

the

Lyme Times

VOL. 3 No. 2

FALL 1992

International conference shows progress

Arlington, Virginia- The V International Conference on Lyme Borreliosis was attended by over 800 people from the US and abroad. There were 63 oral presentations and 316 posters from 23 nations. A novel feature for a scientific meeting was tried: concurrent poster discussion groups were held at the end of each day. This allowed further discussion in a group setting of numerous special topics which had been presented during the poster session.

Following are summaries of the abstracts with conclusions of the researchers and some of the questions which came from the audience. These are presented to give the reader some idea of the range and depth of the research which is currently in progress all over the world. Two oral sessions plus a poster session were devoted to Clinical Manifestations, Diagnosis, Treatment, Pathogenesis, Immunology, Biology, Ecology,

See **International** on page 36

Inside:
Lyme Foundation medical advisory board recommends treating tick bites. See pages 10 & 12.

Missouri Lyme disease controversy still simmers

Dr. Ed Masters and CDC haggle over definition of "Lyme-like" disease

Cape Girardeau, Missouri - Family physician Ed Masters of Cape Girardeau, Missouri, is caught between a rock and a hard place. On the one side, he finds overwhelming clinical evidence of Lyme disease in his practice. On the other side, the Division of Vector-Borne Infectious Diseases of the national Centers for Disease Control (CDC) has labelled Missouri a "non-endemic" state. While requiring him to report his Lyme cases, the CDC is also questioning his diagnoses, placing his patients in a sort of diagnostic limbo.

Ed Masters, MD, believes that he is dealing with a spirochetal infection

in southeastern Missouri. He sees characteristic skin lesions (erythema migrans), biopsies these lesions and sends them to labs all over the world where spirochetes are actually visualized. Dr. Masters' patients have also had Bb-positive serological tests from labs all over the country. 46% of 37 erythema migrans cases from Missouri were antibody reactive to *B burgdorferi* by whole cell sonicate ELISA at the CDC. Dr. Masters even uses some of the newer technology and obtains positive PCR tests for Lyme disease from no fewer than seven different research labs. His

See **Missouri** on page 32

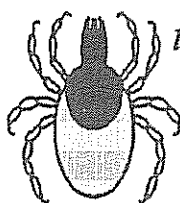
The Lyme Vaccine: hope or hype?

Commentary by Richard Lynch

New York- Recently, the mass media has been reporting on a potential vaccine for Lyme disease. The reports were based on a study conducted by researchers at the Yale University School of Medicine and Howard Hughes Medical Institute, New Haven, Connecticut. An abstract of

this work, #276, was presented at the V International Conference on Lyme Borreliosis. The abstract reports on the protection of laboratory mice from *Borrelia burgdorferi* (Bb) after injection with purified outer surface proteins (Osp) A and B from the

See **Vaccine** on page 27



In this issue...

Mission Statement

The Lyme Disease Resource Center was conceived in 1988 and incorporated in 1990, as a non-profit education and communications center for the public, for Lyme disease victims, for physicians, and other interested people.

The goals of the Lyme Disease Resource Center are:

To educate the public about Lyme disease, including risk factors and prevention (workshops, media, slide show, brochures);

To provide services for Lyme disease victims and their families and friends, including a telephone hotline, physician referral service, support groups, newsletter;

To provide a forum for physicians and health professionals for the exchange of ideas and information about symptoms, diagnosis, and treatment of Lyme disease (workshops, symposia, reference library);

To be a communications center for individuals and groups who are working to help victims of Lyme disease (newsletter, training program);

To create a network of support groups devoted to education and support of the people who must wrestle daily with this puzzling and sometimes devastating disease.

Board of Directors

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Special Articles

- 41 Kristoferitsch, . Neurological Manifestations of Lyme Borreliosis. Reprinted from Infection 19, No. 4 (1991).

Two well known neurologic disorders have been found to be caused by chronic borreliosis. Other neurological phenomena are under investigation.

- 45 Stanek, L. Laboratory and Seroepidemiology of Lyme Borreliosis. Reprinted from Infection 19, No. 4 (1991).

Direct detection methods are time consuming and expensive. Indirect detection methods have varying degrees of accuracy. The diagnosis of CNS borreliosis is the most highly developed method.

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The Lyme Times is a publication of the Lyme Disease Resource Center, a non-profit organization for education of the public and support of Lyme disease victims and their families.

The Lyme Times is interested in publishing your articles. Send to:

Phyllis Mervine, Editor
The Lyme Times
PO Box 1423
Ukiah, CA 95482

If possible, submit articles on single or double-density 3.5-inch floppy disk in either Microsoft Word or ASCII files. We can translate IBM-compatible files in ASCII and MS-DOS. Original articles will be preferred. Articles which have appeared in other Lyme disease publications may not be accepted.

This publication is not intended to replace the professional and individualized attention provided by your own personal physician. Because of the possibility of typographical error or other misinterpretation, physicians and other readers are cautioned to confirm any recommendations with the authors themselves.

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Guest Editorial

It's time to see some change

by James Katzel, MD

"The more things change, the more they stay the same," seems to be an applicable quote in the diagnosis and treatment of Lyme disease. The many new findings regarding transmission, pathology, successes and failures in treatment of the disease, either go unnoticed or are ignored by the mainstream medical community. The family doctors, general internists, and primary care doctors have a very limited handle on the current trends in Lyme disease. Things are moving at a frustratingly slow pace.

Instead of a situation where the proper information trickles down to the doctors on the front lines, we have a situation where there is confusion at the top. Decisions on Lyme disease are being devised and dictated by a different Department of Health in each of our fifty states. Since not all states are recognized as having Lyme disease, this means that at least thirty or forty state departments of health are making varied decisions on behalf of the practitioners in their respective states.

While some states produce logical guidelines, others are absolutely unreasonable and at times, unthoughtful. Are their decisions based on the best and latest scientific evidence, or are they based on political pressures and fears? For whatever reason, the medical practitioners are left with either nothing, or with protocols which vary widely from state to state. What may be a reportable case in New York may not be accepted in California or Florida. What is considered Lyme disease in Oregon may not be in Missouri or New Jersey. To remedy this confusion for

both the practitioners and the public, we need nationwide criteria and guidelines for Lyme disease.

It is hard to change the status quo. Despite the fact that Lyme disease is the nation's number one vector-borne disease, and despite patient victimization from delayed or improper diagnosis and treatment, those on top really don't want to make things change. It's not a conspiracy, or harmful intent, or even a case of not

"Situations will not improve spontaneously; inertia prevents that from happening. We must make it happen."

caring. We have intelligent, well-educated, caring folks in charge of policy making. They just need better guidance.

There are many factors which mitigate against change. Should health insurance companies change? Why? There is no need to pay on a disease that doesn't exist. They benefit from the confusion.

Should state agencies change? It's hard to predict if their budgets or their personnel will hold out. Improving one department means cutting another.

Should the medical profession change? Why? They rarely change until forced to be more responsive to the medical needs of their patients.

Are the insurance companies, the

state agencies, and the medical profession uncaring and incompetent, or are they merely passing the buck? My sense is that they are passing the buck. As I was reminded by a friend, the sign over the desk says: "The flogging will continue until morale improves." We have a long haul with a lot of flogging ahead of us. Situations will not improve spontaneously; inertia prevents that from happening. We must make it happen. To effect any change, we must speak out, be logical, be clear in what we want, and we must be persistent.

If your insurance company will not pay, start a letter-writing campaign. Send complaints to the company president, to your legislators, to the insurance boards and your state insurance commissioner. If you do nothing, nothing will happen. We must force the insurers to pay for testing, treatments, and consultations.

If your local doctors are resistant, become a local educator. Bring in lecturers, work at public education, talk to nurse practitioners and physicians' assistants. Provide consultants for your local doctors and reinstate that desire to learn back into your apathetic family doctor. It can be done.

If your public health officials are pessimistic, lobby your local and state representatives. They respond when they feel you are out there in numbers, in great numbers. You are the people who can change attitudes in public health.

We need to work from the bottom, and we also need to change from the top. In 1993, as we move closer to some form of national health care for all Americans, we need also to move toward a unified, national approach to dealing with Lyme disease. Like so many things in medicine, Lyme disease has been neglected too long.

*James Katzel, M.D.
514 S. School Street
Ukiah, CA 95482
707-482-1097*

Letters to the Editor

In this column we print opinions, therefore we expect differences. We do not recommend any of the doctors or treatments which may be mentioned here by writers. You should discuss any treatment options with your physician. We cannot print defamatory opinions about individuals. Signed letters of general interest may be printed. Please indicate if you do not wish your letter to be printed. Send letters to Editor, the Lyme Times, PO Box 1423, Ukiah, CA 95482.

She wants to help the children with Lyme

Thank you for the information you sent me. It was great, but I must say, I cried and cried when I read these children's stories.

I am 49. Most of my life is over. I have had Lyme for 10 years now. I am blind in one eye. My left knee needs to be replaced and the right hip is deteriorating quite quickly. My MRI shows scattered lesions. I do not know if eventually my brain will be totally demyelinated. I can't think about that. I have been on antibiotics for almost 2 years now.

I am much better than I was. At least I can walk now. If there would be any way I could walk across the U.S. for these children, I would. If we could raise money for them this way, please let me know!

I pray someone will reach out and help those who cannot see a light at the end of the tunnel. God bless you for helping those out there.

Connie Lawrence
Terre Haute, Indiana

Lyme patient would like to have another baby

I am interested in hearing from anyone suffering from late Lyme who has had a baby after such an infection, or any medical person that has knowledge of such a case. I am 38 years old and would like to have a second child but cannot find any information as to the safety of having another child. Will the child be subject to any problems generated by my problems?

I was first infected in January of

'91 during the last three days of breastfeeding my daughter, who is now a healthy 2 1/2 year old. Is it possible she might have ill effects in the future from being breastfed?

My symptoms are loss of memory, poor concentration, and periodic headaches which are accentuated by my menstrual cycle. My medications

"I am 49. Most of my life is over. I have had Lyme for 10 years now."

Connie Lawrence

have been amoxicillin, doxycycline, tetracycline, three months of IV ceftriaxone, and I am presently finishing my second month of minocycline. I would like to hear from anyone who has taken biaxin or suprax.

Is my daughter in danger and would a future child be in jeopardy? Any information will be greatly appreciated.

Sue Coffee
10 Saunders Hollow Rd
Old Lyme CT 06371

Theoretically your daughter could have been infected through your milk, but likely not with the sheer numbers of bacteria she might have received had she been bitten by an infected tick. She is probably in as great danger from the environment as she was from your breastfeeding. If she ever gets Lyme, you will not know if

she got it from you or from an unnoticed tick bite.

Not much is known about Lyme and pregnancy (See the Lyme Times, Vol 3 # 1). It is likely that the greatest danger to the unborn is if the mother is infected for the first time during the pregnancy. There appear to be many normal births to women with Lyme living in endemic areas. Your feelings are understandable, however, would your doctor approve of a pregnancy if your health is impaired and you are on medication?

She is starting a group

Would you kindly send me a copy of the new publication you offered in Lyme Times Spring '92, to people who are interested in starting a support group. I am in the process of starting a support group here in Peekskill. I need any and all help that you can give me.

Helen Morey
Peekskill, New York

The Lyme Connection is specifically for support group leaders. It will come out as regularly as the health of the editor permits, which seems to be the case with all our activities. We also send about 20 Lyme Times to support group leaders to distribute to new members, doctors, clinics, etc. Please write LDRC, Box 9510, Santa Rosa, CA 95405.

They need help

Please send me any free information on Lyme disease, the treatment, diet, vitamin supplements, doctors treating Lyme disease in my area. I have explained my symptoms to a ton of doctors. No one will help me. My husband and I are broke just trying to find out what's wrong with me. I need help!

Kathy Bennett
Chester, Virginia

Help in on the way in the form of

Continued on next page

a complimentary copy of the Lyme Times. That way you get some needed information, resource suggestions, and support contacts. Good luck!

Children finally diagnosed

I would like to compliment you on your Lyme Times issue featuring children with Lyme disease. I only wish that the information in your publication had been available three years ago.

In 1989, my daughter was diagnosed by an infectious disease physician after she had Bell's palsy. She was placed on Rocephin for 4 weeks. She improved, then relapsed when treatment was stopped. Eventually she got married, joined an HMO, and then was denied further treatment for nearly 2 years, because of a test that is still not any good.

In 1990, I was diagnosed with an EM rash. The internist who treated me suggested that I study Lyme disease and fight for my daughter's treatment. While I was studying the disease, I was given a copy of an article on Lyme disease in children, written by Dr. Dorothy Pietrucha. I realized that my young son also had symptoms of Lyme disease.

My son started treatment in 1991. His diagnosis came nearly 2 years after I first suggested that his ongoing and increasing medical problems might be caused by Lyme disease. Because of going undiagnosed so long, this child, a former B student, was devastated by having to repeat fourth grade. Although he is much better, he developed his most painful symptoms during the last months before treatment for Lyme, after being placed on prednisone for a second time. These recurring symptoms have been the hardest to cure.

Often, when I was trying to get help for my daughter, or when I expressed concern that my son might have Lyme disease, almost every doctor quoted the statistics on the ticks that carry Lyme (1-2% in

California), as though this was supposed to mean that a person can't get the disease. I had one doctor tell me that I needed to rethink my thinking. Another told me, tactfully, that I was on a witch hunt, looking for a doctor that would diagnose Lyme disease, and this was not good for my son. The last doctor told me Lyme was a garbage disease (everyone that has a piece of garbage is being treated for Lyme) and the hoopla over it disgusted him. This was unfortunate, because he was examining someone who had Lyme disease and his attitude kept him from seeing it.

"He was examining someone who had Lyme disease and his attitude kept him from seeing it."

Susie Merrill

My son was diagnosed by a rheumatologist, placed on Rocephin for six weeks by an infectious disease physician, and then placed on minocycline by a family practice physician. While I was watching this last doctor examine my son, I suddenly realized that all three of these doctors had done the same things during his examination, and had asked the same questions. The other doctors didn't do these things, nor ask these questions, and so they couldn't diagnose Lyme disease. They didn't know what the symptoms were, and they didn't know what to look for.

Five months later, my six-year old nephew, who is also a neighbor, tested positive for Lyme. Despite a history of tick bites, symptoms of Lyme disease (including swollen knees), and positive tests, his doctor under-treated and did not report him. This was yet another doctor who

believed surely these were false positive tests; it was impossible that a fourth member of the same family could get Lyme disease. My nephew's symptoms went away after he was treated by a doctor who had experience with Lyme disease.

According to a doctor with the CDC, there are many opportunities for physician self-education on Lyme disease. During the past 2 years, there have been approximately 40 articles on the disease, published per month in medical journals. I have also been told that the medical community is traditionally conservative, and that we cannot force doctors to learn about anything that they don't want to learn about. Frankly, I resent that I had to study the disease to get help for my children. This was not my job.

Until they develop a test for the doctor who cannot practice medicine without one, the best doctor to rule out Lyme disease, especially in children, is the doctor who has experience with it.

The doctor who diagnosed by son said, "The risk of treating your son for Lyme, if this should turn out to be the wrong disease, does not compare to the potential disaster of failing to treat Lyme disease at all." It was a disaster.

**Susie Merrill
Sonoma, California**

Mom has Lyme

I'm writing you this letter to ask you for information on Lyme.

My mom is 49 years old and has just been diagnosed as 3rd stage of Lyme.

Right now none of us really understands this and we can't afford to purchase any material, but we do want to know all we can about this disease that has infected my mom.

**Kelly Ward
Cody, Ohio**

Lyme disease has only been

See Letters on next page

Letters, cont.

known about 10 years, so there is a lot we don't know yet. There are still many different tests and treatments, different doctors preferring different ones. It can be confusing for the patient. The sickness of one member of a family can be stressful on the family, even without all questions Lyme patients have to live with. Many people find great support in a local support group, and from tying into the network which actually exists all across the country. Patients can find the empathy they need from other patients if their families are kind of burned out from dealing with it. They can also find out what works for other people, and just get support in general.

She has suicidal thoughts

Hello. My name is Solitaire. I am concerned about children and young adults coping with Lyme disease and the stresses of growing up. I am 16 and have had Lyme for 12 1/2 years. I've been on treatment for 2 1/2 years. During this time I've thought of running away or committing suicide. If other have, please write or call:

Solitaire Metheny
11224 Hwy A-12
Montague CA 96064
916-459-5571

Lyme spirochetes invade the brain, and according to research by Dr. Brian Fallon, there is more depression in Lyme than in other chronic illnesses. Treating the Lyme disease can help, and there are medications specifically for depression as well.

If you do get suicidal at times, pay close attention to your feelings, because they are both unhealthy and dangerous and need to be dealt with. Get into the habit of making the effort to reach out for help, and you will be more likely to do it at a crucial time. People who do, feel much better. It is

important to line up a dependable person or hotline to call while you are feeling fine. Make a list of numbers to call: family, friends, or 24-hour Crisis phone numbers, if your community has one. Do not wallow in depression or give yourself time to carry out a suicidal plan. If you hide from it, you won't solve it. The first line of defense against suicide is to reach out for help.

His disease always comes back after treatment

I have had Lyme disease for many years and have tried many different antibiotics for many different durations, but the disease always comes back within weeks after treatment.

Do you publish a newsletter or updates on current medical thinking on the treatment of the disease? If so, please advise how I would get your published information.

Jack Odell
New Jersey

Research has shown that the disease organisms can survive standard antibiotic treatments. Many people experience improvement with

additional treatment.

The Lyme Times can help you to keep abreast of current medical thinking, as well as keep you in touch with support groups and other individuals who are interested in Lyme disease. See the subscription coupon inside the back page.

Write to magazines about inaccurate stories

I just finished writing a letter to Glamour magazine. In its August '92 issue there was an article about Lyme under the title "The truth behind health-scare stories." The article was filled with wrong information, for example: the author of the article said that Lyme had only been reported in twenty states! Hopefully they'll print my letter.

Kelly Pertak
New York

We hope they will, too, Kelly, and your effort is important in undoing the miseducation of the public by ignorant writers. Please send a copy of any article you see, plus the address of the publication, and I will send an informative retort to the editor on LDRC stationery.

Support CDC pregnancy registry

From Lyme Disease Surveillance Summary, Vol 2, No. 2, March 29, 1991

Gestational Lyme-disease and its effect on the fetus continues to be controversial. Few scientific studies have been reported and many basic questions, including magnitude of risk, remain to be answered. CDC plans to contract for a new epidemiologic study of this issue in the current fiscal year. In addition, CDC is encouraging clinicians to register their Lyme disease patients who are pregnant.

