



Dr. Rath Research Institute



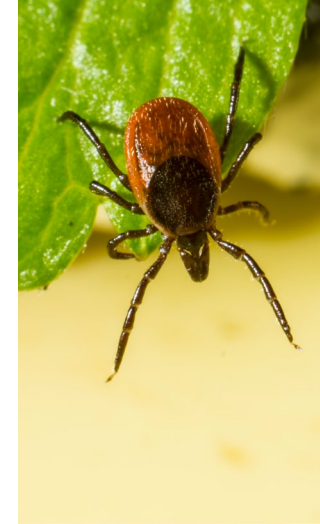
Lyme

D I S E A S E

Anna Goc, Ph.D.

Aleksandra Niedzwiecki, Ph.D.

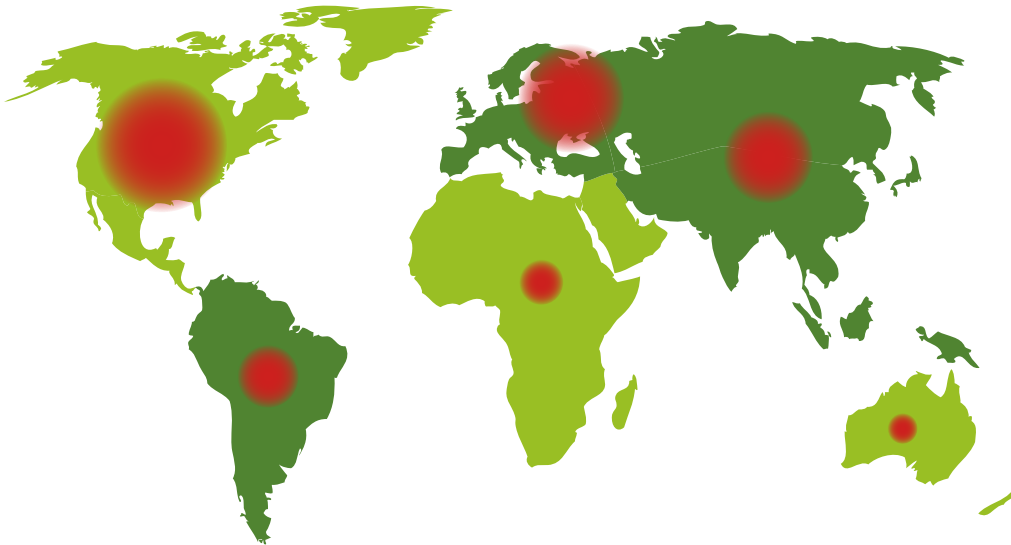
Matthias Rath, M.D.



Lyme disease

Lyme disease (LD), also called Borreliosis or Lyme borreliosis, is a bacterial infection transmitted by ticks. It was first described in the USA in 1975 in Old Lyme, Connecticut, however, reports of Lyme disease can be found in medical literature in Europe as early as 1883. Lyme disease has been reported in all continents except Antarctica. In the USA most Lyme disease cases (~95%) have occurred in North-Eastern states. This disease occurs in almost all countries in Europe, especially the Scandinavian countries, Germany, and Slovenia.

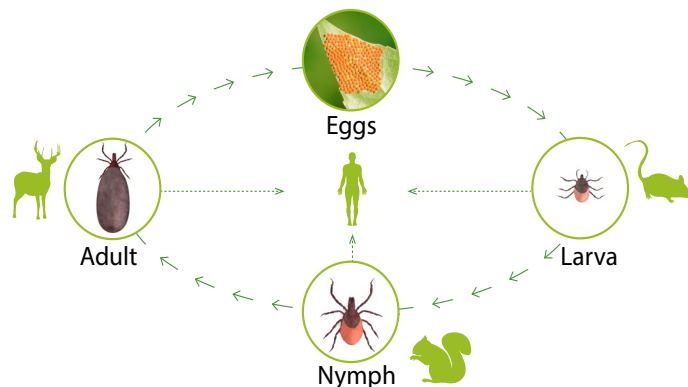
Public awareness of Lyme disease has been steadily growing over recent years. It is the most common vector-borne disease in the USA (with ~30,000 cases annually) and in Europe (with ~65-80,000 cases annually). While these numbers reflect only reported cases, the real number of patients affected with *Borreliosis* may be even up to 10 times higher due to frequent misdiagnosis and false-negative results that may occur in as many as 50% of cases.



