories and microbiologists as an established method of verifying pathogens (as it used to be to diagnose syphilis by detecting the spirochete Treponema pallidum).

In seronegative, but clinically suspect cases of LD, it is still possible- by using Dark Field Microscopy- to find evidence of Borrelia and certain co-infections as well as other risk factors (e.g. heavy metals or hyperacidity). Dark field microscopy can also be used to find out if there is any Borrelia left after a course of antibiotic treatment. In general, it takes 10 days to get the results of this particular dark field investigation method. The patient himself can clearly observe the changes and/or improvements in his own blood sample because the doctor as well as the patient is given a print-out of the images of the microscope and, if desired, even a DVD with video sequences of (moving) spirochete Borrelia (see **Appendix** for an address for where to get Dark Field Microscopy done).

- 9.) One can also find the spirochete Borrelia in skin and tissue samples through **histological methods** by applying special staining agents such as the immune histochemical method of the **Focus Floating Microscopy (FFM)**, which uses polyclonal antiborrelia antibodies. FFM analysis has achieved a sensitivity of 96% compared to the PCR method which has only reached a sensitivity of 45%. Additionally, FFM reached almost the same specificity like PCR (FFM 99,4% compared to PCR 100%). Many skin conditions which until now could not easily be identified, can now be attributed to a Borrelia infection by this method (Information given by Dr. Dr. Eisendle 5/10).

Known factors, that can lead from acute Borrelia infection to a chronic one

In completely healthy individuals without previous stress on the immune system, the body's own defense system, such as the production of antibodies against Borrelia, can be sufficient to prevent the onset of further Borrelia-related symptoms. Epidemiological studies show that out of 100 Borrelia-infected patients who developed antibodies, only 10 showed clinical signs of the disease. However, the follow-up observation period for these studies was, in all cases, so short that no definite conclusions should be made because many Borrelia-related symptoms appear only much later.

This latter opinion is supported by clinical, longtime observations made by Dr. Hassler, M.D., who, over years, monitored his patients with a confirmed infection of Borrelia. Many of these patients were seropositive but asymptomatic (such as the "healthy lumberjack" type). Nevertheless, many of them only first began to show symptoms and complaints of a Borrelia-related disease as late as eight years after infection.

However, those who begin to show symptoms shortly after infection (such as the "Borreliosis flu") are more likely to later suffer from chronic Lyme Disease with its confusing variety of symptoms. Additionally, this can be dependent on some other risk factors and (genetic) conditions, of which, so far, we only know a few and for which some new laboratory tests can check.

For those without a really strong immune system, the main reason for the progression to a **chronic course** of Lyme disease is **the lack of or insufficient treatment with antibiotics** at the time when there was an Erythema migrans, a lymphocytoma or, equally as important as both of these, a "summer flu" shortly after a tick bite.

It is hard to think of having an infection with Borrelia if there is no known bite by a tick. Yet lately there are reports of Borrelia transmission to humans by fleas and horseflies. In all of these cases it is much harder to identify a particular condition as Lyme disease. It should also be noted that Borrelia infections can be transmitted sexually or from mother to child during pregnancy. Even these rare forms of transmission should be considered when examining a complex yet undiagnosed illness.

Antibiotic treatment is considered insufficient if the antibiotics are given for too short a period of time or in too low a dosage. This is often the case when one strictly follows the current applicable guidelines of different (e.g. neurological or dermatological) organizations for the treatment of LD, as these recommendations are often not sufficient. For example, guidelines published by the "Deutsche Gesellschaft für Neurologie" make neither a statement about the treatment of a recently acquired Borrelia infection without neurological symptoms nor about the treatment of chronic persistent LD, if there are no neurological symptoms/complaints. These guidelines were formulated only for cases of (acute) Neuroborreliosis, which are nevertheless only **one** of the many possible manifestations of Borrelia infection. Other symptoms of acute or chronic LD, for example, are cardiac, cognitive, gastrointestinal or muscle-skeletal symptoms, to name but a few.

All of these guidelines are very similar to those of IDSA (Infectious Diseases Society of America). These are not mandatory for doctors, but serve only as a reference or recommendation for treatment. For example, these guidelines recommend that an acute Neuro-Borreliosis should be treated

with Ceftriaxon iv, Cefotaxim iv, Penicillin G iv or 200 mg (maximum 300 mg) of Doxycycline orally for 14 days to a maximum of 21 days. To treat a recently acquired Borrelia infection (so called Stage 1), most medical textbooks and articles about this subject suggest 2 x 100 mg (max. 300 mg) of Doxycycline for 14 (max. 21) days except for children under 9 years of age. Amoxicillin only is recommended for pregnant women and children (50 mg/kg bodyweight) and is also applicable to adults in a dosage of 3 x 1000 mg.

However, the suggestion of a maximum of 21 days treatment does not take into consideration the very long replication-time of Borrelia (they divide by transverse fission across their width and then replicate every 12 to 24 hours). It has been calculated, based on this slow replication-time in comparison of that of only 20 minutes by E.coli bacteria, that a LD patient should be treated for **at least 30 days** to combat the Borrelia.

In vitro studies at the University of Wädenswil, Switzerland, under the direction of Prof. Martin Sievers, using borrelia bacteria grown in human endothelial cell structures, have shown that a certain level of antibiotic concentration in the blood is needed to prevent Borrelia from replicating. According to the results of these studies, the necessary so-called minimal **bacteriostatic serum concentration** of Doxycycline in the blood would need to be **5µg /ml**. This, in practical application, would need to be **400 mg to 600 mg of Doxycycline** daily, depending on body weight, that is to say more than twice or **even 3 times the dose suggested by the current guidelines** (i.e. 200 mg Doxycyclin).