The National Lyme Disease in Pregnancy registry was established in 1985 (MMWR 1985;34:376-384), but, according to directory coordina-

tor Dr. Roy Campbell, has not seen much activity. The registry is anonymous. The essential requirements for registration are a brief clinical history and information on the resulting birth outcome.

Pregnant patients who become aware of the Registry should request their physicians to register them. Culture media and shipping costs will be supplied by CDC for the collection of clinical samples related to adverse birth outcomes. For more information, or to register patients, please contact Dr. Campbell at 303-221-6453.

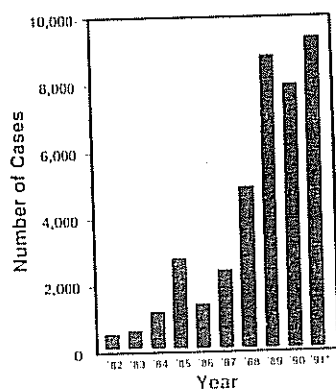
Beginners' Pages

New government leaflet on Lyme disease gives recent information

Reprinted from a public information guide from the Centers for Disease Control, National Center for Infectious Diseases, Division of Vector-Borne Infectious Diseases, US Department of Health and Human Services

Lyme disease

Lyme disease was recognized in the United States in 1975, after a mysterious outbreak of arthritis near Lyme, Connecticut. Since then, reports of Lyme disease have increased dramatically, and the disease has become an important



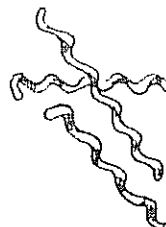
*1991 figures are preliminary.

public health problem in some areas of the United States.

How the disease is spread

Lyme disease is spread by the bite of ticks of the genus *Ixodes* that are infected with *Borrelia burgdorferi*. The deer tick, *Ixodes dammini*, which normally feeds on the white-footed mouse, the white-tailed deer, other mammals, and birds, is responsible for transmitting Lyme disease bacteria to humans in the northeastern and north-central United States. (In these regions, this tick is also responsible for the spreading of babesiosis, a disease caused by a malaria-like parasite.) On the Pacific coast, the bacteria are transmitted by the western black-legged tick, *Ixodes*

Lyme disease is an infection caused by *Borrelia burgdorferi*, a member of the family of spirochetes, or corkscrew-shaped bacteria.



pacificus, and in the southeastern states possibly by the black-legged tick, *Ixodes scapularis*.

Ixodes ticks are much smaller than common dog and cattle ticks. In their larval and nymphal stages, they are no bigger than a pinhead. Adult ticks are slightly larger.

Ticks can attach to any part of the human body but often attach to the more hidden and hairy areas such as the groin, armpits, and scalp.

Research in the eastern United States has indicated that, for the most part, ticks transmit Lyme disease to humans during the nymph stage, probably because nymphs are more likely to feed on a person and are rarely noticed because of their small size (less than 2 mm). Thus, the nymphs typically have ample time to feed and transmit the infection (ticks are most likely to transmit infection after approximately 2 or more days of feeding).

Tick larvae (seed ticks) are smaller than the nymphs, but they rarely carry the infection at the time of feeding and are probably not

important in the transmission of Lyme disease to humans.

Adult ticks can transmit the disease, but since they are larger and more likely to be removed from a person's body within a few hours, they are less likely than the nymphs to have sufficient time to transmit the infection. Moreover, adult *Ixodes* ticks are most active during the cooler months of the year, when outdoor activity is limited.

Ticks search for host animals from the tips of grasses and shrubs (not from trees) and transfer to animals or persons that brush against vegetation. Ticks only crawl; they do not fly or jump. Ticks found on the scalp usually have crawled there from lower parts of the body. Ticks feed on blood by inserting their mouth parts (not their whole bodies) into the skin of a host animal. They are slow feeders: a complete blood meal can take several days. As they feed, their bodies slowly enlarge.

Although in theory Lyme disease could spread through blood transfusions or other contact with infected blood or urine, no such transmission has been documented. There is no evidence that a person can get Lyme disease from the air, food or water, from sexual contact, or directly from wild or domestic animals. There is no convincing evidence that Lyme disease can be transmitted by insects such as mosquitoes, flies, or fleas.

Campers, hikers, outdoor workers, and others who frequent wooded, brushy, and grassy places are commonly exposed to ticks, and this may be important in the transmission of Lyme disease in some areas. Because new homes are often built in wooded areas, transmission of Lyme disease near homes has become an important problem in some areas of the United States. The risk of exposure to ticks is greatest in the woods and garden fringe areas of properties, but ticks may also be carried by animals into lawns and gardens.

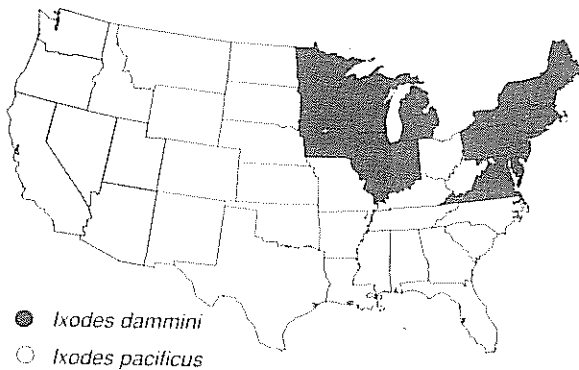
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Lyme, cont. from previous page

Geographic distribution

Lyme disease has a wide distribution in northern temperate regions of the world. In the United States the highest incidence occurs in the

- Northeast, from Massachusetts to Maryland
- North-central states, especially Wisconsin and Minnesota
- West Coast, particularly northern California



For Lyme disease to exist in an area, at least three closely interrelated elements must be present in nature: Lyme disease bacteria, ticks that can transmit them, and mammals (such as mice and deer) to provide food for the ticks in their various life stages. Ticks that transmit Lyme disease are found in regions with temperatures of 15° to 95°F, with only short period spent at either extreme, and a constant relative humidity of close to 100% at ground level.

Life cycle of Lyme disease ticks

Knowing the complex life cycle of the ticks that transmit Lyme disease is important in understanding the risk of acquiring the disease and in finding ways to prevent it.

The life cycle of these ticks requires 2 years to complete. Adult ticks feed and mate on large animals, especially deer, in the fall and early spring. Female ticks then drop off these animals to lay eggs on the

ground. By summer, eggs hatch into larvae.

Larvae feed on mice and other small mammals and birds in the summer and early fall and then are inactive until the next spring when they molt into nymphs.

Nymphs feed on small rodents and other small mammals and birds in the late spring and summer and molt into adults in the fall, completing the 2-year life cycle.

Larvae and nymphs typically become infected with Lyme disease bacteria when they feed on infected small animals, particularly the white-footed mouse. The bacteria remain in the tick as it changes from larva to nymph to adult. Infected nymphs and

adult ticks then bite and transmit Lyme disease bacteria to other small rodents, other animals, and humans, all in the course of their normal feeding behavior.

Lyme disease in domestic animals

Domestic animals may become infected with Lyme disease bacteria and some of these (dogs, for instance) may develop arthritis. Domestic animals can carry infected ticks into areas where humans live, but whether pet owners are more likely than others to get Lyme disease is unknown.

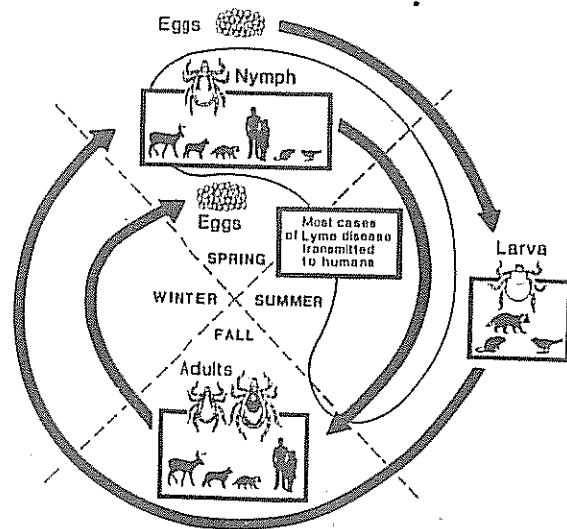
Symptoms and signs of Lyme disease

Early Lyme Disease: The early stage of Lyme disease is usually marked by one or more of the following symptoms and signs:

- fatigue
- chills and fever
- headache
- muscle and joint pain
- swollen lymph nodes
- a characteristic skin rash, called *erythema migrans*

Erythema migrans is a red circular patch that appears usually 3 days to 1

Life cycle of Lyme disease ticks



Continued on next page

month after the bite of an infected tick at the site of the bite. The patch then expands, often to a large size. Sometimes many patches appear, varying in shape, depending on their location. Common sites are the thigh, groin, trunk, and the armpits. The center of the rash may clear as it enlarges, resulting in a "bull's-eye" appearance. The rash may be warm, but it usually is not painful. Not all rashes that occur at the site of a tick bite are due to Lyme disease, however. For example, an allergic reaction to tick saliva often occurs at the site of a tick bite. The resulting rash can be confused with the rash of Lyme disease. Allergic reactions to tick saliva usually occur within hours to a few days after the tick bite, usually do not expand, and disappear within a few days.

Late Lyme Disease: Some symptoms and signs of Lyme disease may not appear until weeks, months, or years after a tick bite:

- Arthritis is most likely to appear as brief bouts of pain and swelling, usually in one or more large joints, especially the knees.
- Nervous system abnormalities can include numbness, pain, Bell's palsy (paralysis of the facial muscles, usually on one side), and meningitis (fever, stiff neck, and severe headache).

- Less frequently, irregularities of the heart rhythm occur.

- In some persons the rash never forms; in some the first and only sign of Lyme disease is arthritis, and in others, nervous system problems are the only evidence of Lyme disease.

Lyme disease and pregnancy

In rare cases, Lyme disease acquired during pregnancy may lead to stillbirth, but adverse effects to the fetus have not been conclusively documented. The Centers for Disease Control (CDC) maintains a registry of pregnant women with Lyme disease to advance the understanding of the effects of Lyme disease on the

developing fetus.

Diagnosis

Lyme disease is often difficult to diagnose because its symptoms and signs mimic those of many other diseases. The fever, muscle aches, and fatigue of Lyme disease can easily be mistaken for viral infections, such as influenza or infectious mononucleosis. Joint pain can be mistaken for other types of arthritis, such as rheumatoid arthritis, and neurologic signs can mimic those caused by other conditions, such as multiple sclerosis. At the same time, other types of arthritis or neurologic diseases can be misdiagnosed as Lyme disease.

Diagnosis of Lyme disease should take into account:

- History of possible exposure to ticks, especially in areas where Lyme disease is known to occur.
- Symptoms and signs.
- The results of blood tests used to determine whether the patient has antibodies to Lyme disease bacteria.

These tests are most useful in later stages of illness, but even then they may give inaccurate results. Laboratory tests for Lyme disease have not yet been standardized nationally.

Treatment and prognosis

Lyme disease is treated with antibiotics under the supervision of a physician. Several antibiotics are effective. Antibiotics usually are given by mouth but may be given intravenously in more severe cases. Patients treated in the early stages with antibiotics usually recover rapidly and completely. Most patients who are treated in later stages of the disease also respond well to antibiotics, and full recovery is the rule. In a few patients who are treated for Lyme disease, symptoms of persisting infection may continue or recur, making additional antibiotic treatment necessary. Varying degrees of permanent damage to joints or the nervous system can develop in patients with late chronic Lyme

disease. Typically these are patients in whom Lyme disease was unrecognized in the early stages and for whom the initial treatment was unsuccessful. Rare deaths from Lyme disease have been reported.

Prevention

Tick Control: Removing leaves and clearing brush and tall grass around houses and at the edges of gardens may reduce the numbers of ticks that transmit Lyme disease. This is particularly important in the eastern United States, where most transmission of Lyme disease is thought to occur near the home.

Applying acaricides (chemicals that are toxic to ticks) to gardens, lawns, and the edge of woodlands near homes is being done in some areas, but questions remain regarding its effectiveness and environmental safety. Wide-area acaricide application should be supervised by a licensed professional pest control expert.

A relationship has been observed between the abundance of deer and the abundance of deer ticks in the eastern United States.

Reducing and managing deer populations in geographic areas where Lyme disease occurs may reduce tick abundance. Removing plants that attract deer and constructing physical barriers may help discourage deer from coming near homes.

Personal protection from tick bites

The chances of being bitten by a tick can be decreased with a few precautions.

- Avoid tick-infested areas, especially in May, June, and July (many local health departments and part or extension services have information on the local distribution of ticks).

- Wear light-colored clothing so that ticks can be spotted more easily.

- Tuck pant legs into socks or

See Lyme, on page 10

Lyme, cont.

boots and shirt into pants.

- Tape the area where pants and socks meet so that ticks cannot crawl under clothing.
- Spray insect repellent containing DEET on clothes and on exposed skin other than the face, or treat clothes (especially pants, socks, and shoes) with permethrin, which kills ticks on contact.
- Wear a hat and a long-sleeved shirt for added protection.

- Walk in the center of trails to avoid overhanging grass and brush.

After being outdoors remove clothing and wash and dry it at a high temperature; inspect body carefully and remove attached ticks with tweezers, grasping the tick as close to the skin surface as possible and pulling straight back with a slow, steady force; avoid crushing the tick's body. In some areas, ticks (saved in a sealed container) can be submitted to the local health department for identification.

Preventive Antibiotic Treatment: Antibiotic treatment to prevent Lyme disease after a known tick bite may not be warranted. Physicians must determine whether the advantages of using antibiotics outweigh the disadvantages in any particular instance. If antibiotics are not used, physicians should alert patients to the symptoms of early Lyme disease and advise them to return for reevaluation if symptoms occur.

Lyme disease research

Research continues to discover

- Where ticks are most likely to be and how best to protect against them.
- Which chemicals and other approaches are best for controlling ticks in each kind of habitat.
- Better diagnostic tests.
- Improved antibiotic treatment.
- An effective vaccine.
- Effects of mother's infection on

the developing fetus.

- How Lyme disease bacteria cause chronic infections of the joints and nervous system and how to prevent these complications.

For further information, contact the CDC Voice Information System at (404) 332-4555, your physician, or your local health department.

To obtain copies of the leaflet containing this information, with color illustrations, contact your local State Health Department. If your state does not have any, or if you wish to obtain a large quantity, contact Karen Peterson, CDC, PO Box 2087, Fort Collins, Colorado 80522, Tel. 303-221-6453.

Statistics show Lyme cases still increasing

The table on the following page are official CDC statistics on the incidence of Lyme disease on a state-by-state basis. 1991 figures are still preliminary. In 1992, a total of 4,999 cases have been reported through Sept. 3, 80% of this total from the mid-Atlantic and New England regions. Human cases of Lyme disease have been reported from every state except Montana. Infected ticks have not necessarily been found in all the states from which cases have been reported.

Lyme Foundation doctors recommend prophylactic treatment for tick bites

The Medical Advisory Committee of the Lyme Borreliosis Foundation now recommends antibiotic prophylactic treatment upon a known tick bite. Treatment is indicated for:

A. People at higher health risk bitten by an unknown type of tick or tick capable of transmitting *Borrelia burgdorferi*, including pregnant women, babies and young children, people with serious health problems.

B. Persons bitten in an area endemic for Lyme Borreliosis by an unidentified tick or tick capable of transmitting *B. burgdorferi*.

C. Those bitten by a tick capable of transmitting *B. burgdorferi*, where the duration of the tick bite is greater than four hours and/or the tick was improperly removed by being squeezed between the fingers, covered with petroleum jelly, or mangled.

D. A patient who, when bitten by a known tick, clearly requests oral prophylaxis and understands the risks. This is a case-by-case decision.

The physician cannot rely on a

laboratory test or clinical finding to definitely rule in or rule out Lyme Borreliosis infection, but must use clinical judgement as to whether to use antibiotic prophylaxis for Lyme Borreliosis. Since an established infection by *B. burgdorferi* can have medical consequences, since the likelihood of harm arising from prophylactically applied spirochetal antibiotics is low, and since treatment is inexpensive and painless, it follows that the risk benefit ratio favors tick bite prophylaxis.

It is the Medical Advisory Committee's recommendation that antibiotic prophylactic treatment for tick bite in many circumstances is not only justified but warranted. The ultimate decision for treatment on tick bite should be determined jointly between the physician and patient.