How humans can get Lyme disease

The human transmission of Lyme disease starts from ticks which are small common external insects of the spider family that feed on blood sucked from humans and animals. If the tick feeds on the animal carrying *Borrelia sp.* then it can become infected with this bacterium in a form of spirochetes. Subsequently, spirochetes multiply in the tick's midgut and are ready to be transferred into the next host (such as animals and humans). The animals that most often carry ticks are white-footed field mice, deer, raccoons, skunks, weasels, foxes, chipmunks, squirrels, and horses.

In nature, ticks mature following a few sequential transformation stages, starting from egg, to larva, to nymph, and finally they become an adult form called imago. The infection can be spread at all development/maturation stages, however, the most concerning are the nymphs since they are abundant during spring and summer. Nymphs are small (1-2 mm) and since their bite is painless they are very difficult to detect. They can attach to any part of the human or animal body but are often found in the areas most easy to be missed, such as the scalp, the armpits, and groin.



What causes Lyme disease

The causative pathogen of Lyme disease is a bacterium of genus *Borrelia*, which has at least 37 known species. Twelve of them are Lyme-related and the number of genomic strains is unknown. All *Borrelia sp.* are host-dependent,



invasive, micro-aerophilic and slow-growing and this is the primary reason of the complications with diagnosing Lyme disease.

Lyme disease is manifested as an inflammatory disease that can affect many organs in the body. In its early (localized) stage it affects mainly the skin. In later stages (disseminated and/or persistent) the inflammation spreads to the joints, nervous system and also to the heart, muscles or other organs.

Lyme disease is often misdiagnosed as its symptoms may suddenly disappear even without any treatment or after a mild treatment. Also, not all symptoms have to always appear in a patient, and different symptoms may appear at different times.

Several medical disorders, recognized over the years as separate clinical cases, are currently accepted as the indicators of Lyme disease. They include acrodermatitis chronica atrophicans (ACA), lymphadenosis benigna cutis (LABC), erythema migrans (EM) and lymphocytic meningoradiculitis (Bannwarth's syndrome).

How Lyme disease progresses

There are four recognized stages of Lyme disease:

1. Early localized stage

(appears 3-30 days after tick bite):

- **Skin lesion** called erythema migrans (EM): A red spot/redness at the site of the tick bite, which will expand over time forming a bull's eye pattern. However, only about 10% of patients develop the appearance of a classic bull's eye. In some the rash can appear at more than one area of the body. In some people this small bump or redness at the site of a tick's bite may disappear over the next 1-2 days.
- **Flu-like symptoms:** Symptoms include fatigue, chills, fever, headache, muscle and joint aches, swollen lymph nodes, and nausea. It is important to note that these symptoms may vanish without treatment. Some people may get these non-specific symptoms as the only sign of infection, in others they can be accompanied by a red rash.



2. Early disseminated stage

(appears days to weeks after tick bite):

- Rashes appearing in other places on the body
- Fatigue, nausea, diarrhea
- Depression, anxiety, mood swings
- Cognitive impairment, light/sound sensitivity
- Severe headaches and/or neck stiffness due to meningitis
- Pain and swelling in the large joints
- Shooting pains with or without sleep disturbance
- Facial or Bell's palsy (loss of muscle tone on one or both sides of the face)
- Heart palpitations and dizziness due to changes in heartbeat



3. Late disseminated stage

(appears months to years after tick bite):

- **Neurological complications:** Up to 5% of patients with untreated Lyme disease develop neurological symptoms such as shooting pains, weakness or itching/tingling in the hands and/or feet, impaired short-term memory, muscle impairment, and severe fatigue. Also, heart problems (an irregular heartbeat), and inflammation of the eyes and liver (hepatitis) can appear.