To find the correct individual dosage, it would be useful to test the serum concentration of the antibiotic during treatment, especially during prolonged antibiotic therapy for chronic persistent LD. (see Appendix for suitable labs). However, with the currently recommended antibiotic dosage, even for severe neurological cases, the necessary 5µg/ml Doxycycline serum concentration cannot be achieved. The dosage recommended by the IDSA guidelines will, at most, simply prevent further replication of the Borrelia. Professor Sievers as well as others (Prof. E. Sapi as well as MacDonald, MD, Univ. of New Haven, Conn.) have also discovered that, by using Ceftriaxon or Penicilline G, persister forms will be developed i.e. cysts, blebs or biofilms, which are partly the cause of chronic LD.

I would like to mention another disadvantage of such “guidelines adequate” low dose antibiotic therapy. **Low dose antibiotic as well as cortisone** treatment in the early stages of the infection **prevents a strong initial immune system reaction**. Consequently, the production of antibodies and immunoblot bands is compromised. Therefore, LD infected patients will later not be easily diagnosed and, thus, remain untreated.

Antibiotic therapy in the early stages of LD with **cell wall synthesis inhibitors** like **beta lactame** (i.e. Amoxicillin or Cefuroxim) as well as **cephalosporines** (Ceftriaxon or Cefotaxim), leads to an increase in organisms **without cell walls (stealth pathogens)**, which form a biological base for later relapses. A well thought-out and effective first treatment, after Borrelia infection has taken place, should take into account all of these facts to avoid unnecessary risk that the patients become chronically ill with LD.

Another reason for an inadequate elimination of pathogens could be -as already mentioned- a weakness in the patient’s immune system. This could be due to an inborn **lack of immune-**

globulin or due to a previous treatment with **immunosuppressant medication** for another severe illness, thus inhibiting the body's ability to defend itself against invading bacteria.

Other factors that increase the **risk of developing** chronic LD infection are **environmental toxins** such as **solvents, softeners (phthalates), fungi and heavy metals**. These include, to name only a few, lead (from old pipes), Cadmium (manure, cigarette smoke, waste burning) and nickel (jewelry or food), as well as aluminum (in deodorants, antacids and in many vaccines where it is used as a stabilizer).

More serious is the **toxic load** after exposure to **dental/medical interventions**. Several alloy materials used by dentists for tooth inlays or crowns (Gold, Palladium etc.) and their "glue" (Methylmethacrylat or MMA) can contribute to the development of chronic LD. The worst culprits are amalgam fillings, since roughly 50% of amalgam is mercury, which is a strong (neuro)toxin. Many vaccinations can be even toxic for those with an **impaired genetic detoxification function** for, among others, heavy metals (for example GST-enzyme deletions or weakened activity of GST-enzymes and SOD 2-variants). Until recently, many vaccinations (e.g. Twinrix® against Hepatitis B) contained **Thiomersal** (in the USA Thimerosal or Phenylmercury) as an antibacterial preservative, as well as **Aluminium-Hydroxide** (Al-OH) as a stabilizer. This could potentially have very serious consequences, especially for infants and young children, as their immature nervous and immune systems are often not strong enough to cope with these powerful neurotoxic substances.

In this connection it is worth noting that in the United States a triple vaccination (!) is often given to newborns on their first day of life. The growing number of autistic children has become quite a problem. Epidemiological investigation by the National Survey of Children's Health (NSCH) from the year 2007 discovered that in the United States almost one in every 100 children, between the ages of 2 and 17, suffers from a form of autism (Autism spectrum disorder or ASD). There has been a drastic increase in the number of previously healthy children who develop autistic or ADD/ADHD behavior patterns after a Borrelia infection and/or who have a "Thiomersal-load" caused by either vaccinations and/or amalgam fillings of the mothers during pregnancy.

More information about the relationship between **Mercury , LD and ASD, ADD/ADHD** see www.liafoundation.org

<http://articles.mercola.com/sites/articles/archive/2009/09/10/1-in100-Now-Have-Autism-Spectrum-Disorder.aspx>

[Cheuk, D.K.L., Wong, V.\(2006\): Attention-Deficit Hyperactivity Disorder and blood mercury level: a case control study in Chinese children, Neuropediatrics 37: 234-240](#)

Mercury poisoning primarily affects the peripheral and central nervous system, resulting in polyneuro-pathic disturbances, as well as psychological and cognitive dysfunctions. Those suffering from chronic LD often show a **Type IV-allergy** to amalgam composites (e.g. Mercury (Hg), Methyl-Hg and Phenyl-Hg and sometimes even tin), even long after the removal of the amalgam fillings. Often, evidence of mercury can be found in the stool from residual deposits in the body, even though the patient has not recently consumed any mercury-containing foods such as seafood, especially tuna.

The build-up of the toxic effects of these substances is directly related to the degree to which the patient can or cannot detoxify them (genetic detoxification dysfunction). There are various genetic tests available for testing the enzyme activity to check the individual's potential for detoxification (stage I or II). Usually, **detoxification enzymes of phase II** are analyzed for this, such as Glutathione-S-

Transferases (GST-M1, GST-T1, GST-S1), SOD2, NAT2 and COMT. Normal functions of these are needed to **excrete heavy metals and solvents**. If there is an intolerant reaction, when applying a normal dose of medicines, it is also recommended to check the **phase I enzymes of the Cytochrome P 450-System** (i.e. Cyp 2D6, Cyp 2C19 or Cyp 3 A/4 et.al.) to avoid the risk of incorrect dosing (under dosing or overdosing according to the metabolizing ability of these enzymes).

Taking this into consideration, it is apparent that many chronic LD patients have, additionally, a noticeable reduction in their enzyme activity or even a genetic absence (so called **deletions**) of **certain detoxification enzymes of phase II**. This missing ability to detoxify explains the build-up of heavy metals and also the **continuing weakening of the immune system**, compromising the patient's ability to deal with new pathogens (especially with the persistent intracellular ones, such as the spirochete Borrelia).

However, in the author's experience, the immune system can improve and become more effective again after detoxification, through certain supplements and herbal medicines.