*Andrew D. McBride, M.D., M.P.H.
Director of Health and Medical Advisor
Stamford, Connecticut
Chair, LBF Medical Advisory Committee*

STATE	REG	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	TOTAL	1990 pop	inc_91
ALABAMA	ESC	0	0	0	0	1	1	1	25	33	18	79	4165000	0.432
ALASKA	PAC	0	0	0	0	0	0	0	0	0	1	1	525000	0.190
ARIZONA	MT	0	0	0	0	0	0	0	0	0	1	1	3666000	0.027
ARKANSAS	WSC	0	1	4	0	0	0	16	10	22	29	82	2421000	1.197
CALIFORNIA	PAC	0	11	24	70	107	182	200	250	345	323	1512	29287000	1.102
COLORADO	MT	0	0	0	0	0	0	2	1	0	1	4	3331000	0.030
CONNECTICUT	NE	135	73	483	699	0	215	362	774	704	1221	4666	3266000	37.38
DELAWARE	SA	1	4	1	0	0	6	4	25	54	72	167	682000	10.55
DC	SA	0	0	0	0	0	0	0	0	5	5	10	603000	0.829
FLORIDA	SA	0	0	0	2	0	1	0	6	7	23	39	12942000	0.177
GEORGIA	SA	0	0	1	1	2	4	53	715	161	31	968	6598000	0.469
HAWAII	PAC	0	0	0	0	0	0	0	1	2	0	3	1133000	0
IDAHO	MT	0	0	0	0	0	0	1	42	1	2	46	1013000	0.197
ILLINOIS	ENC	0	0	0	2	0	6	5	79	30	25	147	11682000	0.214
INDIANA	ENC	0	0	1	0	1	3	0	8	15	13	41	5617000	0.231
IOWA	WNC	0	0	0	1	1	4	15	27	16	22	86	2814000	0.781
KANSAS	WNC	0	0	0	0	0	1	0	15	14	22	52	2522000	0.872
KENTUCKY	ESC	0	0	0	0	0	3	5	21	18	43	90	3745000	1.148
LOUISIANA	WSC	0	0	0	0	0	0	2	2	3	6	13	4368000	0.137
MAINE	NE	0	0	0	1	4	0	1	3	9	9	27	1236000	0.728
MARYLAND	SA	7	4	11	20	15	27	66	138	238	274	800	4774000	5.739
MASSACHUSETTS	NE	15	13	33	69	163	95	80	129	117	290	1004	5921000	4.897
MICHIGAN	ENC	0	1	0	1	0	4	21	165	134	110	436	9292000	1.183
MINNESOTA	WNC	22	55	86	64	94	94	67	92	70	85	729	4377000	1.941
MISSISSIPPI	ESC	0	0	0	0	0	0	6	7	7	7	20	2649000	
MISSOURI	WNC	0	0	2	1	1	4	5	108	205	193	519	5207000	3.706
MONTANA	MT	0	0	0	0	0	0	0	0	0	0	0	797000	0
NEBRASKA	WNC	0	0	0	0	0	0	0	0	0	0	20	1604000	1.246
NEVADA	MT	0	0	0	0	0	0	0	7	2	7	16	1130000	0.619
NEW HAMPSHIRE	NE	0	1	0	0	7	0	8	3	4	35	58	1140000	3.070
NEW JERSEY	MA	57	70	155	175	219	257	500	680	1074	852	4039	7808000	10.91
NEW MEXICO	MT	0	0	0	0	0	0	0	5	0	0	5	1539000	0
NEW YORK	MA	170	267	466	1235	482	877	2637	3224	3244	3357	15959	17868000	18.78
NORTH CAROLINA	SA	0	1	16	14	6	2	19	61	87	81	287	6688000	1.211
NORTH DAKOTA	WNC	0	0	0	0	0	0	1	12	3	2	18	658000	0.303
OHIO	ENC	0	0	3	2	2	14	39	99	36	173	368	10907000	1.586
OKLAHOMA	WSC	0	0	0	0	2	2	4	16	13	31	68	3190000	0.971
OREGON	PAC	0	1	10	5	10	19	4	5	11	5	70	2822000	0.177
PENNSYLVANIA	MA	2	0	5	29	31	65	306	626	553	1022	2639	12043000	8.486
RHODE ISLAND	NE	29	20	20	41	57	74	121	415	101	177	1055	998000	17.73
SOUTH CAROLINA	SA	0	0	1	3	3	3	10	18	7	10	55	3560000	0.280
SOUTH DAKOTA	WNC	0	0	0	0	0	2	2	3	2	1	10	716000	0.139
TENNESSEE	ESC	0	1	1	4	1	1	13	30	28	45	124	5009000	0.898
TEXAS	WSC	0	1	18	172	8	33	18	82	44	15	391	17053000	0.087
UTAH	MT	1	1	0	0	1	0	2	3	1	3	12	1729000	0.173
VERMONT	NE	0	0	0	0	0	0	1	1	11	7	20	571000	1.225
VIRGINIA	SA	0	0	1	2	7	27	25	54	129	202	447	6229000	3.242
WASHINGTON	PAC	0	0	0	0	0	8	9	33	30	3	83	4797000	0.062
WEST VIRGINIA	SA	0	0	0	0	0	0	5	15	11	44	75	1842000	2.388
WISCONSIN	ENC	58	69	176	135	162	358	246	762	337	424	2727	4892000	8.667
WYOMING	MT	0	0	0	0	0	0	0	6	5	9	20	468000	1.923
U.S. TOTAL		497	594	1518	2748	1387	2392	4882	8803	7943	9344	40108	249894000	3.739
NE SUBTOTAL	NE	179	107	536	810	231	384	573	1325	946	1739	6830	13132000	13.24
MA SUBTOTAL	MA	229	337	626	1439	732	1199	3443	4530	4871	5231	22637	37719000	13.86
ENC SUBTOTAL	ENC	58	70	180	140	165	385	311	1113	552	745	3719	42390000	1.757
WNC SUBTOTAL	WNC	22	55	88	66	96	105	90	257	310	345	1434	17898000	1.927
PAC SUBTOTAL	PAC	0	12	34	75	117	209	213	289	388	332	1669	38564000	0.860
SA SUBTOTAL	SA	8	9	31	42	33	70	182	1032	699	742	2848	43918000	1.689
WSC SUBTOTAL	WSC	0	2	22	172	10	35	40	110	82	81	554	27032000	0.299
ESC SUBTOTAL	ESC	0	1	1	4	2	5	25	83	86	106	313	15568000	0.680
MT SUBTOTAL	MT	1	1	0	0	1	0	5	64	9	23	100	13673000	0.168

Case totals as reported to CDC by state health departments

CDC/NCID/DVBD/BZB

1. Total reported cases, 1982-1991 (Preliminary data for 1991)

2. Incidence per 100,000 population, 1991

Docs make strong case for treating tick bites

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Recent news reports have led to much confusion and concern over the issue of antibiotic treatment upon tick bite in order to prevent Lyme borreliosis. Some researchers and clinicians have publicly advocated against the use of antibiotics for tick bites and have advised waiting for either clinical symptoms or laboratory serologic confirmation to occur. Parents removing engorged infected ticks from their infants and young children are being told to wait for the establishment of disease before antibiotic therapy is being initiated. However, scientific evidence, current clinical results, and emerging public health considerations seriously challenge this conclusion. Our recommendations are based on the following:

1. There is no complete data on the length of time it takes for a tick to transmit *Borrelia burgdorferi* (the causative agent) to the human host. Any such study must employ a perfected direct detection test for humans who knowingly volunteer for the study, receive full disclosure of potential outcome, and sign informed consent forms. Also, the study must monitor the patient for several years for the full spectrum of disease. Only then, would researchers be able to determine who is infected and who is bacteria free. Until such time, experimentation, including treatment on tick-bite studies, should not be done on humans. It is imperative to make sure that we do not repeat the mistakes of the Tuskegee Study. In this study, researchers let patients with a very similar spirochetal disease go untreated (no informed consent) so researchers could fully document the disease course.

Reliance upon tick analysis is

unrealistic since too few facilities have the ability to conduct these tests. Also, every researcher conducting a tick test will admit to design and logistical flaws that could result in falsely missing information. The often cited work of Drs. Piesman, Mather, et. al. only established a relationship of duration of attachment and relative risk of disease transmis-

“Experimentation, including treatment on tick-bite studies, should not be done on humans....”

sion. It did not establish minimum length of time to transmit disease.

2. Reliance on definitive early clinical symptoms is extremely difficult (e.g., children - who are less likely to develop a rash) and in some cases impossible. The skin rash is often overlooked or unapparent, particularly in darker skinned people. Early Lyme borreliosis symptoms can be missed or mistakenly attributed to other causes, including muscle aches and pains, headache, low grade fever, or fatigue.

3. The current antibody test, the serum test most often used by the clinician, relied upon to indicate the presence or absence of infection is often inaccurate. The test can be negative in the presence of infection and the results can take weeks to be reported to the physician. This test, often negative at the time of initial infection, may take as long as 4-6 weeks after the bite to become

reactive. An increasing number of patients with Lyme disease have immune systems that never “sero-convert.” A negative serum test after antibiotics is common and cannot be interpreted as the patient not having had Lyme disease. Unfortunately, seronegative patients with disease are almost always excluded from many studies.

4. The current state of research and practice has not developed accurate and complete data on the incidence, prevalence, or spectrum of disease for Lyme borreliosis. The Centers for Disease Control new case surveillance definition is artificially narrow and excludes many cases of well recognized presentations of actual disease. Reporting of Lyme borreliosis, which is not mandatory in every state, is limited to those cases complying with the new criteria and has been notoriously low. Many physicians openly admit to never having reported known cases. It is now recognized that many cases are missed due to falsely negative antibody tests. The true prevalence, incidence, and spectrum of Lyme borreliosis is significantly greater than presently reported or studied.

5. The bacteria causing Lyme borreliosis spread rapidly throughout the body in a few days via the blood stream, at which time the microbe is most reachable and susceptible to antibiotics. It is during this time that the bacterium is disseminated to various organs of the body. Recent scientific reports have shown that *B. burgdorferi* can disseminate to the central nervous system within days after the tick bite - much earlier than previously thought. **It is within these several days that the physician has the highest chance of totally preventing disease.**

6. Once the bacteria establishes itself in the body tissue, Lyme borreliosis can progress and affect any organ. The bacteria can disseminate to areas where many or all

Continued on next page

antibiotics cannot penetrate; e.g., inside cells or sequestered. Some people have chronic disease not curable by current antibiotic therapy.

7. When the organism is present in the brain and nervous system, the blood-brain barrier presents a serious obstacle to antibiotic therapy. As time passes, *B. burgdorferi* has a chance to

11. The antibiotics typically used for Lyme borreliosis are safe and are used prophylactically for many other diseases. Therefore, the most reasonable conclusion is to treat adequately and immediately upon known tick bite.

Statement on Tick Bite Treatment to Clarify Issue

“The most reasonable conclusion is to treat adequately and immediately upon known tick bite.”

establish itself in the body, making antibiotic treatment less effective (or ineffective) and a chronic infection could result.

8. Scientific and medical literature has established, and clinical experience suggests, that once the bacteria has disseminated, it can be harbored in human tissues (parenchyma) in a latent form for many years. Once established in the tissues, the bacteria is very slow to reproduce, making it less susceptible to antibiotics.

9. Certain aspects of Lyme borreliosis disease may be due to the alteration of the body's immune system and not just the infection alone, thus causing a diagnostic dilemma. At this time, when scientific understanding of this bacterium is still in its infancy, the physician does not have the technology to resolve this diagnostic dilemma with great certainty - thus putting the patient and physician at risk.

10. An increasing number of scientific and medical reports indicate that some cases, approximately 1/3 of the originally studied and adequately treated Lyme, Connecticut pediatric group, have suffered chronic illness from what appears to be caused by persistent *Borrelia burgdorferi* presence. For this group of chronic sufferers, the appropriate treatment is not yet clear.

This statement on antibiotic prophylaxis for known tick bites is being made because of the confusion resulting from an announcement regarding unpublished observations that the treatment of tick bites may not be warranted.

It is important to know these observations (studies) advocating non-treatment have several shortfalls:

The study was released directly to the media bypassing scientific peer review. Therefore, physicians were unable to fully review the criteria and methods in order to evaluate if the conclusion was justified or applicable to their own area's practice. One of the study collaborators did not agree with the conclusion either. The study involved an area of extremely high public awareness where the individuals partake in prevention measures - including early and proper tick removal. All studied tick bites had the ticks removed within several hours of attachment. This awareness and early removal is good, but according to researchers involved in the study, causes an inherent bias in favor of significantly reduced disease.

The stated definition of disease was extremely narrow. The first criterion was the appearance of a rash. This rash is known to develop in less than 50 percent of the light skinned population and may exclude

people of color. The second criterion stated was the development of a positive blood test, coupled with selected symptoms. Both the antibody tests and the symptoms mentioned were equally restrictive.

The incidence of disease in the non-treated group could have been reduced to zero if they had received prophylactic treatment. The ticks were assayed using the direct detection test (PCR) for infection while the humans were assayed using the less reliable antibody test. The antibiotically treated group would not be expected to develop a positive blood test. Therefore, by the authors' stated definition, they could not have disease.

The real conclusion should be that heightened education about early tick removal can decrease the chance of becoming infected. The incidence of disease in the non-treated group could have been reduced to zero if they had received prophylactic treatment.

Lyme Foundation president named Woman of the Year

Karen Forschner, founder of the Lyme Disease Foundation (formerly Lyme Borreliosis Foundation) of Tolland, Connecticut, was named Woman of the Year by Family Circle Magazine. Forschner and her husband, Tom Forschner, started the Lyme Disease Foundation in 1988 after realizing that their son, Jamie, who died in 1991 at the age of 5, had been infected with the Lyme spirochete before birth. Lyme disease can pass from mother to child *in utero*.

The Lyme Disease Foundation conducts educational efforts and supports medical research. Ms. Forschner has been featured in popular magazines and on TV shows. She hopes to eradicate the disease and educate the American public about prevention and treatment.

Guidelines for diagnosis and treatment

by Joseph J. Burrascano, Jr., MD

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Although a similar entity was reported in the United States in 1970, Lyme disease remained unnamed until 1977, when Steere and colleagues reported a high incidence of this disorder in Lyme Connecticut, and surrounding communities. The disease is becoming ubiquitous; in 1987 and 1988 cases reported to the Centers for Disease Control were acquired in 43 states. But 80 percent of cases during that period occurred in six northeastern states: Massachusetts, Rhode Island, Connecticut, New York, New Jersey and Pennsylvania. The annual incidence of Lyme disease has also increased dramatically - from 492 cases in 1982 to 4,572 cases in 1988. Today, Lyme disease is the most commonly reported vector-borne infection in the United States.

Diagnosis

Lyme disease is caused by infection with the spirochete *Borrelia burgdorferi*, transmitted via ixodid ticks. *Ixodes dammini* ticks are the most common causative agents in the northeastern and midwestern areas of the United States, and *I. pacificus* is the causative agent in western areas. The white-footed mouse is the preferred host for both larval and nymphal stages of *I. dammini*, and the white-tailed deer is the preferred host for the adult stage. But these "deer ticks" have been found on at least 30 types of wild animals and 49 species of birds.

Lyme disease has a wide variety of manifestations. Because Lyme borreliosis can mimic other disorders not treatable with antibiotics, proper diagnosis is crucial. There is some concern that Lyme disease may be over-diagnosed. For example, a report

of 100 patients referred to a Lyme disease treatment center showed that only 37 actually had Lyme disease.

Diagnosis of Lyme disease can be difficult, relying on subjective and clinical evidence obtained from history, physical, and laboratory findings. For practical purposes, the disease may be considered to consist of two stages: early and late.

"Within a few hours of infection, Borrelia organisms migrate through the bloodstream into all tissues by burrowing between endothelial cells, potentially affecting all the tissues."

The early stage is characterized by a distinctive localized rash, while the late stage manifests as a disseminated infection that can involve the nervous, musculoskeletal, and cardiovascular systems, in addition to the skin.

History

There must be a strong likelihood of exposure to ixodid ticks in an endemic area. Infection is usually acquired via bites from ixodid nymphs during their May-to-June feeding season and may also be acquired from adult ticks during their autumn feeding. While awaiting a host, ticks assume a "questing" posture on grasses or shrubs about three feet above the ground. Clinical studies have shown that the tick must

often remain attached to the host for at least four hours or more before transmission of spirochetes occurs. Deer ticks are very tiny, however, and only about half of those who acquire Lyme disease remember being bitten by a tick.

Physical examination and symptoms

Early-stage Lyme disease is not always detectable and may go unnoticed even by the patient. Careful questioning about the appearance of symptoms is often necessary. Often there will be low-grade fever (99° to 100° F) in the late afternoon. The best single indicator of early-stage disease is the typical "bull's eye" rash of erythema migrans (formerly called erythema chronicum migrans), which occurs in 60 to 80 percent of patients. In the remaining patients, erythema migrans may not be present or may be unnoticed. About 18 percent of patients have multiple lesions, and the rash may be atypical - ununiform, vesicular, purpuric, or violaceous. Fever, fatigue, and other constitutional symptoms are absent or very mild. It has been established that within a few hours of infection, *Borrelia* organisms migrate through the bloodstream into all tissues by burrowing between endothelial cells, potentially affecting all the tissues.

Once systemic symptoms appear, the disease is considered to be late stage. Erythema migrans may still be present; other symptoms of late-stage Lyme disease include fever, fatigue, arthralgias or myalgias, headache, stiff neck, and regional lymphadenopathy. If the disease remains untreated, symptoms become more severe. Neurologic manifestations include meningitis, facial palsy, motor or sensory radiculoneuritis, and sometimes mild encephalitis. Cardiac involvement most often manifests as atrioventricular block; there may be acute or chronic myopericarditis. Asymmetrical oligoarthritis commonly affects the knees; bones, tendons, and bursae may be painful. Ophthalmic symptoms include

Continued on next page

conjunctivitis, iritis, and panophthalmitis. Less common manifestations are hepatitis, adult respiratory distress syndrome, and microscopic hematuria or proteinuria. There is some evidence that the more severe the extracutaneous signs and symptoms, the slower the response to antibiotic treatment and the greater the risk of serious sequelae.

Immunologic disorder predominates in late-stage disease, and manifestations may mimic those of other disorders, including acute rheumatic fever, gonococcal arthritis, or enteroviral meningitis. Arthritis may become chronic and persistent; occasional pannus formation with erosion of bone and cartilage may resemble rheumatoid arthritis. Symptoms of central nervous system disorder may be subtle, such as memory loss and behavior changes, or more overt, such as encephalopathy, ataxia, paresis, and dementia.

Laboratory studies

Baseline laboratory studies to evaluate patients with suspected Lyme disease include complete blood count and chemistry panel, tests for antinuclear antibody, rheumatoid factor, C-reactive protein, creatine phosphokinase, erythrocyte sedimentation rate, urinalysis, and electrocardiogram. Additional tests indicated to rule out other illnesses may include blood cultures, serum vitamin B-12 levels, thyroid studies, and diagnostic imaging.

Serologic evidence of *B. burgdorferi* infection can be useful in diagnosis, but there is a high incidence of false negative and a significant but lower incidence of false positive results. In addition, standards vary among laboratories. Currently, the Centers for Disease Control and the Association of State and Territorial Public Health Laboratory Directors are working to establish standards for analysis, reporting, and interpretation of results. Even positive serology indicates exposure only and cannot confirm the presence of disease.

Enzyme-linked immunosorbent

assay (ELISA) testing has been found more sensitive and specific than indirect immunofluorescence testing. False-negative results may occur because of low antibody concentrations during the first several weeks of infection. If Lyme disease is strongly suspected but the initial serology is negative, the test should be repeated in four to six weeks. Results may be confirmed using Western blot analysis. In all stages of the illness, due to the antibodies being bound in immune complexes, patients may remain seronegative.

False-positive results may occur if the patient has antibodies to *Treponema pallidum*, but Venereal Disease Research Laboratory and rapid

“The more severe the extracutaneous signs and symptoms, the slower the response to antibiotic treatment and the greater the risk of serious sequelae.”

plasma reagin testing can differentiate syphilis from Lyme disease. False-positive results may also occur if the patient is infected with another species of *Borrelia* or has rheumatoid factor IgM antibody.