- **Arthritis:** About 60% of patients with untreated Lyme disease develop arthritis (severe joint pain with swelling), usually in the knees, although pain can move from one joint to another. Note: arthritis manifests differently than arthralgia (pain, but not swelling).



4. Persistent (chronic) stage

(called PTLDS, Post-Treatment Lyme Disease Syndrome):

- Muscle and/or joint pains
- Cognitive defects
- Sleep disturbance
- Fatigue

These symptoms can develop in approximately 10-20% of patients with Lyme disease and continue for months, or even years after treatment. They allegedly result from an autoimmune response and cause lasting damage to the tissues.

Lyme disease patients are also facing*:

- Neurological abnormalities such as decreased sensation on one side of the face, asymmetry of the face, restricted movement of the eyes, hearing loss, loss of vibration sense in the feet compared with the hands, abnormal brain MRI showing non-specific white matter disease, abnormal brain SPECT scan showing changes in blood flow in the brain
- Low CD57 count
- Co-infections with *Babesia sp.*, *Ehrlichia sp.*, and *Bartonella sp.*
- Mild elevation of auto-immune disease markers including: RT (rheumatoid factor) and ANA (antinuclear antibodies)
- Micronutrient deficiencies, including low levels of vitamin B12 and folic acid
- Changes in vitamin D metabolites: low 25-Hydroxy-vitamin D (25-OH-VitD) and high 1,25-Dihydroxy-vitamin D (1,25-OH-VitD)

Note: Jarisch-Herxheimer reaction has been reported in about 15% of Lyme disease patients and appears within 24 hours or longer after treatment. It is manifested by elevated temperature, myalgia, and arthralgia, resulting from increased levels of circulating antigens derived from dead spirochetes and latent forms.



How Lyme disease is diagnosed

Diagnosis of Lyme disease is not easy and is often a challenge for a physician. Currently Lyme disease is diagnosed based on:

- **History of possible exposure** to infected black-legged ticks.
- **Symptoms.** This diagnosis is not very dependable as many symptoms are non-specific and often mimic other medical conditions. In addition, there are ~7-10% of patients without symptoms (called asymptomatic patients).
- **Laboratory blood tests, such as:**

❖ **ELISA** (Enzyme-Linked Immunosorbent Assay, also called enzyme immunoassay or EIA): This test is most often performed to verify the infection by detecting antibodies produced by the patient's body against spirochete *Borrelia burgdorferi*. This test evaluates the

body's response to infection rather than presence of the bacteria. People with early stages of Lyme disease may not produce enough of specific antibodies for several weeks from infection to reach the level detectable by this diagnostic test

❖ **Western blot** (or Immunoblot): This blood test is usually performed when the ELISA test is positive in order to confirm the diagnosis. Different laboratories use different methods and validation criteria, and a patient can have a positive test result from one lab and a negative test result from another. Western blot test is more reliable when performed at least a month after a tick's bite when the infection has already developed, although none of the current tests are 100% accurate.

❖ **PCR** (Polymerase-Chain Reaction): This test detects bacterial DNA in fluids obtained from a patient's infected joint or spinal cord fluid (CSF). It can detect the bacteria presence, but also gives many false negative results. It is not very effective in diagnosing *Borrelia* infection in the blood or urine, however, it is useful to indicate chronic Lyme disease.

❖ **Cultivation:** This method allows for direct detection of the presence of bacteria in the body. Confirmation of the presence of Lyme bacteria in blood is a "gold standard" test which is done by culturing serum/blood or biopsies taken from a patient. Although this method gives evident proof of infection, it is not routinely performed because Lyme disease bacteria grow very slowly and the results are not available quickly. Also, there are no commercially available culture tests for Lyme disease.