(see **Vitamin and mineral supplementation** p. 24 ff)

Heavy metals, like so many other toxins, (i.e. pesticides, biocides, and fungi) lead to an increased accumulation of free radicals. This causes an abnormal metabolic reaction, the so-called nitrit/ peroxynitrite-cycle or better known as **NO/ONOO-Cycle** (according to Martin Pall, Ph.D.), which leads to an increased formation of Nitrogen Oxide (e.g. Peroxynitrite, Nitrotyrosine, Nitrophenylacetic acid just to name a few). This causes nitrosative stress in cells (and also in the immune cells) and therefore a decrease in immune system function.

Several laboratory parameters are indicators for such cell "emergency" situations: i.e. a deficiency of intracellular ATP and Glutathione, increased values of Peroxynitrite, Citrulline, Phenylacetic acid and Methylmalon acid in the urine, and Homocysteine, which acts as an indicator for a Vitamin B1, B6, B12 and/or a folic-acid deficiency. Carnitine, Selenium, Zinc and Coenzyme Q10 are often low in value as well. If these parameters are different from the norm, therapy should try to substitute these missing substances for the chronic persistent infected patients (see "**Vitamin and mineral supplementation**" p. 24 ff).

As Borrelia spirochetes cause a **chronic-systemic inflammation** in their host, cytokines (inflammatory markers) are often measurably increased. For Borrelia, which are typically intracellular in the chronic stage of LD, these cytokines are the so-called **Th 1-Cytokines** (TNF alpha, Interferon gamma, Interleukin 1 β et al.) which normally help to defend against viruses and cancer cells, as well as against all intracellular pathogens.

As long as a chronic infection is present, the **Natural Killer(NK)-cells** in the blood are decreased in numbers, as they are needed in the tissue to fight the chronic systemic infection. The number of the NK cells and especially their subgroup, the **CD 57+-NK cells**, can be an additional indicator of a long existing systemic infection, such as chronic LD. However, it is not a specific indicator of LD, but rather for a general chronic systemic inflammation.

If the number of **CD-57+ NK cells is lower than 50/ μ l** in the blood (the norm being 60 to 360/ μ l), this would be an indicator of a chronic form of LD (if a Borrelia infection has been previously diagnosed), according to Drs. Stricker and Burrascano Jr. (both members of ILADS, the International Lyme

and Associated Diseases Society). If the value is even lower ($< 20/\mu\text{l}$), this would indicate a very severe case of chronic Borrelia infection. With these very low values, even the Lymphocytes Transformation Test (LTT) can be (false) negative, as the immune system cannot react adequately. Therefore, it is useful at the beginning of laboratory testing to determine the CD 57 value, as to find out the immune system's ability to react to pathogens. If NK cell values increase during or after therapy, the treatment can be considered successful.

It was reported a few years ago, that certain constellations of the **Human Leucocytes Antigen (HLA)** i.e. certain immunologic markers on all those body cells containing nuclei, can lead to a resistance to the usual antibiotic therapy against Borrelia spirochetes or even to a lack of specific antibody production. With the presence of the HLA-DR (B)-1 Subtype *0101, *0102, *0104, *0105 the production of antibodies against Borrelia spirochetes would be prevented and with the presence of HLA-DR B1 *0101, *1501, *0401 and *0402 a resistance to antibiotics would result. On the other hand, still other HLA-subtypes (HLA-DR B1 *0701, *0703, *0704) can cause an especially strong immune reaction towards Borrelia surface protein antigens. However, newer studies have moderated these assertions and called for more scientific research. Nevertheless, these above-mentioned genetic parameters can still give an indication of possible reasons for therapy resistance or for a total lack of antibodies, as well as for an extreme build-up of antibodies against Borrelia spirochetes.

Some information about the biological bases of the therapy recommendations

As already mentioned, an effective antibiotic therapy is needed as soon as possible after an infection with Borrelia spirochetes (or other pathogens). This is because it is now known that, due to their flagellae, the spirochetes are actively moving through their host's body within a matter of hours and then begin to replicate. Spirochetes quickly make their way from the blood stream into cells (for example into erythrocytes, endothelial and glia cells within hours, into the fibroblasts a bit later). In animal tests, it was proven, that in artificially-infected animal hosts (sheep), the Borrelia spirochetes had spread to the brain, to the liver and even to the lining of the bowels within 21 days.

Once they have penetrated the cell walls, Borrelia spirochetes change into their persisters forms (i.e. granula, blebs, cysts or biofilms), and so, all antibiotics which are only extracellularly effective, e.g. penicillin, amoxicillin, cefuroxime or ceftriaxone, do not reach the pathogens. All of these penicillin derivatives impede the synthesis of the bacterial cell walls after the spirochetes have divided themselves into two parts and thus prevent the normal replication and growth. Only antibiotics which are able to attack pathogens intracellularly as well, such as the macrolides (e.g. clarithromycin, azithromycin) or the tetracyclines (e.g. minocycline or doxycycline) should be chosen for therapy of chronic Lyme disease.

Antiprotozoal medication such as **Metronidazole** (e.g. Clont[®], Arilin[®], Flagyl[®]) or **Tinidazole** (e.g. Trimonase[®], Fasigyn[®], Tindamax[®]) is also effective intracellularly and thus can enhance macrolides or tetracyclines antibiotic therapy, especially since an undetected parasite (especially e.g. giardia/lambliia or trichomonas) can prolong and intensify chronic Borrelia infection. Also the persisters forms of Borrelia (e.g. cysts, blebs, granula, biofilms) can be treated with Metronidazole as well as Tinidazole.

Hydroxychloroquine sulfate (Quensyl[®], Plaquenil[®]) is an anti-malaria medication, but it also enhances the intracellular effect of these antiprotozoals through increasing the intracellular cell-pH

(alkalinization). **Artemisinin** or **Chininsulfate** (Chininsulfat D4) can be used as well, as an herbal alternative for Hydroxychloroquine to enhance the effects of the antibiotics.