To confuse the situation even further, residual antibodies may be present in a patient who had subclinical Lyme disease and now has a non-Lyme illness with symptoms similar to those of Lyme disease.

Researchers are now conducting clinical trials of a urine test to detect *Borrelia* antigen. Early results show that this test may be extremely helpful but must be interpreted cautiously. As with serologic testing, false-positives and false-negatives may occur.

Spinal taps are most useful to rule

out other conditions, as a negative result does not rule out *Borrelia* infection. Culturing of blood, cerebrospinal fluid, bone marrow, or other tissues is slow, expensive, and usually yields little helpful information. Tissue staining of biopsy specimens yields low numbers of *B. burgdorferi* and is not widely recommended.

Lyme Borreliosis Foundation Diagnostic Criteria

In March 1990, a workshop supported by the Lyme Borreliosis Foundation developed diagnostic criteria that gives a relative point value to a series of criteria: tick exposure in an endemic region, 1; systemic symptoms/signs consistent with published descriptions of Lyme borreliosis — single system (e.g., monoarthritis and facial palsy), 2; erythema migrans, 3; seropositivity, 2; seroconversion (paired sera), 2; tissue microscopy, silver stain, 2; tissue microscopy, monoclonal immunofluorescence, 3; culture positivity, 4; *Borrelia* antigen recovery (when validated), 2; *Borrelia* DNA recovery (when validated), 3. A total of four or greater is indicative of definite Lyme borreliosis; three or greater, probable Lyme borreliosis; and two or greater, possible Lyme borreliosis.

This simple point system has been proven useful in helping to clarify the diagnosis not only for clinicians but also for third-party payers and hospital utilization review committees. It should be noted that the CDC Lyme Disease Case Definition criteria were developed for epidemiologic surveillance and should not be used routinely to establish a diagnosis.

Treatment

As with diagnosis, treatment of Lyme disease must be based on subjective assessment. Because there are no objective clinical or laboratory tests, therapeutic progress is judged by the regression of symptoms, and there is no clear end point of therapy. Not all drugs are effective in every

See **Guidelines** on next page

Guidelines, cont.

patient, there are probably antibiotic-resistant *Borrelia* organisms, and relapse is common. Some late cases of Lyme disease may not be curable.

The Nature of *Borrelia* Infection

Because the Lyme spirochete is rapidly distributed to all parts of the body, antibiotic concentrations in all tissues must reach bactericidal levels. The spirochete has a very long generation time and may have dormant periods. Therefore, Lyme disease should be considered a chronic infection, requiring long-term treatment to alleviate all active symptoms and prevent relapse.

Antibiotic Therapy

Three types of antibiotics are effective for Lyme disease treatment: tetracyclines, penicillins, and cephalosporins. Of the tetracyclines, doxycycline and minocycline are effective in early-stage Lyme disease but are not recommended for late-stage disease except as a last resort. There is some evidence that these drugs may be bacteriostatic rather than bactericidal unless doses are very high. The use of tetracycline is not advised because of its limited capacity to penetrate into the cerebrospinal fluid. Amoxicillin is the most effective of the penicillins but should be administered with probenecid to increase its short half life. Penicillin G and penicillin V have poor penetration into the central nervous system and are associated with beta-lactamase resistance.

First-generation cephalosporins are not effective against Lyme disease; second-generation agents have efficacy comparable to that of doxycycline and amoxicillin. Third-generation agents are the most effective antibiotics for Lyme disease because of their very low minimal bactericidal concentrations, excellent tissue penetration, and resistance to borrelial beta lactamases. These drugs have also proven effective when treatment has failed with amoxicillin and other penicillins. One drawback

has been the need to administer these drugs intravenously. Early clinical trials have shown that cefixime, a once-daily oral third-generation cephalosporin recently approved for marketing, is by far the most effective oral agent available to treat Lyme disease.

Although erythromycin has been highly effective in *in vitro* studies, practical clinical use has shown poor results. Quinolone antibiotics are not effective against *Borrelia*.

Duration of Therapy

Experience has shown that duration of therapy is as important as the choice of antibiotic. Early reports in the literature considered treatment successful if major symptoms (e.g., arthritis, facial palsy, carditis) were eliminated. The fact is that these symptoms usually regress even without therapy. Recently it has become more clear that the continuing "minor" symptoms of fatigue, headache, and arthralgias are not part of a "post-Lyme" syndrome but indicate that disease has not been eradicated. Discontinuing treatment before all active symptoms have cleared usually results in relapse, particularly in sicker patients. Longer therapy may be indicated for patients with multiple bites, active synovitis with a high erythrocyte sedimentation rate, heart murmur, or for women who are hormonally active. The average duration of treatment in advanced Lyme disease is four months. A definition of successful treatment is the elimination of all signs of active disease, including major and minor symptoms, and no posttreatment relapse.

Virtually all Lyme disease patients experience a symptomatic flare, similar to the Jarisch-Herxheimer reaction of syphilis, after beginning antibiotic therapy. Most often this appears within the first five days and can last up to two weeks. Patients should be warned that this is likely to occur and not to discontinue therapy on the mistaken idea that this is a treatment failure or an allergic

reaction.

Intravenous therapy is more likely to be indicated for patients with duration of symptoms greater than one year, active synovitis and a high erythrocyte sedimentation rate, major cognitive dysfunction, inflammatory spinal fluid, prior use of corticosteroids, failure of oral antibiotic therapy, or age greater than 60 years. If intravenous antibiotics are given for more than three weeks, there is commonly a severe flare of symptoms, similar to a serum sickness reaction during the fourth week of drug therapy, presumably due to increased immunoreactivity that results from the monthly antigenic shifts in *B. burgdorferi*. If this occurs, the dose should be decreased or interrupted for one to three days, resuming carefully with a lower initial dose. This can be a trying time, but if antibiotics can be continued there will be a dramatic improvement at about the sixth week. If treatment is stopped entirely, relapse is likely.

Treatment failure is guaranteed to occur if there is noncompliance with therapy or if the patient uses alcohol regularly or fails to obtain proper rest. Patients should be advised to rest before the onset of typical midafternoon fatigue. A daily diary of symptoms will help to assess treatment.

Physical Therapy

Like any debilitating multisystem illness, a carefully guided, aggressive program of rehabilitative physical therapy is required for the patient with chronic Lyme borreliosis to return to a normal level of functioning. Such a program must begin with simple, symptom-directed local treatments, including heat, massage, ultrasound, and possibly electrical stimulation. It then should progress to include generalized muscular conditioning and ultimately lead to an aerobic program when and if the patient can tolerate it.

Joseph Burrascano MD
139 Springs Fireplace Road
East Hampton NY 11937
Tel. 516-324-7337

Personal Stories

by Jorjann Kuypers

I recently read in a newspaper article that researchers cannot substantiate Lyme disease actually being contracted in Florida. Perhaps one of the reasons is that doctors refuse to believe that it can be contracted in Florida, so they consequently misdiagnose the disease.

April, 1991 - Girl Scout Camp Out - I spent one weekend at Faver Kykes State Park in St. Johns County, Florida. On Sunday evening I removed a nymphal tick from my abdomen at the waistline. Thinking nothing of it, as I had removed about 5 or 6 nymphal ticks throughout the weekend, I smashed the tick on my kitchen counter and went on about my business. By Wednesday of that week I began suffering from extreme fatigue, irritability, dry cough, chest pain, swollen glands, headache, and neck pain. This continued for about 4 days. I thought I had come down with the flu. Then on Monday evening, 8 days after removing the tick, I noticed a dime-size rash around the tick bite. The tick bite itself looked like a little pimple. It was clear immediately surrounding the bite and a reddish rash encircled the clear area.

At that time I was unaware of the symptoms of first stage Lyme disease, but I did know that a "bull's-eye rash" around a tick bite was indicative of Lyme disease. I immediately researched the literature and discovered that my earlier symptoms were textbook symptoms of stage one Lyme disease. Within 2 days of the appearance of the rash, it had expanded to about 3 inches (8 cm) in diameter.

I began oral antibiotic therapy (Doryx) for two weeks. All blood tests (3 total) were negative for Lyme. Approximately 8 weeks after I finished taking the antibiotics, symptoms reappeared - stiff and painful neck, fatigue, and this time,

loss of appetite. During this period I lost 10 pounds in one week. I would awaken about 4 am feeling as though I'd been beaten with a baseball bat. I was unable to move my head without turning my whole upper body. Since I was told that 2 weeks of medication would completely cure the disease, I was hesitant to seek medical help again, even though I was certain it was Lyme. I waited for one month before going back to the doctor. I started antibiotic therapy again, this

"Since I was told that 2 weeks of medication would completely cure the disease, I was hesitant to seek medical help again."

Jorjann Kuypers

time for 3 weeks. Symptoms disappeared just 4 days after the same antibiotic as before.

About 12 weeks later I had mild recurrence of symptoms - migrating joint pain (very mild, just in one knee at a time), stiff neck, pain starting at the base of my skull and radiating into the back of my head. These symptoms were so mild that I doubted that they were even Lyme-related. However, after putting up with the recurrent symptoms I did go back to the doctor and we decided to go ahead and retreat with the same antibiotic for 30 days. This time it took approximately 10 days for symptoms to go away.

I remained symptom free for 4 months. Just in the past 2 weeks symptoms have returned, as mild as before: throbbing pain in knee (lasted

one day), stiff neck, pain in rear of head, pain just below kneecap, lower back pain. Symptoms come and go. I'm not sure these little aches and pains are a result of Lyme. I'll wait and just see what happens.

So, as you see, Lyme disease is alive and well in Florida. You wouldn't believe the number of medical personnel I've spoken to who categorically deny the possibility of anyone contracting Lyme in Florida. Some may say I'm crazy, but I'm not. Nor am I an attention seeking and antibiotic seeking person. I do not like to take medication.

I feel sorry for all of those people in Florida who have Lyme and don't know it.

*Jorjann Kuypers
17 Blaketown Place
Palm Coast, Florida 32137*

by Jean Schluckebier

Being sick is never fun, but being sick and not knowing what is wrong can be one of the most frustrating experiences in your life. Even worse is having the medical profession label you a hypochondriac or refer you for psychological help because they can't find an answer, so it must all be in your head.

Thirteen months ago, I had a hysterectomy after three doctors concurred I had adenomyosis. My symptoms were severe enough to warrant the surgery, and I was so miserable I just wanted to feel normal again. Unfortunately, following surgery I developed new and worse symptoms. My neck hurt and I could hardly hold my head up. The pain in my back and shoulders was so great I went through six weeks of physical therapy to strengthen my muscles. It seemed to help, but the pain would continue to come and go. My dizziness and loss of balance suggested an inner ear problem, so I was referred to an ear specialist. Tests

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Stories, cont.

indicated a lesion on the brain stem. I feared a tumor on the brain, but a neurologist doubted that and had me undergo an MRI (Magnetic Resonance Imaging). The test indicated multiple lesions on the brain consistent with multiple sclerosis. I thought I finally had an explanation for my symptoms. My neurologist felt it was a minor form of MS and that I would not end up in a wheelchair. He suggested exercise, vitamins, and a good diet. Eager to be healthy, I followed his suggestions. Instead of getting better, however, I developed new and even more severe symptoms.

My legs began to have spasms and I could hardly stand up. My heart would pound and my pulse was rapid. My body would go into shaking seizures, and every joint would ache. Headaches were worse and nearly constant throughout the day. My family doctor referred me for psychological evaluation. I am sure he felt that I just was not able to deal with the MS diagnosis.

The turning point in my life came when I was a poster at my local pharmacy about Lyme disease. The symptoms of this disease caused by the bite of a small tick were very similar to many other diseases. In fact, many people were diagnosed with MS when they actually had Lyme. When a friend told me about a young man in our community who had been diagnosed with MS but actually had Lyme, I knew I had to act on my intuition. My family doctor was excited at the prospect that we had a possible cause for my varied symptoms. I had had a rash and I had been to Wisconsin. He put me on tetracycline and my Herxheimer (temporary worsening of symptoms due to immune response) was so violent I had to take a medical leave of absence from my teaching position. It wasn't until later that I realized I had been bitten in Michigan and had had the symptoms of Lyme before my hysterectomy.

In the meantime, I contacted our local support group here in Michigan where I obtained the latest guidelines for treating Lyme disease. I forwarded this information to my family physician, who then put me on Suprax. Life began to change for the better. After three months on orals, I was put on intravenous Rocephin. I am nearly symptom-free and life is looking healthier by the day.

In the face of negatives, it is sometimes difficult to find positives in your life. However, for me, my ordeal has become a positive experi-

"People must take responsibility for their own health. On the most part, doctors want to find solutions to our health problems, but they do not know all the answers. We have to seek out answers as well."

Jean Schluckebier

ence. Because of what I learned through the support group, I was able to identify the Lyme rash that both of my small children had had this past summer. They both are on antibiotics and doing great. We recognized the symptoms in our family cat, had her tested, and discovered she had Lyme. She has since been donated for research at Michigan State University in the hopes that they can learn more about Lyme in animals and perhaps help humans as a result. My greatest thrill came when I told a fellow teacher about Lyme. She was in a wheelchair as a result of MS. I referred her to my doctor who ordered the Lyme tests. Her results

came back completely negative, but he put her on Suprax to see if she would respond. Three weeks later she called to tell me that she walked across her living room for the first time in a year. She has been slowly improving ever since. She had Lyme!!! Knowing that my experience has brought about help for others has made all the suffering worthwhile.

I am now working with members of our local support group to establish the Michigan Lyme Disease Association. We are in the process of incorporating and applying for tax-free status. If we can get grants and support from business and industry, we intend to distribute literature to every school child in our state. Any readers who would like more information about Lyme disease should send \$2.00 to MLDA, PO Box 165, Frankenmuth, MI 48734.

If I have learned anything from this experience it is that people must take responsibility for their own health. On the most part, doctors want to find solutions to our health problems, but they do not know all the answers. We have to seek out answers as well. Medical science has a long way to go before they have all the answers to Lyme disease, but they will have the answers eventually. We are the guinea pigs. What doctors learn from us will benefit generations to come. That may be of little comfort while we suffer with shakes, arthritis, headaches, etc., but perhaps through us, our children and grandchildren will be spared our agony. In the meantime, a positive attitude and a determined spirit will see us through the long road to recovery.

Jean Schluckebier
Michigan Lyme Disease Association
PO Box 165
Frankenmuth, MI 48734.

**Support Group
listing is back!
See pages 50-1**

Patient Support

Alternatives to medications

by Kathy Cavert

This is the last of a three-part series which originally appeared in MidWest LymeAid, March/April 1991. Reprinted by permission.

Alternatives or additions to medication, so-called "adjunctive" therapies, are very important in patient management. What alternatives do we have?

1. Counseling: Most Lyme borreliosis patients were once healthy and active and not in need of counseling, but things have changed. Many of us are no longer able to work. We have dramatically altered lifestyle and we feel fatigued, weak, and stiff. But we still have many of the same responsibilities of life like raising children and being a good wife/husband. Although we once prided ourselves in being able to handle life's stresses, this has become a bit much. Your regular physician is usually not the right person to burden with your continuing tale of woe. Perhaps getting into a sliding-scale counseling program can help provide an outside, objective listener, someone besides the poor spouse, parents, and friends who tire of hearing the dreadfully prolonged story of misery. Nothing beats having professional help to buffer the new stresses, and nothing beats verbalizing all the psychological problems that go along with being disabled. It is amazing how talking to an outside neutral party reduces stress and tension that may otherwise be held inside and make the pain worse. It is like a pressure cooker - when the heat gets too high, if the steam vent isn't open, the pot explodes. Before you get to that point, try counseling to let off steam.

2. Biofeedback: This is administered by a trained professional and teaches us to become aware of our own physiologic response to stressors such as pain. Electrodes are connected to the finger and muscle

groups, and as we relax and calm our heartbeat and muscle tension and blood pressure, it registers in the form of sound. The slower the heartbeat, the deeper the tone. An electrode is

"Remember that although these suggestions are successful for some, they do not work for others. It is for this reason that there are many alternatives to reduce pain and tension."

placed on the finger to measure galvanic skin response to stress. As we learn to control our own reaction to pain or painful thinking processes, the calming response is registered on the machine and we can see it or hear it. The feedback can be specific - it can take individual muscle spasms and allow us to work with just that group of muscles, relaxing them one by one. Talking and thinking about stressful things in our lives can also cause a physiologic response. We can gradually learn to reduce the adrenalin rush of fear and anger around specific issues that plague us. Biofeedback works as a psychological stress reliever and a physical pain reducer.

3. Pacing: Simply put, this is a way to reduce stress from pain by

moving more slowly and doing normal household chores in time increments rather than all at once. Pacing is individual. Pacing means changing our old ways of doing things and making life simpler. Cleaning the bathroom, for example, and be done in two or three days instead of one. The tub and sink one day, the toilet the next, and the floor on the third day. When groceries are brought home, refrigerated items can be put away immediately, but the rest can wait until we have energy to complete the job.

Many people in pain have a tendency to move fast because the pain is less noticeable when we are in motion. When we are still, we can feel the pain more and so we don't like to be still. The down side of this is that as we continue at a frenzied pace, trying to avoid the fatigue and pain, we produce a vicious circle of continued pain and fatigue. We tend to spend one good day doing everything and the next 3 days recuperating on the couch!

4. Prayer/Meditation: Either one has the power to calm. Prayer is comforting because we let go and let God take over our worries and cares, and we relinquish the things over which we have no control. The AA prayer is appropriate: "God grant me the serenity to accept the things I cannot change, courage to change the things I can, and the wisdom to know the difference." Quiet talks with God or our higher power can be comforting in times of pain and illness.

One way which is popular is to take a one-syllable word and close the eyes. Get comfortable in a sitting position if possible and begin saying the word over and over, slowly. As your mind wanders, don't worry, just bring your mind back to that one word and continue saying it. Continue saying that word for 20 minutes and keep your eyes closed. It is ok to check the clock for time, and you will always be aware of phones and sirens, etc., but just continue to draw

See **Alternatives** on next page

Alternatives, cont.

your mind back to that one word. Pick a word that is calming and stick with it. Do this twice a day and by the time your 20 minutes are up, your body will be so relaxed that you will hardly be able to move. It is an almost anesthetized feeling - a wonderfully peaceful feeling. The blood pressure drops, the blood sugar drops (be careful if you are a brittle diabetic) and your heart rate drops. There is an overwhelming sense of peace and tranquility and this can often be more refreshing than a nap!