If Lyme disease goes undetected or is treated incorrectly at its early stages, patients can progress to more advanced stages with more severe symptoms appearing weeks, months or perhaps even years after the tick's bite. **Therefore, it is important to correctly diagnose Lyme disease to undergo adequate treatment therapy.**

Treatment of Lyme disease

Current medicine cannot offer an effective cure for Lyme disease. There are no vaccines against Lyme disease available for humans.

A. Conventional treatments are based on antibiotics:

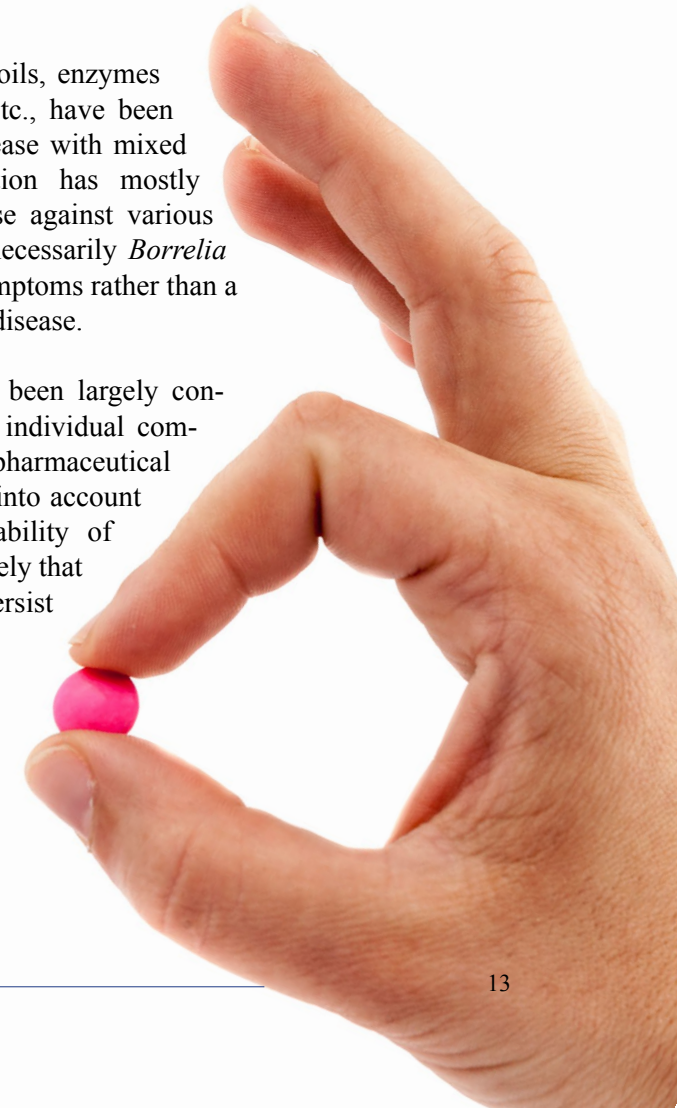
- **Oral antibiotics:** Antibiotics commonly used for oral treatment include β -lactam antibiotics such as doxycycline, amoxicillin, or cefuroxime axetil. These are typically recommended for an early form of Lyme disease and prescribed for 14-21 days of administration. Macrolide antibiotics, such as Azithromycin, Clarithromycin, and Erythromycin are used in patients with counter indications to β -lactams.
- **Intravenous antibiotics:** Antibiotics commonly used for intravenous treatment include ceftriaxone, cefotaxime and penicillin administered for up to 28 days and are typically advised for treatment of late stages of Lyme disease. They are administered longer than oral antibiotics which can cause various side effects, including a lower white blood cell count, mild to severe diarrhea, or colonization or infection with other antibiotic resistant organisms unrelated to Lyme bacteria.