The **biofilm-matrix phenomenon** was, only recently, the subject of more intense research (Prof. Eva Sapi, Alan B. MacDonald, University of New Haven, Connecticut 7/2008) showing how effectively the polymeric matrix of the biofilms shields the spirochetes *Borrelia* from antibiotics (up to 1000-fold!) and from the immune system. This could be the cause of the often ineffectiveness of current recommended therapies and relapses (i.e. reappearances of symptoms) even after antibiotic treatment. Almost tragic in this context is the fact that the often-used antibiotic treatment based exclusively on penicillin and its derivatives, has been proven to be the cause of the later difficult-to-treat persister forms (granula, blebs, cysts). (Research by Prof. Dr. Sievers, University of Wädenswil, Switzerland).

LD patients often experience a deterioration of their condition every 4 weeks possibly because of the very long replication cycle of *Borrelia* (12-24 hrs as compared to 20 minutes for *E. coli*). Theoretical calculations by microbiologists suggest a necessary time period of 30 days for elimination of **one** spirochete generation and therefore an antibiotic treatment of at least 30 days is recommended.

Therapy Recommendations

The following antibiotic treatment recommendations and other complementary therapies are based on my personal experience through years of treating chronic LD patients, on the information and guidelines of the German Borreliosis Society (see www.borreliose-gesellschaft.de), and on the different therapies published by German and, more often, American colleagues. These **therapy recommendations claim to be neither complete nor final**, as new findings and insights on LD and its causes constantly change the therapy proposals and bring about new ideas. All the following therapy schemata should always be performed by a doctor, who of course, is then responsible for the treatment.

The following antibiotic treatments are recommended in accordance with the above-named so far known biological facts. All these antibiotics should be increased gradually to prevent a so-called **Herxheimer reaction**

1. Early stage of *Borrelia* infection always needs a treatment of 30 days

A. For adults

Tetracyclines

Minocycline 2 x 100 mg daily (blood-level necessary for effectivity > 2,5 ug/ml)

Minocycline dosage should be increased slowly, starting with one dose of 50 mg/day, then increasing by 50 mg every 3 days up to 2 x 100 mg (i.e. 2 x 50 mg = 100 mg morning and evening). Dosage may vary depending on body weight and blood level of the antibiotic.

Doxycycline 2 x 200 mg (up to 2 x 300 mg), starting with 100 mg twice a day. Dosage may vary depending on body weight and blood level of the antibiotic (necessary blood-level > 5 ug/ml).

Macrolides (also in case of allergies to Tetracyclines or side effects of Tetracyclines)

Azithromycin 500 mg 1 x /day

(After 4 days treatment, a 3 day break is necessary because of an intracellular accumulation of the antibiotic)

Clarithromycin 2 x 250 mg for 4 days at the beginning, then continue with 2 x 500 mg

B. For pregnant women:

Amoxicillin 3 x 1000 mg

In case of penicillin allergy and if an infection occurs during pregnancy, **Clarithromycin** is a possible alternative

C. For children under 8 years:

Amoxicillin, Cefuroxim, Clarithromycin - dosage always adapted to body weight

D. In cases of severe neurological symptoms or serious effects on other organs

e. g. Facial palsy, paralysis of an extremity or life-threatening heart dysfunctions (AV- Block III, myocarditis and/or pericarditis with effusion)

Cephalosporins (in these cases, only the intravenous forms of cephalosporins should be given)

Cefotaxime (Claforan®) 3 x 2 g (up to 4 g) iv or 200 mg/kg bodyweight for children or patients who are under weight/over weight (usually with less side effects than Ceftriaxon)

or

Ceftriaxon (Rocephin®, Cefotrix®) 2 g- 4 g iv or 100 mg/kg body weight for children (only once a day due to the long half-life of Ceftriaxon)

2. Chronic persistent stage of the Borrelia infection

Initially, treatment should be 30 days, then paused/stopped in order to be able to check via a Lymphocytes transformation test (LTT), the effectiveness of the prescribed antibiotics. Treatment should then be continued until no more symptoms are present and the LTT becomes negative.

Tetracyclines

a.) **Minocycline starting with 50 mg in the morning**, followed by 3 day intervals increasing the dosage by 50 mg until **2 x 100 mg** is reached.

Combine with Hydroxychloroquine 200 mg (e. g. Quensyl®, Plaquenil®) in order to alkalize the infected cells, daily or even only every second day due to the extreme long half-life of 30-60 days).

Of all the above-mentioned antibiotics, **Minocycline is the most effective** in crossing the blood-brain-barrier (40% can enter the CFS). Thus, in my experience, Minocycline should be

preferred to Doxycycline with regard to neurological, psychiatric, cognitive and vegetative symptoms in the chronic persistent stage of LD.

As an alternative to Hydroxychloroquine, **cAMP® D 30** (ampoules), a homeopathic medication, can be used. It can be administered once a day intravenously, intramuscularly, subcutaneously or orally, diluted with water. A second alternative is **Artemisinin®** (Artemisia annua anamed) 3 x 200 mg daily in **combination** with Tetracyclines or Macrolides.

- b.) Doxycycline 2 x 200 mg** (up to 2 x 300 mg). Less effective in crossing the blood-brain-barrier (14%) in comparison to Minocycline (40%). It could also be administered intravenously in case of side effects of skin/stomach due to Doxycyclin. In the case of overweight patients needing a higher dosage, Doxycyclin may also be administered intravenously to avoid gastrointestinal side effects. Combinations of intravenous and oral treatment are possible, too. For example 100 mg Doxycycline iv (dissolved in 100 ml of 0.9% saline (NaCl)-solution) in the morning, followed by either 200 mg Doxycycline or alternatively 100 mg Minocycline orally in the evening.

Macrolides

- c.) Clarithromycin** (Klacid®) **2 x 250 mg**, after 4 days **2 x 500 mg, combined with e.g. cAMP D 30 or Artemisia annua or Hydroxychloroquin 200 mg** daily or every 2nd day, especially effective in the case of musculoskeletal symptoms.
- d.) Azithromycin** 500 mg (Zithromax®, or 600 mg Ultreon®), especially as post-treatment after an initial treatment with Macrolides in order to further reduce Borrelia activity. Patients suffering from impaired intestinal flora or from stomach sensitivity will benefit from Azithromycin because it is taken only once a day. The same once-a-day dosage can also work well for those who must go to work. After a 4-day intake, a pause of 3 days is recommended, as Azithromycin accumulates intracellularly. In particularly severe and difficult cases Azithromycin may be given intravenously (500 mg Azithromycin in a 500 mg saline (0.9% NaCl) solution) in order to reach higher blood- and tissue levels. To avoid irritation of the veins it should be administered slowly (over 2-3 hours).