There are times when relaxation via meditation might be especially important. Generally speaking there are people whose central nervous system disease has caused them to become agitated and to have a sleep disorder. Although they might meet these suggestions with resistance, anything that can calm this heightening of sensation would be wonderful.

5. Water therapy: Many YMCAs provide warm water rehab swim time for people with disability. If one is arthritic, there are often arthritic water exercise classes. Nothing beats moving one's arms and legs about in the water as opposed to on land where gravity has its say. Water provides gravity-free exercise allowing for free and painless movement. Water can also be used as a kind of muscle re-education medium. When one swings one's arms slowly through the water, there is resistance. This resistance is a mini-form of weight lifting. The resistance provided by the water gives one's muscles a chance to strengthen gradually and with little effort and without damaging the joints. Try swinging the leg around or back and forth in the water and feel the hips loosen and feel the leg muscles push against the water. Ideally one should learn some water exercises from a professional and then apply them to the individual situation. Many hospitals and rehab centers now use water/pool therapy so it is easier to come by. Once you have learned the techniques for loosening joints and

strengthening muscles all over the body, then you can go it alone for the rest of your life. Just remember to go slow. If you are a swimmer, do not start in by swimming 20 laps, just move around in the water and perhaps swim just a couple of laps.

Remember that although these suggestions are successful for some, they do not work for others. It is for this reason that there are many alternatives to reduce pain and tension. Some people report renting VCR tapes and allowing themselves to become absorbed in a good "flick." For those who have a hard time lying down and staying quiet, a soap opera addiction might work wonders. The libraries now have shelves filled with audio-books, many of which are best sellers: mysteries, romance, history, humor, self-help, and so on. Plugging a good book into the stereo or walkman and putting on the ear-phones can help one take one's mind off the pain by becoming engrossed in a good book on tape. I have eye damage so audiobooks are good for me. I also have a weakness in my arms, so I have purchased a light-weight book holder that can be placed over my body when I want to thumb through a magazine (see picture below). It allows me to read without needing to hold the book up.

Although there are many ways to reduce pain and stress, it still must be stressed that this is a serious infectious process attacking the body at the cellular level. This means that what might work to reduce the pain of muscle spasms in the arm or back might not work to reduce the swelling of a huge, infected nerve root along the spinal cord. Aspercreme rubbed onto aching muscles and joints is wonderful but it may not rid you of your headache. Learn which techniques work for you and which do not, and do not knock them until you try them. Often these techniques are applied in conjunction with the pain medication and/or muscle relaxers. But no matter how you attack the problem, antibiotics are the only thing

that we know of that can attack the cause of the problem. Our primary goal is to find the antibiotic or combination that works for us.

When friends, family, or co-workers make fun of you or start losing enthusiasm for your mysterious ailment, remember that there is a whole country of people who will take up your cause in a minute and come to your side. It might be by phone only but we are there for you. Friends might see us as "weaklings" but we know different. We know that we have suffered with an infectious disease that can act like a combination of lupus, ALS, MS, Alzheimers, rheumatoid arthritis, fibromyalgia syndrome, heart problems, sometimes even seizures, all rolled into one. So let them poke fun at us or give us those "weird looks." We know that we are strong and that we have developed the strength of the Incredible Hulk.

Remember: You do not go home with an abscessed tooth and endure it. You call a dentist. You do not sit and endure a heart attack. You call a cardiologist. If you are suffering too much, let your doctor or some doctor know. If your physician is not empathetic to your pain and suffering, there are plenty of them out there who will be. Sitting around and playing "martyr" will do nothing but stress one to the brink and cause the disease to become worse due to the unnecessary stress of "holding" the pain. If you are prone to chemical addiction, then this needs to be discussed with your doctor. Perhaps you may need to suffer a little more than the others, but then again, perhaps not.

To recapitulate - generally when pain medication is taken for pain, it is seldom addictive. It is when one takes pain medication for the "high" that it becomes an addictive problem. Addiction is partly psychological. The reason they invented pain medication was not for abuse, but rather for legitimate medical use.

Continued on next page

Lyme disease emphasizes need for teamwork

by Linda Hanner

The need for teamwork between physicians and patients has been emphasized by the discovery of Lyme disease. If health officials had not listened to the concerns of a New England housewife in 1975, Lyme disease would probably not be a household word today, and patients who have since been diagnosed as having it would remain undiagnosed or misdiagnosed.

Teamwork is especially important during the prediagnosis period, which can be a traumatic time for patients and their families. Yet patients' emotional and psychological needs during this stage of illness are seldom recognized or addressed by medical professionals. This is unfortunate as the manner in which patients are dealt with during the prediagnosis period can impact the quality of the patient/caregiver relationship and the patient's ability to cope with symptoms even after the diagnosis is made. Lack of teamwork also increases the chance of errors in making a diagnosis.

During the past year I have visited

a number of patient support groups, including those for people afflicted with Lyme disease, lupus, MS, and rheumatoid arthritis, and have solicited information through interviews and questionnaires. About 70 percent of the patients in these groups confided that prior to their diagnosis, they were told their symptoms had no physical basis. About 60 percent said they were treated better by medical professionals after the diagnosis was made.

There are many possible reasons for delays in diagnosis of illness, and all of them apply to Lyme disease. Many chronic conditions tend to produce vague and fluctuating symptoms for a number of years before showing up on tests or producing objective signs. Poor communication or improper interpretation of tests sometimes confound the diagnostic process. Some diseases have no specific tests; some have tests that are unreliable. And, of course, diseases that have not been discovered yet can't be diagnosed.

It is important for patients to realize that a concrete diagnosis might take a long time, and is important for physicians not to assume that difficult-to-diagnose patients are hypochondriacs. The good news is that a growing number of medical professionals seem to be recognizing the need for change. Many physicians agree that psychological diagnoses have become convenient catch-alls when physical diagnoses are elusive. Some are recognizing the need for tact, compassion, and patience during the prediagnosis period.

In recent years a national organization called The Task Force on Doctor and Patient has been presenting seminars at medical schools around the country. After sharing my concerns with doctors who are members of this Task Force, I have been invited to speak at one of their seminars. This is an exciting opportunity as I will be speaking to physicians who train other physicians.

I plan to incorporate the results of surveys and information gathered from patients and caregivers into a third book with the goal of encouraging teamwork between the two.

Input from nurses, physicians, and fellow patients has been invaluable in making my speeches and writings meaningful and effective. As I work on my next book, I am particularly interested in hearing from those who have had positive physician/patient encounters with examples of actions and choices of wording that were helpful both before and after the diagnosis.

Any suggestions or comments can be mailed to:

Linda Hanner
9050 County Road 11
Maple Plain, MN 55359

Linda Hanner is author of Lyme Disease: My Search for a Diagnosis, and co-author of When You're Sick and Don't know Why. Both are available through LDRC Mailorder. See page 54.

Alternatives, cont.

Infected patients fall into the category of legitimately ill and pained persons. Infected patients need help. Infected muscles need to be relaxed if they are in spasm. Muscle relaxers were invented to reduce the spasms of muscles caused by neurologic abnormalities causing the muscles to spasm. Spinal cord injured patients know this - why shouldn't we? And many of us have spinal cord, central nervous system damage.

So be smart and prudent both. Ask for help. Your doctor is there to help you. If not, find another one.

If a good doctor/patient relation-

ship cannot be worked out, then move on. Pain and Lyme are synonymous. In summary: IF YOUR PAIN MEDICATION IS NOT WORKING, TELL YOUR DOCTOR. As Dr. Ronald Melzaek and other pain experts put it, "...You are ultimately responsible for your own well-being." Good luck and God bless.

Kathy Cavert
Midwest Lyme Disease Support Group
PO Box 3135
Independence MO 64055
816-252-6159

Stretching: one way to fight back against Lyme

by Alec Isabeau, DC

Lyme disease, as most of you know, may adversely affect the joints and surrounding soft tissues. While some Lyme patients appear to have little trouble at all with their joints and muscles, others are completely disabled by pain and stiffness. Therefore, the long-term successful management of Lyme often requires a program of treatment and/or self-care aimed at improving joint and muscle function. This will prove valuable in reducing pain and improving overall functional capacity.

Stretching is a key component of joint and muscle care and every Lyme patient (in fact, every person, period!) should stretch his/her limbs and torso on a regular basis. Why?

All of our moving parts require regular use, through their full ranges of motion, in order to stay healthy. If a muscle is allowed to languish for days on end it will become weak, short, and inelastic. Consequently, the joints which are controlled by these muscles will also suffer from the effects of immobility - they will become stiff, painful, and poorly lubricated.

Stretching, then, is a simple, highly-effective means to help your body regain or maintain optimum function. There are very few contraindications to stretching, as long as you follow a few guidelines. If you have Lyme, particularly if you are suffering from significant joint or muscle pain, check in with your doctor to make sure that you can safely begin a stretching program.

Some key points to remember are:

1. Stretching must be performed on a regular basis to achieve long-term results. You'll need to stretch at least three times a week to accumulate the positive effects of stretching. Better yet, stretch daily.

2. Stretching must be gentle and prolonged: hold all stretches comfortably for 20-30 seconds. Don't stretch a muscle so hard that after 3 or 4 seconds of grimacing you quit - that's counterproductive. And don't bounce.

3. Ideally, stretching should isolate specific muscle groups, without stressing other areas of your body in the process. For example, bending forward to touch your toes, as we were all told to do in high

"It shouldn't hurt. Pain which is sharp, jolting, stabbing, or catching is a warning that something is amiss. Don't ignore it and don't "work through it."

school gym class, will certainly stretch the hamstring muscles in the backs of the thighs, but it will be at the expense of your low back, which may be injured by this maneuver. There are safer, more specific ways to stretch the hamstrings.

4. It's best to stretch when your muscles are warm - therefore, a hot bath, shower, massage, or exercise beforehand will be helpful. Then, slowly and gently begin your stretching program. All of the major muscle groups of the body may be effectively stretched in only 10 minutes. That tiny investment of time may provide dramatic benefits!

5. Stretching may be uncomfortable, but it shouldn't hurt. Pain which is sharp, jolting, stabbing, or catching is a warning that something is amiss.

Don't ignore it and don't "work through it." Consult your doctor.

6. An optimum stretching program must be individualized for each Lyme patient, but a great resource for learning some basic head-to-toe stretches is the classic book *Stretching*, by Bob Anderson (Shelter Publications, 1980, Bolinas, CA). I highly recommend this well-illustrated manual (*Ed.- available through LDRC mailorder, page 54*)

Stretching, while vital, is not effective alone in combatting the joint and muscle problems we see in Lyme. We must also pay attention to strength, aerobic capacity, diet, rest, and stress management. I think it is fair to say that there's not a single patient who has ever walked out of my office without having enjoyed or endured a discussion on the importance of these fundamental factors of health.

It is also fair to say that those patients who do prioritize these factors, as a whole, can't help improving their health. There's no magic in health care, just a lot of hard work and perseverance. Fight Lyme relentlessly! I wish you all the best!

Alec Isabeau, DC
4310 Lacheau
Penngrove, CA
Tel. 707-792-2325

Lyme found in large city parks

A letter in *The Lancet*, Vo. 338: Sept 7, 1991, discusses the incidence of *Borrelia burgdorferi* in two parks in London. Ticks were collected in parks where one canine case of Lyme disease had been confirmed, and where large numbers of deer roam free. Of a total 65 adult female *Ixodes ricinus* tested by polymerase chain reaction, 5 were positive for *B burgdorferi*. The writers emphasize that identification of potential foci of infection can assist clinical diagnosis of Lyme disease.

1990 Disabilities Act now protects the disabled

by Lawrence J. McLaughlin

Article originally appeared in Ag Alert, the weekly newspaper for California agriculture published by the California Farm Bureau Federation, May 22 and June 5, 1991. Reprinted by permission.

On July 26, 1990, President Bush signed the "Americans with Disabilities Act." The act, which was enacted with strong congressional support, broadly prohibits virtually all forms of discrimination against individuals with physical or mental disabilities with regard to employment, public services, public accommodations and services by private businesses and telecommunications.

The act imposes sweeping obligations on employers with respect to such things as pre-employment procedures, hiring, discharge, compensation, and other terms and conditions of employment.

However laudable its aims may be, the act in its present form may prove to be an administrative and financial burden of huge proportions, and will surely pose substantial problems for employers by reason of its ambiguities and vague terminology in many crucial areas. Its definitions and requirements are imperfectly articulated and will require much costly litigation before the act's terms are clarified.

For the purpose of this article, which focuses upon the employment aspects of the act, is simply to alert employers to those vague requirements and to provide a basis for understanding the cautious approach needed as these occasions arise. Through a question and answer format it addresses some of the more pressing issues facing employers.

When did the act go into effect?

For employers with 25 or more full time employees, the effective date was July 26, 1992. For employ-

ers of 15 or more full time employees, the effective date is July 26, 1994. Employers with fewer than 15 employees are not covered by the act.

Who must comply with the act?

In addition to employers, the act covers employment agencies, labor organizations and joint labor-

"The act contains many vaguely defined phrases that employers will be forced to apply to real-life situations."

management committees. Presumably included would be covered activities of such agencies as apprentice committees, temporary employment agencies, outside employer training programs and the like.

Who is protected by the act?

Any "qualified individual with a disability" is protected. The protection under this act encompasses both applicants for employment and employees. Thus, persons holding jobs, as well as those who merely wish to hold a position are covered. Furthermore, the act protects qualified individuals with respect to training, advancement, compensation, discharge, and other terms and conditions of employment. In brief, these provisions are all-inclusive with regard to every aspect of employment, and, even though it is called the

"Americans with Disabilities Act," it protects non-citizens as well as citizens.

A qualified individual is one who, with or without reasonable accommodation, can perform the essential functions of the employment position that such individual holds or desires. Obviously, employers are immediately confronted with two fundamental questions; i.e. what is "reasonable accommodation," and secondly, what are the "essential functions" of a job. As may be noted, the act contains many vaguely defined phrases that employers will be forced to apply to real-life situations.

Disabilities are broken down into three categories:

- A physical or mental impairment which substantially limits one or more of the major life activities of such individual;
- A record of such an impairment;
- Being regarded as having such an impairment.

Examples of disabilities falling in the first category include any physiological disorder or condition, cosmetic disfigurement or anatomical loss affecting one or more of the following body systems: neurological; musculoskeletal; special sense organs; respiratory, including speech organs; cardiovascular; reproductive, digestive; genito-urinary; hemic and lymphatic; skin; and endocrine. Furthermore, any mental or psychological disorder, such as mental retardation, organic brain syndrome, emotional or mental illness, and specific learning disabilities are included.

Even a cursory review of the foregoing summary will quickly illuminate the difficulties confronting employers in complying with the act. Physical impairments that are not at all obvious, and seldom thought to be disabling, are included. A simple example might be a person with emphysema who requires oxygen on

See **Disability** on next page

Disability, cont.

smoggy days, yet seeks a position requiring public contact in an open-air setting. Must the employer furnish an oxygen mask and permit the employee to function in this manner as a "reasonable accommodation?"

The second category was intended to protect persons who have recovered from an impairment. An example would be a person who had, but no longer has, cancer. The third category encompasses persons who are perceived to have an impairment, whether or not they in fact do. Examples may be a disfigured burn victim, or person with a hearing aid, who has learned to compensate for this condition and, in fact, functions adequately on the job.

What are the "essential functions" of the employment position?

The act does not define this term. However, the Senate and House reports explain that a disabled person may not be disqualified for the job merely because s/he has difficulty performing certain marginal tasks connected with the job. Rather, only if the job task is "fundamental" can it be considered an "essential function."

Consideration is given to the employer's judgment on what job functions are essential. However, it is not controlling. Furthermore, written job descriptions may be evidence of the essential functions of the job, although such descriptions will not be conclusive. The Senate Committee Report states broadly that a "fact-specific" inquiry may be required for each position a disabled person may hold or be seeking.

Are certain behaviors and conditions excluded from the act?

Yes, these include homosexuality, bisexuality, transvestism, transsexualism, pedophilia, exhibitionism, voyeurism, gender identity disorders not resulting from physical impairments, other sexual behavior disorders, compulsive gambling, kleptomania, pyromania, and psychoactive substance use disorders resulting

from current illegal use of drugs. However, even though discrimination may not be charged under this act, various state laws which may cover the condition must also be taken into account.

Are users of illegal drugs protected?

Current users of illegal drugs are not protected. On the other hand, an individual who has been rehabilitated or is a participant in a rehabilitation program, is protected.

What if an applicant has a degenerative condition and, although qualified now, may not be in the future?

The applicant's qualifications must be determined at the time of the

"The requirements of 'reasonable accommodation' are bound to be difficult to determine in many instances."

"job action" (e.g. hiring or promotion). The possibility of future impairment cannot be a basis for finding a person unqualified.

Must an employer give preference to disabled individuals?

No, the employer may still select the most qualified individual for the job. Employment decisions must simply be based on factors other than the disability.

Must an employer employ a disabled individual with a currently contagious disease?

Not if the individual would pose a direct threat to the health and safety of others in the workplace which cannot be eliminated by reasonable accommodation. On the other hand, if an individual has been infected with, for example, the AIDS virus, but does not pose such a threat, s/he is protected by the act.

May an employer ask if an applicant is disabled or require the applicant to undergo a medical examination?

No. The act prohibits any pre-offer medical examinations. Likewise, an employer cannot inquire about the existence of, nature or severity of a disability. For example, the employer cannot ask about prior medical treatments or prior receipt of Workers' Compensation benefits.

However, an employer may condition an offer of employment upon a medical examination under the following circumstances:

- All entering employees in the same job category must be subject to the examination;
- The information from the examination must be kept confidential and collected and maintained in a separate file;
- The examination results cannot be used to discriminate against a disabled person who is qualified for the job.

If an applicant is shown unqualified as a result of the medical examination, and no reasonable accommodation is feasible, the job offer may be withdrawn.

What can an employer ask to determine if an applicant can do the job?

An employer may ask questions about the applicant's abilities to perform job-related functions. For example, with respect to a truck driving position, it is permissible to inquire whether the applicant has a driver's license, however, the employer may not ask if s/he has impaired vision.

What is "reasonable accommodation?"

The act does not define this term but rather gives examples. In short, an accommodation is reasonable if it does not impose "undue hardship" on the employer. Undue hardship is defined as an action "requiring significant difficulty or expense."

Continued on next page

Whether an accommodation will cause undue hardship will depend on the size of the employer, the site involved, and the nature and cost of the accommodation.