B. Alternative treatments.

Many desperate patients dissatisfied with a lack of efficacy of prescribed medicines are turning to natural approaches which are generally safe without severe side effects that are associated with pharmaceutical approaches.

Several plant extracts, oils, enzymes (proteases), vitamins, etc., have been used against Lyme disease with mixed results. Their application has mostly been based on their use against various types of bacteria, not necessarily *Borrelia sp.*, and on targeting symptoms rather than a causative factor of this disease.

These substances have been largely considered and applied as individual components mimicking the pharmaceutical drug approach. Taking into account an extreme adaptive ability of *Borrelia* it is quite likely that this bacterium can persist these substances.



C. Cellular health and micronutrient synergy.

This approach offers a new tool in designing effective natural approaches against various pathologies. At the Dr. Rath Research Institute we pioneered this concept in developing natural strategies against various chronic conditions, and most recently we also included Lyme disease.

We have tested 37 natural compounds against *Borrelia burgdorferi* sensu stricto (pathogen causing Lyme disease in the USA) and *Borrelia garinii* (pathogen causing Lyme disease in Europe). The initial results have been very encouraging and after testing these natural components against all known morphological forms of *Borrelia* (spirochetes, rounded forms and biofilm), we selected specific phytochemicals (e.g., phytochemicals and vitamins) simultaneously affecting all of these forms and restoring affected homeostasis of the organism. To learn more about their effectiveness and our research visit our website at www.drrathresearch.org.

Based on this research we composed these selected compounds (phytobiologicals/nutriceuticals) derived from plants (i.e., specific phytochemicals and vitamins) in a way to work synergistically to display higher therapeutic efficacy compared to the individual ingredients. To learn more visit our website at www.drrathresearch.org.

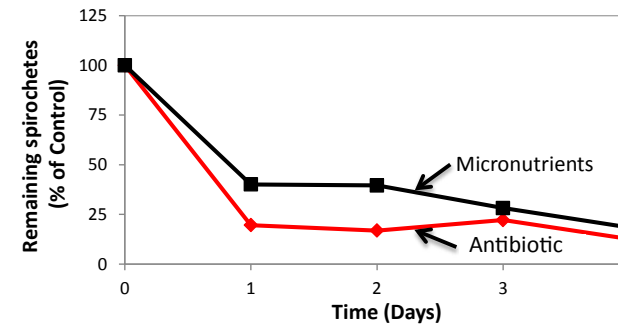


Figure 1. Synergistically composed micronutrients are equally effective to antibiotic doxycycline in inhibiting growth of spirochetes of *Borrelia garinii*.

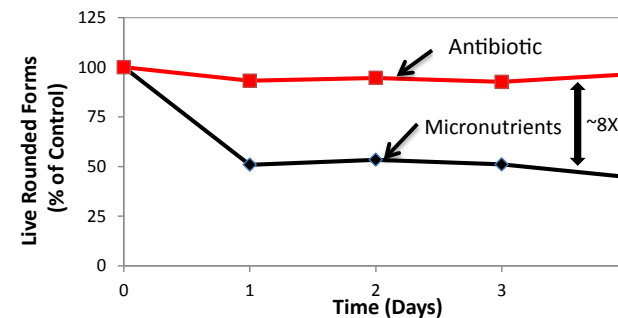


Figure 2. Synergistically acting micronutrients are more effective than antibiotic doxycycline in eliminating rounded forms of *Borrelia garinii*.