Depot Penicillin

- e.) Benzathine-Benzylpenicillin** 1.2 Mega (Tardocillin®) intramuscularly 2–4 times a month, especially in cases of penicillin-sensitive co-infections such as Streptococcus, Staphylococcus and Pneumococcus

Antiparasitic Medication

- f.) Metronidazole** (Clont®, Arilin®, Flagyl®) 400 mg – 800 mg orally or, better yet, 1.2 g intravenously daily for 10 days as additional treatment, especially if a parasitic co-infection is present (often detectable through Dark Field Microscopy or for example a positive Giardia/Lambli-LTT). Additionally, Metronidazole is suitable to treat intracellular persisters forms of Borrelia as well as co-infections with Chlamydia pneumoniae and others. A 4 week pause has to be observed due to possible side effects (e.g. chromosomal damage) before another 10 day

treatment can be repeated. Some even state that Metronidazol should only be given once in a lifetime!

- g.) Tinidazole** (Fasigyn®, Trimonase®, Tricolam®, Tindamax®, Simplotan®) 500 mg 1-2 Tablets in the morning as a very effective co-treatment together with Tetracycline and Macrolides. Very recent studies (Prof. E. Sapi and Allan B. MacDonald at the University New Haven, Conn., 2011) have shown its high efficacy against intracellular persisters forms and biofilms as well as against the spirochetal *Borrelia*.

Antiviral drugs

- h.) Amantadine** (Symmetrel®, Symadine®) 100 mg (up to 200 mg) daily can be quite effective in viral co-infections (e. g. Bornavirus, Parvovirus B 19, Herpes zoster or HSV 1/2) as well as in cases of severe fatigue. Due to its stimulating effects, however, intake is recommended until noon.

Modafinil (Vigil®, Alertec®, Provigil®)

It can also be effective in cases of chronic fatigue and exhaustion; it is officially approved for treatment of narcolepsy, chronic fatigue in Multiple Sclerosis, shift work sleep disorders and obstructive sleep apnea, but in other conditions with severe tiredness e.g. chronic borreliosis or CFS and other diseases with chronic fatigue due to mitochondrial dysfunctions it may be tried as well.

Summary

After an initial antibiotic therapy, **Borrelia-LTT** should be repeated after a pause of 4-6 weeks. Depending on the LTT-result (either still positive or already negative) and on the continuing presence of clinical symptoms, the decision should then be made, whether to start with another type of antibiotic or continue with the same one.

For the same reason, **Dark Field Microscopy** should be done after the first course of antibiotics. In this way, it is possible to detect if viable/mobile *Borrelia* spirochetes can still be seen. As mentioned above, the spirochetes can emerge out of the “dying” erythrocytes and macrophages after an observation period of 3-4 days.

There is **no reason to retest for Borrelia antibodies or the immunoblot**, not only because of the cost, but also because it is not necessary: the question is not whether an infection with *Borrelia* has occurred at all, but whether there is still activity of the *Borrelia* spirochetes after the antibiotic treatment.

Further supplemental therapies (to correct the previous proven vitamin and mineral deficiencies and other pathological laboratory findings)

The chronic form of Lyme Disease (LD) has already been discussed in several contexts in this article. I would, nevertheless, like to briefly summarize here **what is known about this persistent form of the Borrelia infection today** (even if it is still somewhat controversial to established medical opinion and guidelines).

Chronic LD is a chronic-systemic inflammation with continuous slightly elevated **inflammation parameters** of the **Th 1-type** e.g. TNF alpha, Interferon gamma or IL 1 β . These inflammatory reactions are exacerbated by other pro-inflammatory factors such as a build-up of free radicals due to heavy metals and/or other environmental toxins as mentioned previously (see page 15 ff).

Free radicals, and subsequently the increase of nitric oxide, start to change the metabolism of the body resulting in the so-called **NO/ONOO-Cycle** (nitrite/peroxynitrite cycle according to M. Pall, Ph.D.). (Interestingly enough, nitric oxide seems to cause the Borrelia spirochetes to become more mobile, too, as seen in biofilm matrix observation).

An immediate consequence of this abnormal metabolism is a change at the cellular level e.g. the **reduction of intracellular Glutathione** and **Adenosine Triphosphate (ATP)**, a **deficiency of Vitamin B 12** seen by elevated **Homocysteine** in serum and by **elevated Methylmalonic acid** in serum as well as in the urine. Infection with parasites (especially with Giardia/Lambliia), which are easily identified with Dark Field Microscopy, results in an **increase of immunoglobulin E (IgE)** and **elevated eosinophiles** as seen in the differential blood count. The response of the eosinophilic cells reflects the intensity of the allergic process. This may also be seen in an incompatibility with heavy metals and/or other toxins. **A low level of the enzyme DAO (Diaminooxidase)** frequently leads to histamine intolerance and allergic, often urticarial skin reactions. Minocycline as well as N-Acetylcysteine (NAC[®], ACC[®]) lowers the DAO activity, so allergic reactions of this kind are more likely if either one or both is administered. If such allergic reactions do occur, one can prescribe DAOsin[®] or other DAO-formulas to stabilize the levels of the DAO enzyme.

Chronic inflammation - due to various reasons e.g. bacteria, heavy metals, toxins etc.- after a period of time, very often leads to a progressive **weakening of the functioning of the adrenal glands**. This causes hormonal changes (e.g. cortisol, adrenaline, aldosterone and DHEA-S deficiency with lower levels of the sex hormones estrogen, progesterone and testosterone) causing symptoms such as severe tiredness and exhaustion, muscle aches, cognitive impairment, sleeplessness and emotional disturbances, just to mention a few. This should be kept in mind in treating any kind of chronic disease and/or inflammation.