As may be seen from this brief discussion, the accommodation requirement is certain to become controversial and may frequently impose substantial burdens upon an employer. The requirements of "reasonable accommodation" are bound to be difficult to determine in many instances.

What are examples of reasonable accommodation?

Reasonable accommodation encompasses various actions necessary for the disabled person to perform the essential functions of the job. Such accommodations may include: making existing facilities used by employees readily accessible to and usable by individuals with disabilities, job restructuring, parttime or modified work schedules, reassignment to a vacant position, acquisition or modification of equipment or devices, appropriate adjustment or modifications of examinations, training materials or policies, the provision of qualified readers for the visually impaired or interpreters for the hearing impaired and other similar accommodations.

It is important to note that if there is more than one effective accommodation, the employer may choose which s/he will institute. It must be understood that the scope of the accommodations that may be required may be limited only by the types of disabilities encountered in an employer's work force. It is apparent that employers should first establish clear and reasonable job standards which set forth the true, essential functions required. Secondly, where examinations are considered necessary, they must closely relate to the job, just be given to all applicants, the results must be confidential, and may not discriminate against individuals with disabilities. Thirdly, when a person with a disability becomes

Insurance company wants the money back

Kenneth Beckley of Altamont, New York, needs help. His wife has been diagnosed as having Lyme disease. She is now seeing a nationally recognized specialist for the disease, and is making great progress, although she has been through a great deal of suffering in the process of recovery. It was necessary for her to be treated intravenously and orally for a two-year period.

Empire Blue Cross-Blue Shield authorized payments weekly to the Beckleys' IV company for treatments in 1991. However, in April, 1992, they informed the Beckleys that they had changed their mind and would not pay the outstanding balance owed to the IV company, an amount

totalling about \$22,000.00. In addition, they informed the Beckleys that the Blue Cross-Blue Shield Medical Staff, "after extensive review of all information related to these charges for the treatment of Lyme Disease," had determined that \$16,651.21 of treatments already reimbursed in 1991 were to be paid back to the insurer by the Beckleys. The Visiting Nurse Association utilized by the patient was also being notified of the insurer's decision to ask for a refund. In a letter, the insurance company's Disbursement Services officer stated that Mr. Beckley's prompt attention would be appreciated, and added, simply "attach your remittance, payable to

See Money, third column next page

involved, the accommodation determination must be made, beginning with an analysis of the accommodation required, and concluding with an objective determination whether the accommodation would, in fact, impose an "undue hardship" on the employer.

What if the disabled individual offers to pay part of the cost of accommodation?

If the disabled person or any other person or entity agrees to pay that amount necessary to alleviate what would otherwise be "undue hardship" on the employer, the employer must implement the "reasonable accommodation."

What are the remedies for violating the act?

The remedies incorporate those of Title VII of the Civil Rights Act of 1964. Those remedies are currently injunctive relief, back pay, attorney's fees, reinstatement, and in certain circumstances, front pay. However, notwithstanding President Bush's

veto of the "Civil Rights Act of 1990, a new civil rights act may still be enacted which could expand the remedies of this act to include compensatory and punitive damages.

Although the act is not immediately effective in all categories, employers should now begin taking steps to avoid future litigation. For example, job descriptions should be studied to determine if they accurately describe the "essential functions" of the job. Furthermore, employment tests and applications should be reviewed to make sure they comply with the law.

Along with state laws, and the Rehabilitation Act of 1973, this act provides another layer of protection for disabled persons. Accordingly, employers must be all the more alert to avoid violating the rights of the disabled.

*Lawrence J. McLaughlin
McLaughlin and Irvin
Los Angeles, San Francisco, Newport
Beach, San Diego*

Disabled people may qualify for Social Security benefits

Condensed from "Disability," a booklet issued by the Social Security Administration of the Department of Health and Human Services. The booklet provides a general overview of the disability program.

Social Security does not pay for partial disability or for short-term disability. You will be considered disabled if you are unable to do any kind of work for which you are suited, and if your inability to work is expected to last for at least a year or to result in death.

Certain members of your family may also qualify for benefits on your record, including an unmarried son or daughter, 18 or older, if s/he has a disability that started before age 22. Even a disabled ex-wife or husband who is 50 or older, if the marriage lasted 10 years or longer, may qualify for disability should the recipient of Social Security die.

Many children qualify for disability benefits under the SSI program. For more information, ask Social Security for the booklet, Supplemental Security Income.

To qualify for Social Security disability benefits, you must have worked long enough and recently enough under Social Security. Family members who qualify for benefits on your work record do not need work credits.

You should apply to any Social Security office as soon as you become disabled, however disability benefits will not begin until the 6th full month of disability.

To determine disability, Social Security uses a step-by-step process involving five questions. They are:

1. Are you working? If you are and you are earning \$500 or more a month, you generally cannot be considered disabled.

2. Is your condition "severe?" Your impairments must interfere with basic work-related activities for you claim to be considered further.

3. Is your condition found in the list of disabling impairments? SS maintain a list of impairments for each of the major body systems that are so severe they automatically mean you are disabled. If your condition is not on the list, SS has to determine if it is of equal severity to an impairment on the list. If it is, your claim is approved. If it is not, SS goes to the next step.

4. Can you do the work you did previously? If your condition is severe, but not at the same or equal severity as an impairment on the list, then SS must determine if it interferes with your ability to do the work you did in the last 15 years. If it does not, your claim will be denied. If it does, your claim will be considered further.

5. Can you do any other type of work? If you cannot do the work you did in the last 15 years, SS then looks to see if you can do any other type of work. They consider your age, education, past work experience, and transferable skills, and SS reviews the job demands of occupations as determined by the Department of Labor. If you cannot do any other kind of work, your claim will be denied.

If your claim is denied, you may appeal the decision. There is a four-step appeal process.

You will be automatically enrolled in Medicare after you have been getting disability benefits for 2

years.

Your benefits will continue for as long as you are disabled, however your case will be reviewed periodically.

For more information or to apply for benefits, call or visit Social Security. The toll-free number - 1-800-2345-SSA (1-800-234-5772) - is open from 7 am to 7 pm each business day.

Consumer advocacy

Is your insurance company denying you legitimate benefits?

Contact David Testone Associates, 1-800-843-2524 for assistance. Fees based on percentage.

Money, cont.

Empire Blue Cross and Blue Shield, to this letter and return in in the envelope provided." In case payment was not received within 60 days, the letter continued, "future claim payments will be applied to the amount due until a full refund has been recovered."

The Beckleys have been covered by this carrier for 22 years with very few prior claims. "Now when we need these funds they are breaking their end of our contract which did not exclude treatment for this disease," states Beckley. His wife is very upset and worried that she will not be able to continue treatment and become well. The Beckleys feel that it is a sorry state of affairs when insurance bureaucrats can dictate health care over and above proven treatments prescribed by medical experts.

According to Empire Blue Cross Blue Shield manager Jean-Marie Muchmore, the Beckley claims are currently under further review and are expected to be completed soon.

How to apply for Social Security Disability

by J.H. Dean

Reprinted from an office handout from J.H. Deans Law Office, 6208 Blue Ridge Cutoff, Raytown MO 64133

When should I apply for benefits?

Once it has been determined by a medical source that your condition(s) will prevent (or has already prevented you) from working for 12 consecutive months. (Note that you do not have to have been off work already for 12 months in order to apply - it just has to be documented that you will be unable to work for 12, or more, consecutive months.)

Who is eligible to apply for benefits?

ANYONE. You, me, your neighbor - anyone may apply for benefits. To be qualified to RECEIVE benefits, however, you must have medical documentation as stated above.

What should I tell Social Security?

Tell them that you are disabled. Make certain you state ALL of your conditions - physical and/or mental/emotional conditions. Social Security benefits should be decided on ALL information you give them - not just one or more disabling conditions you may have, but EVERY condition that is affecting your day-to-day living.

Where do I apply?

Go to your local Social Security office. If you live away from a major city, Social Security may send a representative to a nearby location. Call 1-800-234-5772 to obtain the location nearest you. If possible, apply in person. Let Social Security see you and the difficulties you may have moving around, seeing, hearing, understanding, etc. Don't exaggerate your conditions - just be truthful and let them see you. Answer their questions as fully as possible. Don't let their workers intimidate you - most of the workers will try very hard to complete most of the paperwork

WITH your assistance. Don't accept verbal statements that you don't qualify. Get anything that sounds like a decision IN WRITING.

What do I need to take with me to the Social Security office?

Take your birth and marriage certificates with you. Take your spouse's and child(ren)'s birth certificates and Social Security numbers with you. Have information available regarding your monthly (all) income and expenses as well as any previous marriages. Try to know where you have been employed for the past 15 years and what medical doctors/hospitals you have seen as well as what medications you are presently taking.

What happens if I am denied?

Appeal! Don't let the time expire (usually 60 days). Most individuals (more than half!) are denied at the first TWO levels of the appeal process. Don't get discouraged, and, above all, don't take the denial personally. Appeal!

I have other income (Long Term Disability; Pension/Retirement; Rental Income; etc.) so I don't need Social Security - right?

Probably this is a wrong statement. Is your Earnings Record frozen? Are you eligible for and receiving Medicare (or Medicaid) benefits? Do you know if Social Security coordinates with your other income? What if your other income stops? Don't let it be too late to get answers now! Don't let it be too late to be eligible for your Social Security Disability benefits! There's more at stake than a monthly check!

The information contained in this article is not meant to cover all parts of the law. For specific information about your case, please contact Social Security or a reputable attorney.

Vaccine, from page 1

spirochete.

The researchers also state that this protection is cross reactive with several isolates from the United States, but not with strain 25015. It is known that strain 25015 differs from other Bb strains in its OspA C-terminal amino acid sequence. No attempt was made by the authors to determine the vaccine's efficacy using European isolates, which are known to be much more variable than the American isolates.

What is most unfortunate about the way in which Yale researchers have co-opted the media is that a real difference of opinion exists within the research community with regard to the feasibility of using OspA as a base for developing a human vaccine.

This reality was not even suggested to the national media while interviewing the Yale researchers.

There are several arguments that can be made (all based on the scientific literature) to counter the assertion that OspA will produce a 100% effective vaccine:

- 1) Not all strains of Bb express the OspA protein.
- 2) DNA-DNA hybridization studies have shown that there exists only 82% homology between the various strains of Bb with regard to OspA.
- 3) Recombinant OspA only partially protects hamsters from infection with Bb.

See Vaccine on next page

Vaccine, cont.

4) The variability of OspA may make a vaccine derived from all strains impossible.

5) Bb is capable of antigenic variation of its major outer surface proteins through homologous recombination between plasmid-encoded genes.

In paper # 245, Bettina Wilske (University of Munich, Germany) states that about 90% of Bb strains tested express OspA. This means, of course, that 10% do not, and that a vaccine to OspA would be ineffective against all Bb. She also states that, of the strains tested, there exist 7 major serologic classes of Bb, 6 in Europe and one in America.

In paper # 243, Daniele Postic (Pasteur Institute, France), used DNA-DNA hybridization to differentiate three genomic species of Bb. In fact, one genomic species was so far removed from Bb, that he placed it in its own species, *Borrelia garnii*. This third species had significantly different OspA proteins from the others tested, indicating a wide variance amongst *Borrelia* with regard to OspA and OspB.

In paper # 251, Helmut Eiffert (University Hospital, Göttingen, Germany), showed that there exists only 82% homology amongst three strains of Bb with regard to OspA. This allows a wide latitude in the expression of the OspA protein. Additionally, he states that OspB was not expressed in his strain of Bb due to a OspAB operon inhibiting the expression of OspA. This same operon could be responsible for the failure of 10% of Bb strains to express OspA.

In paper # 274, Barbara Johnson (Brookhaven National Laboratory, NY) showed that recombinant OspA only partially protects hamsters from challenge by Bb-infected ticks. In her study, only 65% of hamsters were protected using the same method by which Dr. Flavell reports 100% protection of his mouse strain. It is

extremely important to realize here that mice and hamsters are not human and that success in one model followed by failure in another should engender debate.

In paper # 253, Diane Caporale (University of New Hampshire, Durham), reports on sequence variation in genes that encode for Osps. She states, "Pathogens like Bb need to survive long periods in their hosts in order to be transmitted to another host. Positive selection for variant outer surface protein molecules might be expected to arise, since new variants will temporarily escape immune surveillance." Her report suggests an ecological reason for variations in outer surface proteins. Again, this variability was not taken into account by the vaccine developers at Yale.

In paper # 214, Patricia Rosa (Rocky Mountain Labs, Hamilton, Montana), reports on numerous OspA mutants emerging after challenge with monoclonal antibodies to wild type OspA. She believes that this is accomplished by homologous recombination between OspA and OspB, a second outer surface protein.

In paper # 213, Ariadna Sadziene (Vilnius, Lithuania), reinforces the notion that Bb evades host immune response by mutating. Mutagenic variation was not considered in the Yale study.

In a paper entitled "An Outer Surface Protein is a Major T Cell Antigen in Experimental Lyme Disease in CB6F1 Mice," Andrew Pachner (Georgetown University Hospital) states, "OspA may have considerable heterogeneity in various strains of the spirochete. Should this heterogeneity be manifest at the level of the primary amino acid sequence and OspA prove to be a major T cell antigen in humans, this data might significantly limit the potential for vaccine development." It is clear that antigenic variation is at the center of a very important debate with regard to vaccine development.

It may even be true that OspB

exists for the purpose of creating Osp mutants that can evade host responses. It is also possible to theorize that mutated Osps may be responsible for seronegativity late in Lyme disease, that in fact researchers are looking for the wrong immune response after the organism has already changed.

There is no doubt a need to find a vaccine and a cure for Lyme disease. This devastating illness has ruined the lives of hundreds of thousands, worldwide. However, extremely preliminary efforts fraught with basic scientific questions about efficacy, should not be offered up to the public as if the plague can now be safely put to rest. Such irresponsible acts on the part of the media only lessen the voice of those now infected, for whom little to nothing is being done. I urge the national media to represent Lyme disease rationally, and not to succumb to sensationalism.

*Richard Lynch, Volunteer Director
Lyme Treatment News
17 Monroe Ave
Staten Island, NY 10301
Tel. 718-273-3740*

Southeast focus of vector study

Original article: Magnarelli, L., et al. Antibodies to Borrelia burgdorferi in Rodents in the Eastern and Southern United States. J Clin Microbiol, June 92, 1449-1452.

Antibodies to *Borrelia burgdorferi* (Bb), has been detected by ELISA in blood samples from mice collected in Connecticut, the Carolinas, Georgia, Florida, Alabama, and Mississippi, and on islands off Georgia and Florida. Seropositivity was highest (68.8%) in Connecticut, ranging down to 27 to 35% in the southerly states. The tick vector has not been clearly identified in the southeastern states, although *I. scapularis* and *A. americanum* in Alabama have been shown to harbor Bb, nor have the spirochetes been isolated and characterized.

Research

Multiple Sclerosis may be misdiagnosed as Lyme

by Kenneth Liegner, MD

Abstract: Difficulty of distinction between borrelial (Lyme) encephalomyelitis and multiple sclerosis.

Numerous cases, most new, some originally included in the 1990 45th INCDNCM series (but with further evaluation and treatment) demonstrate the problematic differentiation of these diseases. Clinically virtually indistinguishable in some cases, CSF parameters, special serologic tests such as anticardiolipin antibodies and immunofixation, presence or absence of oligoclonal bands and myelin basic protein, use of cutting-edge direct antigen detection methods (PCR for Bb-specific oligonucleotides in CSF; CSF antigen-capture immunoassay; RML antigen capture assay in urine), isolation of Bb in culture from CSF in BSK-II, epidemiologic considerations, extra-neurologic features, and response to antibiotic treatment allow correct diagnosis. That capable neurologists have diagnosed these patients as having multiple sclerosis, and have sometimes refused to alter their diagnosis in the face of compelling evidence for neuroborreliosis, highlights the likelihood that in many instances borrelial encephalomyelitis is being erroneously diagnosed as multiple sclerosis, depriving patients of potentially beneficial antibiotic treatment. Implications for individual patients and for public health are profound.

Fibroblasts protect Lyme spirochete from ceftriaxone in vitro

Original article: Kostis Georgilis, Monica Peacocke, Mark S. Klempner: Fibroblasts protect the Lyme disease spirochete, Borrelia burgdorferi, from ceftriaxone in vitro. Journal of Infectious Diseases 1992;166:440-4.

Studies have indicated that the Lyme disease spirochete can persist in the host for prolonged periods of time. Papers by Asbrink, Preac-Mursic, Nadelman, Snyderman, Stanek, and Schmidli, among others, have indicated that viable *B burgdorferi* can be recovered from tissues and fluids of patients years after the initial infection and after antibiotic treatment, even when the patients have high serum concentration of antibody to *B burgdorferi*.

This study was designed to examine the possible role of human skin fibroblasts in protecting *B burgdorferi* from the action of a clinically useful antibiotic, ceftriaxone. The experimenters also used spirochetes of different infectivity and several types of cells besides fibroblasts to narrow down the operating variables.

After 2 to 14-day treatment with a concentration of ceftriaxone at least 10 times the MBC, viable spirochetes were recovered from all cocultures of spirochetes with fibroblasts as well as cocultures with several eukaryotic cell types. Spirochetes were not able to be cultured from samples of glutaraldehyde-fixed (dead) fibroblasts, or from cell-free media. The researchers conclude that the presence of living cells is protective. The relative infectivity of the spirochetes as determined by persistence in a rodent did not affect the ability of the spirochetes to interact with fibroblasts. Noninfective strains cocultured with fibroblasts also survived the antibiotic treatment.

The research indicates that only living cells can provide protection to *B burgdorferi*, but the maximum duration of this effect is unknown.

Possible alternative explanations for the observations are ruled out as unlikely by the design of the experiment and the use of controls. The likely interpretation of the data has already been suggested by other research, and that is that the organism penetrates cells and survives in them. The researchers suggest future studies to define whether antibiotics with different modes of action and different ability to penetrate cells would be more successful at eradicating the spirochete.

Lyme causes immune cascade

by Tom Grier

The presence of *Borrelia burgdorferi* in the human body triggers the release of prostaglandin PGE₂ and this in turn triggers the release of lymphokine TGF beta. The TGF beta is an excitotoxin that turns off the helper T-cell, and turns on the suppressor T-cells, and thereby inhibits the B-cell antibody response. This cascade of events seems to end with the decreased macrophage response, leaving the immune system virtually ineffective.