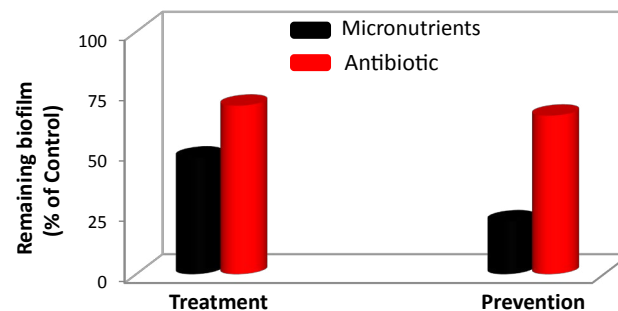
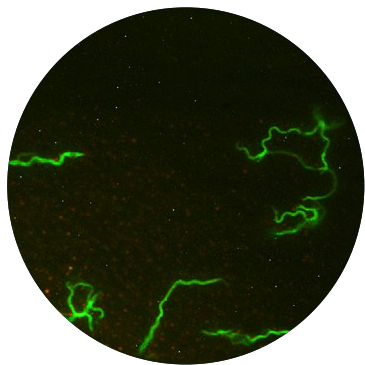


Figure 3. Synergistically acting micronutrients are more effective than antibiotic doxycycline in eliminating existing biofilm of *Borrelia garinii* and preventing its formation.

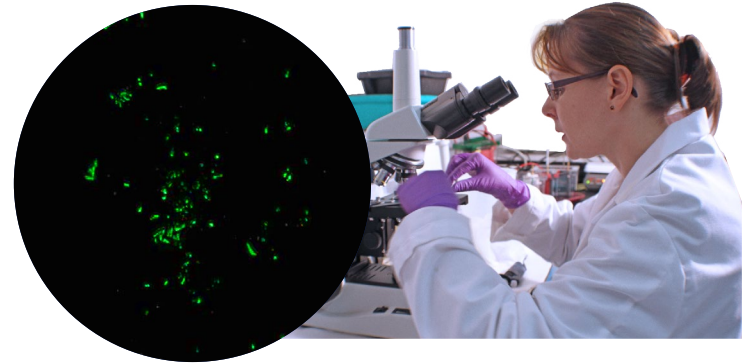
Why it is difficult to eradicate *Borrelia* from the body

Borrelia sp. exists in three morphological forms which allow the bacteria to survive even the most hostile conditions by quickly adapting to the changing environment:

- **Vegetative (active)** bacterium exist as a spiral-shaped form called spirochete, which allows them to be motile and survive viscous conditions, enter into tissue or cells and causing intracellular infection. When these bacteria feel threatened, e.g., by starvation, changes in temperature and/or acidity, exposure to antibiotics, etc., they quickly adapt by transforming into so called, latent forms.

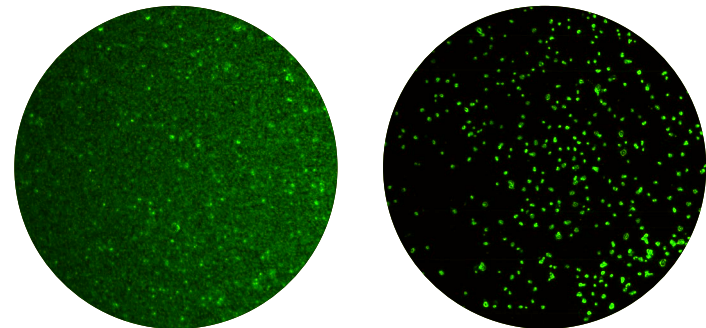


Fluorescent visualization of spirochetes of *Borrelia burgdorferi* cultured from mouse blood.



Visualization of latent rounded forms of *Borrelia burgdorferi* cultured from mouse blood.

- **Latent (atypical) forms** of this bacterium include rounded forms and biofilm, which are structurally and metabolically different from active spirochetes. These forms allow the bacteria to hide and survive any hostile condition for a long time and become active again after these conditions cease. The extreme adaptation of *Borrelia* to environmental changes may be the reason why they can survive for years or even for decades in the host's body.



Fluorescent visualization of established biofilm of *Borrelia garinii* (left) and *Borrelia burgdorferi* (right).