Some medications effective in treating the vicious cycle of these metabolic dysfunctions

For further details and information, see :

Martin Pall, Ph.D: Explaining "unexplained illnesses", Harrington Park Press 2007

James L. Wilson: Adrenal fatigue , Smart publications , Petaluma, USA, 2001

Glutathione as an antioxidant and for regeneration, if deficient

Reduced Glutathione 2 cps. à 100 mg daily or S-Acetyl-Glutathione powder orally.

Tationil[®] or Ridutox[®] amps. 600 mg intravenously 2-3 times/week (depending on the level of Glutathione deficiency).

ACC[®] or NAC[®](N-Acetyl-Cystein) 600 mg 1-4 times daily as a source of Cystein, in combination with Glutamine (Glutamin Verla[®]), both effective as Glutathione precursors.

ACC/NAC is also an important part of the treatment of a Chlamydomphila pneumoniae co-infection with a dosage of up to 2400 mg/daily.

Vitamin and mineral supplementation: (in USA/Canada mostly available over the counter (OTC))

Multivitamins : They should have a high content of Vitamin B, especially Vit. B 12 as well as Vitamins B 1, B 2 , B 3 und B 5 (Niacin), B 6 and B 7 (Biotin = Vit. H) and also Folic acid 400 µg, Vit. C.A 5000 I.U., Vit. C 1-2 g and Vit. E 300-600 I.U.. Additionally, minerals like Magnesium (100 mg -200 mg), Calcium (500 mg-1 000 mg), Selenium (100 µg-200 µg), Chromium c. 150 µg and Zinc c. 30 mg are also to be supplemented (OTC).

Vitamin B 12: If Methylmalonic acid in the urine or serum and/or Homocysteine in the serum is elevated, then there is a more severe Vit. B 12 deficiency. For this, one should take, per day, at least 10 drops (= 1 mg) of Methylcobalamine under the tongue (i.e. sublingually to avoid the decomposition of Vit. B 12 by the HCl-acid in the stomach). Alternatively, an intra-muscular Vit. B 12 “shot” (mostly Cyano or Hydroxycobalamin), often in combination with Vit. B 6 (in Germany: Medivitan®), may be given once or twice a month (OTC).

Vitamin C (Ascorbic acid): as powder or tablets, orally, 1-2 g/day (OTC) or-even much more effective -as an intravenously given formula (in Germany: Pascorbin 7,5 g, **by prescription** only) twice a week. However, Vit. C should not be given, as long as there is a heavy metal load of the body.

Vitamin D: If low levels of Vit. D (1,25-OH) are found in the blood, Vit. D preparations, dissolved in an oil base (capsules or liquid), should be given regularly in an amount of ca. **20 000 IU/week** (in Germany: Dekristol® 20 000 IE), dependent on the Vit. D levels in the blood (OTC).

Zinc (mostly 30 mg/day) and **Selenium** (at the most 200 µg/day, if its plasma concentration was shown lower than 125µg/l) (OTC).

Coenzym Q 10 (Co Q 10, Ubiquinone) 200 mg or more (1mg-12mg/kg body weight) is used as a very effective antioxidant (OTC)

Acetyl-L-Carnitine 500 mg twice daily helps against muscle pains through correcting muscle cell metabolism (OTC).

D-Ribose ca. 4 g-5 g daily (i.e. 4-5 tsp.) as a source of sugar, especially for muscles.

Silymarin (Milk Thistle) ca. 300 mg a day to improve liver function which is often impaired by the borrelia infection (OTC).

Melatonin (1 mg up to 2.5 mg) for sleeping problems with or without Vit. B 6 (which helps against nightmares)(OTC)

L-Tryptophan 500 mg – 1000 mg in the evening (OTC), to help the build-up of Serotonin

Anti-inflammatories (OTC)

Herbal preparations like stinging nettle-extract (in Germany: Hox alpha®, Natulind®), Curcumin in combination, if possible, with Omega-3-fatty acids and myrrh (in Germany: TNF direkt®) or myrrh of the African type (in Germany: Boscari®) or the Indian type (in Germany: H 15 Gufic®), Vit. E 300mg-600 mg (Gamma-Tocopherol, occurring naturally in corn- or sojaoil), Cat`s claw

(Samento TOA-free[®]), Cumanda[®] and Banderol[®] (all 3 by Nutramedix), wild teasel (in Germany: Kardenminzewürze[®] by INK), and an Omega-3-fatty acid preparation 1-2 g (in Germany: Zodin[®])

Detoxification of heavy metals, solvents and other toxins:

Zeolithes (i.e. very small granules of ground lava) like Ferulith[®] (a combination with ferulic acid, a part of curcumin) or Froximun[®] or Montillo[®] or Toxosorb[®] to absorb the toxins in the intestines. Be sure to take them always 2 hrs. before or after meals (OTC).

Cholestyramin (Questran[®], Colesthexal[®]) 2 x 4 g (up to max. 2 x 8) either 2 hrs. before or after a meal. Constipation is a very common side effect, so the regularity of bowel movements has to be observed carefully by the patients (**prescription only**).

Algae can also be very useful in the slow detoxification process of toxin deposits. **Chlorella pyrenoidosa algae** (in Germany: Beta Reu Rella[®] or others) seem to be quite effective (OTC).

Cilantro (in Germany: Cilantris[®]) i.e. coriander is quite effective in detoxifying cerebral mercury deposits, but this should only be taken after some time of enteric detoxification with zeolithes or algae (OTC).

To be able to remove heavy metal deposits (e.g. mercury, lead, cadmium etc.) from the fatty tissues of the body, **chelation substances**, to make these deposits water soluble, are needed. These are, for example, **DMPS** (in Germany: Dimaval[®], Unithiol[®]), only given intravenously (3-10 mg/kg body weight), or **DMSA** (in USA: Chemet[®]) in oral form as capsules. There are several therapy protocols available, but the most convenient one is, taking DMSA orally once a week according to body weight (10 mg/kg body weight) with lots of liquids (zinc should not be taken on the day of this DMSA-therapy). Alternatively **EDTA** (20-50mg/kg body weight) or **Na-Thiosulfate** (15-45 mg/kg body weight) can be given according to the proven heavy metal load. As long as inflammation caused by heavy metals is ongoing, Vit. C should not be given because of its pro-oxidative properties. (all of the chelation substances are available by **prescription only**).