This is further borne out in the mouse model. In experiments using both genetically immunodeficient mice and mice with induced immunodeficiency, researchers found that both sets of mice have exactly the same response to *Borrelia burgdorferi* after being injected as do the normal control mice. Whether or not the immune system is intact seems to have no bearing on the pathogenicity of the disease in mice.

Wisconsin authors write comprehensive overview

Original article: James J. Kazierczak, DVM, MS, and Jeffrey P. Davis, MD. *Lyme Disease: Ecology, Epidemiology, Clinical Spectrum, and Management. Advances in Pediatrics, Vol 39, 1992.*

This comprehensive review of the medical literature by a Wisconsin Public Health Epidemiologist (JJK) and the Wisconsin Chief Medical Officer and State Epidemiologist for Communicable Disease (JPD) contains a list of 256 references. The authors cover topics from historic aspects to vector control and personal protection. The CDC Lyme Disease Surveillance Case Definition is given in detail. Of particular interest is the description of symptoms of Lyme disease, which includes a wide range of dermatologic, neurologic, musculoskeletal, cardiac, ocular, and other manifestations. Among less commonly recognized manifestations noted are cases of lymphadenopathy, hepatitis, splenomegaly, orchitis, microscopic hematuria or proteinuria, nonexudative sore throat, and nonproductive cough.

The authors state that there is a paucity of pediatric research in Lyme. One study reported significantly lower incidence of the marker rash, erythema migrans, in patients under 20 years of age compared to older patients. Children, however, may be at increased risk of having arthritis, although in many cases it appears to be mild and attacks tend to decrease in frequency.

Several pages devoted to gestational and perinatal considerations raise more questions than they answer. Serious consequences, including fetal and neonatal death, have been reported in cases where the mother was infected during pregnancy. It is not known whether chronic Lyme disease preexisting the pregnancy is detrimental to the fetus, and whether asymptomatic women who are antibody positive for *B.*

burgdorferi are at increased risk for adverse pregnancy outcome. Scientists agree that pregnant women with symptomatic Lyme disease should be treated promptly with antibiotics, but the optimal treatment regimen has not been determined. Some physicians recommend IV therapy for pregnant women with disseminated disease. Nursing mothers who contract Lyme disease are advised to stop nursing for several days until antibiotics have had a chance to eliminate blood-borne spirochetes.

The authors point out that chronic Lyme disease may be caused by autoimmune mechanisms or spirochete persistence, or both. Patients with certain HLA alleles may be more genetically susceptible to arthritic syndromes and be more difficult to treat. It is not yet known whether autoreactive disease processes continue even after the organism has been eliminated.

Diagnosis is complicated by the fact that a significant percentage of clinically normal individuals within endemic areas are seropositive. Although long-term prospective studies have not been completed on seropositive, asymptomatic individuals, the authors suggest labelling such antibody response "residual," and consider these patients at risk for being misdiagnosed with Lyme disease should an illness similar to Lyme develop. They do not clarify how to differentially diagnose between Lyme and "Lyme-like" disease when titres are positive. They emphasize, however, that Lyme disease is a clinical diagnosis, and that seronegative Lyme disease does exist.

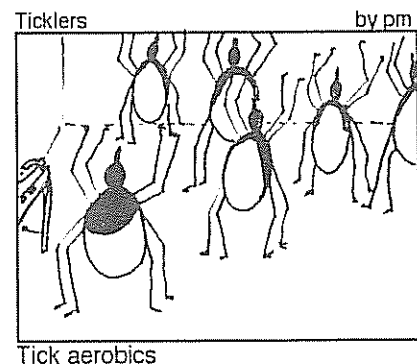
Monitoring antibody levels after

treatment is not recommended, since antibody titers may remain elevated or may decline, and titers do not correspond to clinical manifestations. In short, current serological tests should not be relied on for diagnosis of Lyme disease.

The authors point out that "optimal treatment regimens for the various manifestations of Lyme disease have not yet been definitively established. Additional large, randomized, prospective studies will be required." (p. 234) Treatment recommendations are summarized in a table. No treatment exceeds 30 days in duration, although there is a note that "optimal duration of therapy is ill-defined; some patients may require more protracted therapy." (p. 239) Prophylactic treatment of tick bites is discussed; except in the case pregnant patients, consensus appears to discourage the practice, especially in nonendemic areas. Treatment of asymptomatic, seropositive individuals is not recommended at this time, but this is an important issue deserving further study. [See article on prophylaxis on page 12]

The authors consider several forms of vector control. Each has drawbacks and may be counterproductive. The permethrin impregnated cotton appears to be effective and risk-free. Personal protection is of paramount importance, but directions on tick repellants and acaricides should be carefully followed.

The 256-item list of references can provide a handy guide to periodical literature on the subject of Lyme disease.



CDC recommends biopsy of lesions for diagnosis

Original article: *Biopsy and Culture of Erythema Migrans Lesions recommended As A Diagnosis Test In Lyme Disease. Reprinted from Lyme Disease Surveillance Summary, Vol 3, No. 2, March, 1992*

Bacteriologic diagnosis of Lyme disease by culturing clinical specimens for *B. burgdorferi* has long been considered as unrewarding, a definitive serologic test has not been identified, and the protean clinical manifestations of Lyme disease make it difficult to accurately classify sera for use in serologic test development.

This discussed during the First National Conference on Lyme Disease Testing in Dearborn, MI hosted by the Association of State and Territorial Public Health Laboratory Directors (ASTPHLD), the FDA and CDC. One of the concerns raised at the Conference was the extent to which deficiencies in the BSK medium being employed were responsible for the poor isolation rates of *B. burgdorferi* from blood and other body tissues. Since that meeting, CDC has supported research on the culture of aspirates and biopsies of erythema migrans (EM) lesions and blood of patients and has funded a study to monitor the development of spirochetemia in a primate model.

CDC supported research, as well as recently published data from Berger et al. (J Clin Microbiol 30: 359-361, 1992), demonstrate that *B. burgdorferi* organisms can be recovered from EM lesions in most untreated patients.

The technique for obtaining skin biopsies is minimally invasive and has been well tolerated and accepted by patients. We encourage its use. Requirements for culture are good quality BSK II medium and an incubator which can be maintained at a temperature range of 33 to 34 degrees C. Neither requirement should impose difficulties for most diagnostic microbiology laboratories.

We welcome *B. burgdorferi* isolates and serum specimens from patients with culture positive EM lesions for inclusion in our National Lyme Disease Serologic Reference Collections. These reference materials are being distributed, upon request, for test development and standardization. If you have material to contribute, please call the editors at (303) 221-6453.

Instructions for culture of borrelia from human tissues, including the storage and use of culture medium

Culture of *Borrelia burgdorferi* from clinical specimens is currently the only unequivocal way to diagnose Lyme disease. This organism can readily be isolated from biopsies or aspirates of erythema migrans lesions, with yields in the 50–80% range. Yields may typically be lower from other tissues or fluids, but relatively few studies have been reported. Preferable tissues and fluids for culture include skin (by biopsy or needle aspirate), cerebrospinal fluid (CSF), synovial fluid, fetal tissues, and placenta. Instructions for obtaining and handling specimens are as follows:

A. Storage

Frozen medium in individual tubes containing 4–5 ml BSK II. Keep media frozen at or below –20C. Medium will keep at least 6 months at these temperatures. DISCARD tubes of medium that have turned dark red at the air interface when thawed (a light red or pink color at the air interface is normal and these tubes are satisfactory for use).

B. Inoculation

Thaw tube of medium and, if time allows, bring to room temperature. As soon as possible after sample is collected, inoculate tube of medium

with approximately 0.5 ml skin aspirate, CSF, or synovial fluid. Biopsy material should be placed whole into the tube of medium. Label inoculated tube with (at minimum) patient name, specimen source (e.g., "skin biopsy"), date of collection, and date of onset of illness. Incubate cultures at 33C. Examine cultures by dark field microscopy every 1–2 weeks for 3–4 months.

C. Biopsy and needle aspiration of skin lesions

Skin biopsies typically are done with a standard 2–4 mm diameter punch instrument using standard sterile technique. Generally, the biopsy site is anesthetized (1 cc of a 1% lidocaine plus 1:100,000 epinephrine solution) and then disinfected (iodine tincture followed by isopropyl alcohol). Using a gentle twisting action, the punch instrument is used to cut the skin to a depth of 3–7 mm. The punch instrument is then removed. The skin punch is grasped with fine-tipped forceps, pulled gently away from the body, and snipped at the base with iris scissors. Hemostasis is achieved in the usual fashion; generally, pressure alone is adequate. The biopsy specimen(s) can be divided with a scalpel if more than one test is planned. Biopsy samples are inoculated directly into thawed culture medium.

A successful 2-needle, 2-person aspiration technique ("cutaneous lavage") was developed by Wormser et al. (JAMA, In Press), based on a similar method for use in rabbits described by Piesman et al. (J Infect Dis 1991;163:895–897). After local anesthesia and disinfection (as above), a 25 ga. 5/8" needle connected to a 3 cc syringe containing 2 cc of non-bacteriostatic normal saline is introduced intradermally and enough saline is injected to create a visible wheal at least 1 cm in diameter. While this first needle remains in place, a second operator introduces a 20 ga. 1" needle attached to a 3 cc syringe at a slanting angle into the

See **Biopsy** on next page

Regional News

New Yorkers form Lyme Disease Coalition

On September 19, 1992, Lyme Disease Support Groups and individuals involved in promoting Lyme Disease awareness in New York State voted to form an official statewide coalition. Fourteen counties were represented and are now part of the New York Lyme Disease Coalition (NYSLDC).

The NYSLDC will act as a patient advocacy group. Members seek to focus state and national public, governmental, and medical attention on the issues surrounding prevalence, diagnosis, and treatment.

New York State leads the nation in diagnosed cases of Lyme disease, and thousands of New York residents are now chronic sufferers. New Jersey and Minnesota are the only other states to have organized statewide Lyme disease coalitions.

Biopsy, cont.

wheel at a site opposite to that of the first needle. The second needle and syringe are then removed and used to collect fluid exuding from the second needle tract. The rate and amount of fluid obtained from the second needle site depends on the rate and amount of additional saline injected into the wheal through the first needle and syringe. Aspiration fluid is inoculated directly into thawed culture medium. A good location for isolation of spirochetes from erythema migrans lesions appears to be about 4 mm inside the outer margin (Berger et al., *J Clin Microbiol* 1992;30:359-361).

Missouri, continued from page 1

patients often get Jarisch-Herxheimer reactions with antibiotic therapy, and most importantly, show good clinical responses with antibiotic treatment. In addition, these patients easily meet published clinical diagnostic criteria for Lyme borreliosis. Tick and epidemiology studies have also been done and implicate Lyme. Masters wonders how the CDC can discount these data.

The clinical syndrome experienced by Dr. Masters' patients is consistent with others' experience. The incidence of Bell's palsies is similar (4.3% vs. 3.9% nationally). The incidence of second or third degree heart block is approximately .5%. The incidence of frank arthritis is less than that in Connecticut, but is similar to that experienced in other parts of the world. Dr. Masters does not believe that the clinical picture justifies attempts to classify Missouri borreliosis as a separate and distinct disease.

Since this spirochetal infection is thought to be spread by ticks, Dr. Masters has collected and examined hundreds of ticks. Live, motile spirochetes have been visualized which appear to be *B burgdorferi*, and which stain positive with monoclonal antibody H5332, believed by many to be species specific for Bb. Additionally, positive PCR results have been obtained on Missouri ticks. Unfortunately, the spirochete has proved difficult to grow, and Dr. Masters was advised that this fact invalidated his other data, and that the spirochetes could not be *B burgdorferi*. Cultures from three of Dr. Masters' patients have grown spirochetes. Two of the cultures died, but not before pictures were taken, and they tested positive with monoclonal antibodies and PCR. The third culture is still alive and is *B. burgdorferi*. However, the southern Illinois patient was briefly in Connecticut four months before the

culture. The patient had documented tick bites in southern Illinois and denies any tick exposure whatsoever in Connecticut.

The CDC conducted an epidemiologic investigation of reported Lyme disease cases in Missouri. They claim that the study did not establish the occurrence of *Borrelia burgdorferi* in either field-collected ticks or skin biopsies of case patients, nor in serologic testing of patients. Dr. Masters counters that the CDC did find spirochetes in Missouri ticks that were morphologically consistent with *B. burgdorferi*, as well as staining positive for *B. burgdorferi*, but that the spirochetes would not grow in BSK medium. He suggests that the fact that these spirochetes would not grow in a specific medium cannot refute these data, and that possibly spirochetes from different tick species might have different culture requirements.

The one supposedly irrefutable criterion for Lyme disease is the pathognomonic skin lesion, erythema migrans. The CDC on the one hand requires that cases meeting the clinical case definition be reported, and on the other, denies that Lyme disease exists in Missouri, calling the patients' lesions "Lyme-like." The CDC also concluded, as has Dr. Masters, that erythema migrans does indeed exist in Missouri. Dr. Masters claims that the CDC's current stance places him in a Catch-22 position. If the diagnosis is, in fact, a clinical one, as the CDC claims, then Dr. Masters' cases are Lyme. Moreover, how could there simultaneously be erythema migrans, but no Lyme disease in Missouri? Dr. Masters would like to know the difference between an erythema migrans lesion and a "erythema migrans-like" lesion. No one has attempted to answer that question.

According to Dr. Masters, "The clinical evidence is overwhelming, all clinical criteria are met, and yet the CDC doesn't have it serotyped. These

Continued on next page

patients don't care. I am trying to decide as a clinician whether it even makes any difference.... Do you really believe that there are two separate illnesses this much alike? If so, explain to this clinician and his patients what practical difference it makes."

The critical impact of the current situation is the difficulty patients may have in obtaining a diagnosis.

Physicians who read that there is no Lyme disease in Missouri are not likely to believe that their patients have it. And, if patients are not diagnosed, then they are not likely to be treated. It is well recognized that late Lyme disease can prove refractory to treatment. Third party patient reimbursement can also be affected. "What is the diagnosis code for 'Lyme-like'?" asks Masters.

Dr. Masters not only has his patients' interest at heart; he is defending his own reputation. The first four cases of Lyme disease he reported to the Missouri Department of Health were ordered removed from the computer without so much as a courtesy call. Dr. Masters resents the laws which require physicians to make the clinical diagnosis if no one is "going to act on that information. It is also unfair to then impugn the integrity and professional competency of those physicians who happen to see patients who meet the criteria which were set by the very organizations and government agencies requiring the reporting. They set the criteria, the doctor recognizes patients who meet those criteria and dutifully reports them according to law, and then is challenged for doing so. Those are not his criteria. If they don't like the criteria, then they should change the criteria - not challenge the physician who is ethical and honest and intelligent enough to recognize those cases that do diagnostically fit."

There is also the matter of the much publicized southeast Missouri tick spirochete "isolate" obtained by the CDC. The CDC collected ticks in southeast Missouri in 1991 and obtained what they thought was a

Missouri doc challenges the CDC

The Lyme Times sent the previous article to the CDC for their response. CDC spokesperson Dr. Dave Dennis replied to several points. We then gave Dr. Masters an opportunity to respond to the CDC points. CDC will be given an opportunity to continue the dialogue in the next Lyme Times. The following counterpoint is in their own words:

Dr. Dennis: 1) The CDC has always accepted the possibility that Lyme disease occurs in Missouri, and we have not stated otherwise. In fact, we have spent considerable effort and resources to answer this question.

Dr. Masters replies: The Southern Illinoisan newspaper (6-30-92) reported that Dr. Dennis "explained that a patient exhibiting a bull's-eye rash and arthritic symptoms would probably truly have Lyme disease in Connecti-

cut, where the disease is most prevalent. However, he said that someone exhibiting exactly the same symptoms in Missouri or southern Illinois probably doesn't have Lyme disease."

These patients are clearly and objectively ill and meet all known clinical criteria for the diagnosis of Lyme disease. If I diagnose these patients as anything else when they fit the published criteria for Lyme then I am in violation of the law (19 CSR

See Dialogue on next page

spirochete isolate. In spite of warnings from Dr. Masters to be cautious of jumping to conclusions prematurely, the CDC made inferences about clinical disease in Missouri from this factitious "spirochete." The Missouri Department of Health published in the Missouri Epidemiologist that it would be prudent to refrain from calling the Missouri illness Lyme disease. The Illinois and Ohio Departments of Health included "non-Lyme" inferences in mass mailings. The problem was that the CDC had also previously observed live, motile, antibody-positive spirochetes consistent with Bb in the ticks, and yet this "isolate" was non-motile and non-staining. The CDC temporarily ignored the history of PCR-positive ticks in Missouri. The "isolate" was PCR-negative. "Therefore, all Missouri non-Lyme or 'Lyme-like' theories based on this are specious," explains Dr. Masters. "The rush to discount the clinical evidence turned into a stampede all based on false conclusions from a single factitious isolate. I have extensive documentation of these events and

how they unfolded."

In early 1991, the CDC solicited a research grant application of Lyme epidemiology from the Missouri area. Julie Rawlings of the Texas Department of Health, Dr. Dorothy Feir at Saint Louis University, and Dr. Masters responded to this request with an \$18,000 grant application to the CDC to attempt isolation of *B burgdorferi*, study ticks, and correlate with clinical disease in Missouri. After some unusual delays in communications, in which Dr. Masters discovered that other people knew about the grant being rejected before he did, the CDC informed them that their project would not be funded. Less than one week later, Dr. Masters states, "I was approached by the CDC and the Missouri Department of Health to cooperate with them in essentially doing the same study. I had proposed that we identify patients of mine who had classic erythema migrans and that we collect ticks from those areas where those patients knew that they had been bitten, etc.

See Missouri, on page 53

Dialogue, cont.

20-20-020).

A front page article in USA Today (6-2-92) says Lyme "has been reported in 27 states where there is no evidence of infected ticks, he (Dr. Dennis) says, indicating possible misdiagnosis or that the illness was picked up while traveling." I protested this and asked him whether the patients might not actually have Lyme disease. Dr. Dennis stood by the article as it was written and refused to speculate further. That is exactly my point. My patients would appreciate some speculation as to why they are ill with a disease that is clinically indistinguishable from Lyme disease. This reinforces my experience that contrary to the world's literature, the truth is that Lyme is NOT a clinical diagnosis.