How to be protected against Lyme disease

It is important to take precautions when planning any trip to wooded areas or grasslands and yards where Lyme disease prevails, since these are the preferred dwellings of ticks. Ticks do not handle sunny lawns because they dry out quickly and die. The peak of infection with Lyme disease has been observed in late spring, summer, and in early fall when juvenile ticks are starting to feed. Being bitten by deer ticks during winter months is an exception.

Useful Tips

- Wear long sleeves and tightly laced bright clothes that are tucked into pants and boots when walking throughout wooded or grassy areas or yards.
- After any outdoor trip routinely check yourself, your family and pets and all clothing for ticks.
- Shower and shampoo your hair and wash and tumble dry clothes on high heat for an hour to kill any remaining ticks.
- Any chemical tick repellent should be used with caution as they can cause serious side effects, particularly when used frequently or in high concentrations. They should not be used on infants and children as they are especially at risk for adverse reactions.
 - ❖ DEET (N, N-diethyl-m-toluamide) can be used on clothes, shoes and socks, but can cause irritation in sensitive people if it affects the skin. In addition, chronic exposure to DEET may induce insomnia, cognitive impairments, etc.
 - ❖ Permethrin (0.5% of permethrin) is designed to be used on clothing either alone or in combination with DEET. Permethrin belongs to the family of synthetic chemicals functioning as neurotoxins. It is dangerous especially to fish, honey bees and cats (in cats it can cause seizures and even death). Other repellents registered by the Environmental Protection Agency (EPA) may be found at <http://cfpub.epa.gov/oppref/insect/>.



Useful Information

- ◆ There is no evidence that Lyme disease is transmitted from a person to person, however, Lyme disease developed during pregnancy may lead to infection of the placenta and possible miscarriage.
- ◆ There are reports that spirochetes of Lyme disease can live in blood that is stored for donation, and for that reason donors infected with Lyme disease should not donate blood.
- ◆ Pets can also get Lyme disease and bring infected ticks into the home or garden.
- ◆ There is yet no trustworthy evidence that Lyme disease is an airborne disease. This means that it cannot be transmitted through air. You cannot get it from food, water, or from the bites of mosquitoes, flies, fleas, or lice.



Matthias Rath, M.D.

Dr. Rath is a world-renowned physician and scientist, who is known for his pioneering research in natural and cellular health. He is the founder of the scientific concept of Cellular Medicine - the systematic introduction into clinical medicine of the biochemical knowledge of the role of micronutrients as biocatalysts in a multitude of metabolic reactions at the cellular level.



Aleksandra Niedzwiecki, Ph.D.

Currently the Director of Research at the Dr. Rath Research Institute, Dr. Niedzwiecki is a leading biomedical researcher in the development of nutrient synergy approaches in various aspects of health and disease. Her work in the areas of cardiovascular health and cancer has won her recognition for her research into the biochemical link between disease and nutrients.



Anna Goc, Ph.D.

Dr. Goc is Senior Researcher at Dr Rath Research Institute leading the Microbiological Laboratory where basic, translational, and clinical studies, focused on developing effective and safe therapies for patients suffering from bacterial and fungi infections, are conducted. Dr. Goc has wide-ranging knowledge of molecular biology, biochemistry, and cell biology in fields of microbiology, immunology, cancer, and vascular biology. Results of her research work are published in many reputed scientific journal as well as honored by national and international awards.



Dr. Rath Research Institute

The Dr. Rath Institute in Cellular Medicine is located in the Silicon Valley, in California. The Institute is staffed with experts handpicked from fields of medicine, biochemistry, and nutrition. Here, world-class scientists conduct innovative research utilizing the principle of nutrient synergy, and investigate the role of nutrients in preventing and treating a host of diseases.

Researchers at the Dr. Rath Research Institute are developing new scientific concepts based on Dr. Rath's discoveries in heart disease, cancer, infectious disease, and other diseases. These scientific concepts have been published in various media around the world.

13107