Hyperacidity:

To reduce the hyperacidity of the body cells, mostly caused by the activity of the spirochetes *Borrelia*, different alkalizers can be used e.g. **Alka Seltzer[®]**, **Sodium Bicarbonate[®]**, **Soda Mint[®]** etc. Additionally, an alkalizing diet should be followed. Furthermore, baths in warm water (ca. 100 °F) alkalized with “baking soda” (Na HCO₃) (in USA: Arm & Hammer[®]) 2-3 times weekly for 30-45 minutes will be helpful. Use pH-measuring strips (litmus paper) for sufficient alkalization (above pH 8).

Nitrostress (NO/ONOO-Cycle) and clinical symptoms of **polyneuropathy**, if present, can be treated with **Alpha lipoic acid (ALA)** 600 mg /day orally (OTC) or 300 ml intravenously given by prescription.

Therapeutic Apheresis:

In cases of very serious LD manifestations with neurological disorders and/or consequent autoimmune reactions and/or a coexistent, severe heavy metal load, mostly due to genetic inability to remove them from the body, a so-called **Therapeutic Apheresis** can be done. This means, the blood will be “washed” through special (Japanese) filters within 2-3 hours to extract certain pathogens like germs, heavy metals or autoimmune complexes. The sediment, thus obtained, is called **Eluat**. After-

wards, the examination of the Eluat in specialised laboratories can determine which factors may have contributed to the chronification of LD. The Therapeutic Apheresis will therefore enable the immune system of the chronically ill patient to work more effectively afterwards (for more information see **Appendix**).

Laboratory tests

Listed below you will find some tests, mentioned earlier in this article, and the German labs where they can be performed. As to shipping requirements abroad, one should inquire at the labs themselves. For specialized tests, every lab sends out the necessary test kits and mailing materials (envelopes etc.) when asked. It must be noted that all blood and stool samples have to be sent in unbreakable, shockproof plastic tubes enclosed in specially lined ("bubble") envelopes (for any orders see addresses below).

The tests below are listed in the order of the time needed to reach the labs for correct analysis.

1. Tests which are non-time critical and can be sent from outside Germany

- **Nitrosative Stresstest** (Nitrophenyl acid, Methylmalonic acid Citrullin) of the first urine of the day as well as a test for hyperacidity of the body by measuring several urine samples during the day (so-called Sander test): offered by Labor Ganzimmun, Mainz
- Borreliosis specific **HLA-Subtypes**: offered by IMD Berlin
- **Heavy metals**, single or so-called **Multielement Analysis (MEA)** of the stool or of samples of dental material, solvents in the urine, analysis of heavy metals before and after the so-called DMPS test in the urine, saliva und stool: offered by Medizinisches Labor Bremen, Haferwende 12.
- **Polymorphism of the detoxification enzymes phase II** (e.g. GST-M1, GMST-T1,GMST-S1, SOD 2, NAT 2, COMT et al.) as well as the **Cytochrom P 450 Enzymes** (e.g. Cyp 2D6, 2C19, 2A4 et al.) from EDTA-blood samples: offered by IMD Berlin as well as Labor Langenhagen

2. Tests which need to be at the labs within 2 days after drawing the blood

- **Antibiotic blood levels** (Doxycyclin, Minocyclin) for example in Labor Seelig, Labor Ettlingen-Karlsruhe, IMD Berlin. For this test, it is necessary to give the exact time when the blood was drawn, as well as the actual antibiotic dosage and when the antibiotic therapy was started
- **CK, LDH with its Isoenzymes and TNF- alpha**, only from the serum (i.e. the liquid part of the blood above the sediment after having been spun in the centrifuge): offered by IMD Berlin, Labor Seelig
- **Complete Blood Count (CBC), liver enzyme levels, IgE, ECP (Eosinophilic Cationic Protein), IFN gamma, IL 1 β , IL 10, Diaminoxidase (DAO), Immunoblot and antibodies of Borrelia, Yersinia, Chlamydia, Giardia/Lambliia, Ehrlichia/Anaplasma**: offered by IMD Berlin or Labor Seelig or Borreliose Centrum Augsburg or Labor Ettlingen

3. Time critical (within 24 hrs) and complicated, costly tests

(should be sent preferably by courier and arrive at the lab no later than on a Thursday)

All types of LTT-/Melisa-tests (needed are 2 x Serum-, 1 x Heparin tubes) e.g. for Borrelia, heavy metals, dental material, environmental toxins, co-infections (Yersinia, Chlamydothyla pneumoniae, Chlamydia trachomatis, Giardia/ Lamblia, Herpes simplex virus 1/2, Varicella zoster virus, Epstein Barr virus): offered by IMD Berlin, Laborzentrum Bremen or Labor Ettlingen-Karlsruhe.

Intracellular Glutathion and ATP (Heparin blood): offered by IMD Berlin

EliSpot of Borrelia und Ehrlichia/Anaplasma (needed 2 CPDA tubes): offered by Labor Ettlingen or in Borreliose Centrum Augsburg or Labor Ettlingen-Karlsruhe

APPENDIX

Addresses:

Laboratories: (alphabetical)

- ▶ Borreliose Centrum Augsburg, Morellstr. 33, 86159 Augsburg, Tel. 0821/455471-0
- ▶ Institut für medizinische Diagnostik (IMD) Berlin, Nicolaistr. 22, 12247 Berlin, Tel. 030/77001 220
- ▶ Laborzentrum Bremen, Friedrich-Karl-Str. 22, 28205 Bremen, Tel. 0421/430-70 (LTT)
- ▶ Labor Ettlingen, Otto-Hahn-Str.18,76275 Ettlingen, Tel. 07243/51601
- ▶ Labor Ganzimmun Dr. Kirkamm, Hans-Böckler-Str. 109, 55128 Mainz, Tel. 06131- 7205-150
- ▶ Labor Langenhagen, Ostpassage 7, 30853 Langenhagen Tel. 0511/2030448
- ▶ Labor Laser, An der Wachsfabrik 25, 50996 Köln, Tel. 02336/3911-0
- ▶ Labor Seelig, Kriegstr. 99, 76133 Karlsruhe, Tel. 0721/85000-0
- ▶ Medizinisches Labor Bremen, Haferwende 12, 28357 Bremen, Tel. 0421-2072-0 (especially for heavy metals analysis)

Examination of ticks by the PCR-method for Borrelia-, Ehrlichia/Anaplasma and FSME-DNA: (alphabetical)

- ▶ JenaGen GmbH, Löbstedter Str. 80, 07749 Jena Tel. 03641/6285260
- ▶ Labor Bremen, Haferwende 12, 28357 Bremen, Tel. 0421/2072-0
(even quantitative results of Borrelia or Ehrlichia/Anaplasma i.e. the number of pathogens in each tick will be reported)
- ▶ Labor Dr. Brunner, Mainaustr. 48 a+b, 78464 Konstanz, Tel. 07531/817326
- ▶ Synlab Zeckenlabor, Zur Kesselschmiede 4, 92637 Weiden, Tel. 018050/93253
- ▶ Zecklab, Postfach 1117, 30927 Burgwedel, Tel. 05139/892447

Dark Field Microscopy:

Dr. Ulrike Angermaier, Traubengasse 19, 91154 Roth, Tel. 09171-851-52-17 (1 serum tube of whole blood or a smear sample enclosed in a shockproof plastic tube in a "bubble" envelope can be sent by mail)

Focus Floating Microscopy (FFM)

FFM can be done with all kinds of tissue, but the samples have to be put into formaldehyde or parafin. The material should then be sent in a specially lined ("bubble") envelope to

Prof. Dr. Bernhard Zilger, Department of Dermatology of the University of Innsbruck, Anichstr. 35, A-6020 Innsbruck (Tel. 0043-512-504-81115 for inquiries)

or

D.H. Kutzner, Dermatopathology, Siemensstr.6/1, D-88048, Friedrichshafen, Tel. 07541-60440-0

(www.dermapath.de)

or to Clinic for Dermatology and Dermatological Allergy, Erfurter Straße 35, D- 07740 Jena, Tel. 03641/937375 (www.derma.uniklinikum-jena.de)

Therapeutic Apheresis:

INUS Medical Center GmbH, Gesundheitspark am Regenbogen, Further Str. 19, D-93413 Cham, Tel. 09971/200 320 (www.gesundheitspark-cham.de)

Photos and collages of ticks in natural surrounding: foto.polack@email.de

Some specialized pharmacies: (alphabetical)

Apotheke Eyb, Eyber Str. 74, D-91522 Ansbach, Tel. 0981/46603501 (Glutathion, Ferulith)
Husaren-Apotheke, Kirchenstr. 49, D- 66793 Reisbach, Tel. 06838 86 1420 (S-Acetyl-Glutathion)
Klösterl Apotheke, Waltherstr. 32a, D-80337 München, Tel. 089/54343211 (Methlycobalamin)
Hohenburg-Versand-Apotheke, Kaiserstr. 15, D-66424 Homburg, Tel. 06841/2500 (Samento-TOA free, Cumanda, Banderol)
Peer Stadt-Apotheke Brixen, Adlerbrückengasse 4, I-39042 Brixen, Tel. +39 04728-6173, Fax -2777
e-mail: info@peer.it (Glutathion-Amps., Tinidazol)

Some addresses to order supplements:

- ▶ Heck Bio-Pharma, Karlstr. 5, 73650 Winterbach, Tel. 07181/9902960
- ▶ Institut für Neurobiologie nach Dr. Klinghardt (INK), Habsburgerstrasse 90, 79104 Freiburg/Breisgau, Tel. 07665-93247-10 or Planckstr. 56, 70184 Stuttgart, Tel. 0711/8060870 kontakt@ink.ag
- ▶ NutraMedix, Jupiter Florida 33477, USA, 001-561/7452917 or ordering by internet
- ▶ VIATHEN: Oll-Daniel-Weg 3, 18069 Rostock, Tel. 0381/808-340-033

For further information on chronic Lyme disease

Organizations:

Borreliose und FSME-Bund Deutschland (www.bfbd.de)

Deutsche Borreliose-Gesellschaft (www.borreliose-gesellschaft.de)

Borreliose Nachrichten (www.borreliose-nachrichten.de)

International Lyme and Associated Diseases Society (www.ILADS.org)

Time for Lyme, Inc. (timeforlyme@aol.com)

Turn the Corner Foundation (info@turnthecorner.org)

Canadian Lyme Disease Foundation (www.canalyme.com)

Informative Websites:

www.dr-hopf-seidel.de

www.verschwiegene-epidemie.de

www.lymenet.org or www.lymedisease.org or www.lymeinfo.net

www.lyme-hilfe.npage.de

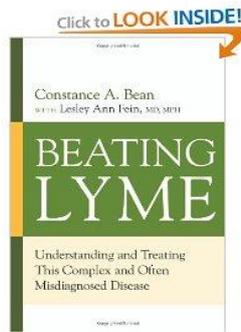
Literature:

Bean, Constance A. and Fein, L.A.: Beating Lyme, understanding and treating this complex and often misdiagnosed disease, Amacom 2008

Burrascano J.J.jr M.D.: Diagnostic hints and treatment guidelines for Lyme and other tick borne diseases, available at www.ilads.org

Dr. Hopf-Seidel: Krank nach Zeckenstich. Borreliose erkennen und wirksam behandeln, Droemer Knauer Verlag 2008, ISBN-13:978-3426873922

Jürschik-Busbach, Birgit: Die verschwiegene Epidemie. 9 Leben Verlag 2011, ISBN-13: 978 3981410501



Fotos: Frau Polack