Dr. Dennis: 2) On invitation by the Missouri Department of Health (MDOH), the CDC conducted an epidemiologic investigation in 1991 of reported Lyme disease cases in that state. This investigation focused on patients reported to have erythema migrans, the rash characteristically found in acute Lyme disease. We were unable to make any association between these Missouri cases and infection with *Borrelia burgdorferi*, the spirochetal bacterium that causes Lyme disease, or any other infectious agent.

Dr. Masters replies: No association? I thought erythema migrans was prima facie evidence of association - at least that is what the world literature says. Secondly, 44% of Missouri EM patients' sera tested positive at the CDC using their whole cell sonicate ELISA while the controls were negative.

No association? The CDC is also aware of positive tests, including seroconversions that I have obtained from labs all over the country. These include IFAs, ELISAs, Lyme western blots from multiple labs, and PCRs from no fewer than seven different research labs. The CDC also reported seeing live

motile "borrelia-appearing" spirochetes in southeast Missouri ticks that stained variably with Bb antibodies, but did not stain. What are they?

No association with spirochetal disease? According to the CDC's own publications, H5332 staining confirms that spirochetes are Bb because H5332 is species specific. (Piesman, et al. JID 1991; 163:895-897) In Missouri apparently this means nothing.

Dr. Dennis: 3) Repeated attempts by CDC to isolate *B. burgdorferi* from patients in Missouri have so far been unsuccessful. In addition to the epidemiologic study described above, an entomologic study was conducted by CDC and MDOH in 1991 to collect and study ticks in areas of southeastern Missouri where reported human cases of erythema migrans reside. Cultures of these ticks were negative for *B. burgdorferi* or other spirochetal bacteria. Additional ticks and samples from patients are being collected for further study during 1992.

Dr. Masters replies: The CDC's new standard of "no culture, no existence" is incomprehensible. What if we had that for syphilis? When Kelly was working with the relapsing fever spirochetes, he had to use different media to culture different borrelia from different ticks. If the Missouri "borrelia-appearing spirochete" is being vectored by ticks other than *Ixodes dammini* (which it would almost have to be as no *I. dammini* have ever been found), then historical experience suggests that there are different growth requirements when the spirochete has adapted to a different tick species. BSK-II medium has been specifically developed to grow spirochetes from ticks such as *I. dammini*, is not a successful medium when a different tick species is involved (eg. *Amblyomma americanum*). To say that because observed live, motile spirochetes that stain with H5332, from non-*I. dammini* ticks in Missouri, do not grow in BSK-II, that they therefore do not exist is premature. We now know that there are multiple isolates of *B. burgdorferi* from Florida

and Georgia, Texas, Oklahoma, the West, the East, and the north-central US. This is in addition to the three we have grown. I don't believe that Missouri is somehow a magical no-spirochete zone.

In their paper "Susceptibility of Laboratory Rats to Isolates of *Borrelia Burgdorferi* from Different Geographic Areas: (Am J Trop Hyg, 42(6), 1990, pp. 596-600(89-340), Dr. Barthold et al. from Yale, made an interesting observation. One European Bb isolate (Germany GT) could not be recovered by culture in any of the inoculated rats, but induced arthritis in all rats. Maybe the CDC should inform Dr. Barthold that the GT isolate never existed.

Dr. Lane from California has indicated to me that he has encountered wild strains of Bb that he has been unable to maintain in culture. The CDC's position of totally discounting ALL clinical, serological, histological, etc. evidence for a myopic position of "No EASY" culture, no tick vectored spirochetal disease in Missouri" leaves me incredulous.

Dr. Dennis: 4) In mid-1991, Dr. Masters informed CDC that he had submitted approximately 35 skin biopsies from EM-like lesions of patients from his clinical practice to Dr. Russell Johnson of the Univ. of Minnesota for culture of *B. burgdorferi*. In addition, he stated that he also had submitted some 70 blood samples from patients from his practice with suspected Lyme disease to Dr. Johnson for culture. He stated that all of these approximately 105 samples of skin or blood had been culture-negative for *B. burgdorferi*.

Since July 1991, CDC has attempted to culture *B. burgdorferi* from more than 40 skin biopsies from apparent EM lesions of patients from south central or southeastern states where *Amblyomma americanum* is common, including some 20 skin samples from Missouri patients alone. These results have been uniformly

Continued on next page

negative. In contrast, *B. burgdorferi* has been cultured from 50-80% of biopsy specimens from EM lesions in studies in New York and Wisconsin.

Dr. Masters replies: True, except I submitted them as EM lesions, not "EM-like" lesions. I addressed this question above. But one more question: Since when is the criteria of easy culturability a *sine qua non* criterion for the existence of human disease? What about many other bacteria, viruses, syndromes, MS, rheumatoid arthritis, etc?

Dr. Dennis: 5) In 1988, Dr. W. Burgdorfer of the NIH Rocky Mountain Laboratories examined by dark field and/or immunofluorescent assay more than 1,000 *Ixodes scapularis* collected from white-tailed deer from 12 Missouri counties, including some from the southeastern portion of the state. All results were negative for spirochetes. PCR studies by CDC of *I. scapularis* collected in Missouri have also been negative, as have PCR of *A. americanum* from Missouri. These data are unpublished.

Dr. Masters replies: As long as we are using Dr. Burgdorfer's work, let's be more inclusive. Dr. Burgdorfer has also personally visualized spirochetes in Missouri ticks, but not in that particular study. In a 1991 summary of the first decade of Lyme Borreliosis, Dr. Willy Burgdorfer mentioned the Missouri experience in the following words: "The state of Missouri... appears to be a new area where disease is endemic. There... the lone star tick, *A. americanum* is suspected to be responsible for maintaining and distributing *Borrelia burgdorferi* or *Borrelia burgdorferi*-like spirochetes." (Burgdorfer, W. "First Decade of Lyme Borreliosis." Infection (Munich) 1991, 19; (4) 3-8.) (Ed.-This article was reprinted in *Lyme Times Vol 3 No 1*) At the recent V International Lyme Disease Conference, Li et al from Washington University and St. Louis University reported on Missouri ticks that were positive by both IFA and PCR (Abstract #315).

Conferences

Certain birds, ticks, mice are better vectors of Lyme

The 47th International Conference on Diseases in Nature Communicable to Man (INCDNCOM) was held at the University of British Columbia in Vancouver, August 16 to 19, 1992.

Durland Fish, from NY Medical College, presented data on tick-infested birds in suburban residential areas in New York State. The American robin as well as other common birds contributed significantly to the maintenance and distribution of *Ixodes dammini* in the environment.

Joe Piesman, CDC, Fort Collins, Colorado, discussed the differences in infectivity of three modes of infection with Bb. Animals were infected at a high rate by tick bites and by inoculation with homogenated ticks; the infection rate was much lower in animals inoculated with cultured Bb. Animals in the first group showed less frequent OspA and B antibody response.

UC Berkeley entomologist Robert Lane discovered that the East Coast tick, *Ixodes dammini* is a more

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Dr. Dennis: 6) *I. scapularis* has been shown to be a competent laboratory vector of *B. burgdorferi*, and unpublished data from the southern Atlantic coast, Oklahoma, and elsewhere suggest that these ticks can occasionally be found to be naturally infected with this spirochete (prevalence in the range of 1%). Ticks of this species feed on humans, but this seems to be uncommon. Given these facts, *I. scapularis* may well account for transmission of *B. burgdorferi* to humans in areas where both occur, although we would expect this transmission to be sporadic in pattern.

To date, however, there is no evidence that *I. scapularis* in Missouri are infected with spirochetes, or that this tick species has any association with Lyme-like disease observed in Missouri.

Dr. Masters replies: I agree. We have never implicated *I. scapularis* in Missouri. Epidemiological studies presented at the international conference strongly urged against *I. scapularis* vectoring disease to humans. What is left out is that other ticks occurring in Missouri are implicated,

not only by us, but by others (Abstracts #173 and #351).

Dr. Dennis: 7) We remain open about the possibility that Lyme disease caused by infection with *B. burgdorferi* occurs in Missouri. We also consider the possibility that disease caused by *Borrelia* other than *B. burgdorferi* may occur in Missouri. Continued research should provide clearer answers to these questions over the course of the next year or two.

Dr. Masters replies: I guess the term "open" is relative. My experience with the CDC over the past few years leaves me with the personal opinion that the CDC embraced "the possibility that Lyme disease... occurs in Missouri" with the same enthusiasm and objectivity that Karl Marx would in evaluating the possibilities that capitalism and free markets are good ideas.

To end on this note without allowing the CDC to respond, would be unfair, therefore the *Lyme Times* will continue this dialogue in the next issue, should the CDC wish to elaborate or introduce any additional points.

International, from pg 1

Epidemiology and Control. There was too much to listen to, too much to see, and much overlapping of the oral and poster sessions, likewise the poster discussion sessions, four or five of which were held simultaneously at the end of each day.

In his opening talk during the first Clinical Manifestations session, Dr. Daniel Rahn expressed a hope that the conference would highlight areas in which clinical investigation is needed. The clinical expression of Lyme borreliosis varies remarkably. There is often a preclinical stage of unknown length, where an individual may be infected but shows no symptoms. We do not know why different individuals exhibit different symptoms, or why the causative organism has a predilection to localize in certain organs and tissues. More study is needed to uncover the mechanisms for variation of clinical expression.

1) John Halperin discovered that

Tick, cont.

competent vector of Bb, even including the California strains. 61% of *I. dammini* picked up infection compared to 17% of *I. pacificus*. Some Ixodes genus ticks have high vector competence, others do not. Isolates from non-Ixodid ticks must be obtained and tested.

Dr. Lane's associate Chindi Peavey reported on the comparative infectivity of 6 tick-derived isolates of Bb for rodents. Using the B31 IFA to test ear biopsies on mice and hamsters, the researchers found that lab mice were more susceptible to infection, and were the only animals from which CA2 strain Bb were recovered. Questions raised which remain unanswered include: Can lack of infectivity be attributed to host specificity? or are certain spirochetes slower growing? or are spirochetes sequestered in organs other than skin? and what is the growth rate of Bb *in vivo*?

serum concentrations of quinolinic acid (QUIN) a soluble neuromodulator, presence of Bb DNA, and intrathecal production of anti-B burgdorferi(Bb) antibody (ITAb) may be useful diagnostic aids in certain cases of neuroborreliosis.

2) Hammers-Berggren et al. found that neuroborreliosis patients with complete clinical recovery after treatment may have persistent production of both serum and intrathecal anti-Bb antibodies. Patients were followed 11.5 months to 8.4 yrs. (median 1.4 yrs) after treatment.

3) Hungarian researchers reported on patients with polyneuropathies and/or cranial neuropathies. Subjective symptoms correlated closely with neurophysiological abnormalities as determined by standardized testing. Abnormalities caused by Lb are multifocal in nature such as is seen in mononeuritis multiplex.

4) Hal Dinerman and Allen Steere found that the signs of Lyme disease in 15 Lyme patients, treated usually with IV ceftriaxone, resolved, except 14 who continued to complain of fibromyalgia. These patients improved during treatment, then worsened. The authors state that persistent Lyme borreliosis was not the cause of this chronic pain syndrome, and that the temporary improvement was attributable to placebo effect.

5) Among Lyme patients studied in Italy, 18% of 168 were seronegative. 21% had erythema migrans; 26% had arthritis alone; 23% had neurologic symptoms alone. 84% of the patients had one symptom of Lyme borreliosis, 12% had two. The clinical pattern in Italy seems less serious than that in USA and Scandinavia. Questions from the floor raised the possibility of selection bias, and whether physicians would find what they do not look for.

6) German researchers report on the distinct manifestation of Lb in ocular inflammation. As in other ocular spirochetoses, the clinical spectrum is variable, including papillitis, retinal

vasculitis, choroiditis. Bb was cultured from a joint specimen 6 months after two courses of antibiotic treatment in one Bavarian patient with recurrent choroiditis.

7) Russian researchers reported a range of symptoms in 190 patients diagnosed with Lyme borreliosis on clinical and epidemiological findings. Most (177 pts) had erythema migrans or tick bite (186), however only 79 showed antibodies by ELISA or indirect IFA. 85 patients had neuroborreliosis, contrasted with 8 with Lyme arthritis. Within up to 2 years of treatment, 9% of the patients relapsed.

Treatment I

Dr. Steere introduced the session by stating that lack of response may be attributable to inadequate antibiotic therapy, with incomplete killing of the causative organism, affected nerves which may not heal, a possibly "parainfectious" phenomenon triggered by the infection (this would include Lyme arthritis and fibromyalgia), and finally, misdiagnosis. However, he conceded that he is currently trying one month of antibiotic treatment on patients who relapse.

8) 230 patients with presumed early LB were treated with 20 days of cefuroxime axetil (CAE) (118 pts) and doxycycline (DOC) (112 pts). Both drugs were statistically equally effective, however CAE caused more diarrhea and DOC more general adverse effects, including photosensitivity.

9) Connecticut researchers contacted by telephone one parent of each of 61 children who had been treated with antibiotics for Lyme disease 1 to 6 years (mean 3.6 yrs) previously. Seven of the children had had subsequent additional erythema migrans that resolved with therapy. None of the children were reported to have developed any neurologic, rheumatologic, or cardiac complications attributable to Lyme disease. The risk of developing long-term complications after appropriate (viz.

Continued on next page

10 to 30 days) therapy appears to be small. Further study is needed.

10) In a Swedish study of 29 patients antibiotic treatment was seen to heal the skin lesions of acrodermatitis chronica atrophicans (ACA), and improve pain and parasthesia, hyperalgesia, and dysesthesia of most patients. However neurophysiological symptoms (polyneuropathy) persisted and were thought to be sequelae rather than caused by active infection.

11) A German study determined that penicillin G sodium and ceftriaxone were equally effective in the treatment of neuroborreliosis in a group of 23 children, with no relapses during a 6-month followup period.

12) Russell Johnson's work on in vitro antimicrobial susceptibility of Bb to 17 agents shows that Bb is susceptible to the action of the macrolides, tetracyclines, semi-synthetic penicillins and late second and third generation cephalosporins. In vivo experiments generally confirm in vitro results, with the exception of erythromycin. Changing treatment schedules improved the in vivo activity of cefotaxime.

13) The efficacy of penicillin (PC) has been questioned. A study by Klaus Hansen, et al. was designed to determine the MBC to Bb, in vitro stability in BSK, and susceptibility to PC in animals. Penicillin is unstable during in vitro incubation. It is effective in experimental Bb infection when administered in divided doses. Previously reported MBC values for Bb and PC are erroneous.

14) Vancomycin was proposed as a possible alternative for the penicillin allergic patient. Other peptides are not effective against Bb. A synergistic effect was observed when using vancomycin and penicillin together in a mouse study.

Diagnosis I

Mark Golightly, Stony Brook neurologist, explained that the predictive value of the serologic tests for Lyme are enhanced by using clinical input. If clinical history is disregarded, the predictive value of a

positive serologic test is 6%. Using clinical input improves the accuracy of the test to 96%.

15) Dressler and Steere studied 100 patients with early or late Lyme disease using Western blot analysis. They achieved a sensitivity of 30% and specificity of 100% by requiring 2 of 10 IgM bands for early disease, and a sensitivity of 83% and specificity of 95% by requiring 5 of 10 IgG bands for late disease. The bands were at 18, 21, 28, 30, 41, 45, 58, 66, 74, 93 kDa. After years of infection, some arthritis patients react to 10 or more spirochetal antigens. German patients were found to respond to fewer antigens (<8, compared to Americans >12).

16) Antibody to 41kDa flagellar protein appears in early disease. Antibodies to OspA and OspB appear later. Use of recombinant OspA, OspB, and flagellin should enable a more specific test earlier in the disease.

17) One of the problems of serologic testing is the considerable indeterminate cross-reactivity on highly sensitive tests. Paul Fawcett's research group from Alfred I. duPont Institute in Delaware found that using enzyme assays prepared from P39 recombinant protein enhanced the specificity while preserving a level of sensitivity similar to standard tests for later stage disease.

18) Bernard Berger and Russell Johnson collaborated on a study to determine the feasibility of using Bb culture of erythema migrans lesions and perilesional (normal-appearing) skin for diagnostic purposes. They were able to culture Bb from 18 (86%) of 21 untreated patients with early Lyme disease. After various treatments, no patients were culture positive at the site of the original EM (this does not preclude survival of organisms in other sites).

19) A Danish study used a PCR assay to identify a fragment of Bb flagellin gene in urine and CSF of patients with neuroborreliosis. While urine appeared to be a more suitable sample

source, all samples obtained more than 4 weeks after therapy were negative. Authors believe results do not point to persistent infection.

20) Michael Millner of Univ. of Graz, Austria, found that 71.4% of the group had positive Bb intrathecal antibody, which was indicated as the most important marker for neuroborreliosis. However, Bb grew from otherwise totally normal CSF of children with symptoms of neuroborreliosis, showing that abnormal CSF parameters should not be required for diagnosis.

21) Swedish researchers measured intrasynovial production of Bb antibodies in patients with Lyme arthritis. About half (6 of 13) showed evidence of local IgG production of Bb antibody compared to the levels in the serum.

The following were presented at the Clinical Manifestations Poster Session:

22) A study of a small group of New York children indicated that the risk of developing Lyme disease after a tick bite is 4%, with a higher risk of 17% if the tick is engorged when removed.

23) Ed Masters of Missouri reported on two cases of secondary erythema migrans associated with treatment with IV cefotaxime therapy of disseminated Lyme disease.

24) Dr. Masters also reported on the clinical differentiation of erythema migrans from the bite of the brown recluse spider, important because early tests are not definitive.

25) Nowakowski et al compared demographic, clinical and immunodiagnostic features of patients with culture positive and culture negative erythema migrans. The only statistically significant variable was found to be antibiotic therapy, which limited the ability to culture Bb from EM.

26) A German woman with acrodermatitis chronica atrophicans (ACA) developed EM following a tick bite. Since both EM and ACA are consid-

See **International** on next page

International, cont.

ered as stage-dependent skin manifestations of one infectious disease, this patient obviously lacked species-specific immunity to Bb.

27) Since early treatment of Lyme disease may prevent late complications, Goldberg et al from NY Medical College urge that vesicular erythema migrans be added to the differential diagnosis of inflammatory vesicular rashes in the appropriate clinical setting.

28) A Spanish patient developed regressive long-evolution scleroderma-like lesions and neuroborreliosis over a 20-year period. Serum antibodies to Bb were found, and the symptoms improved with treatment with ceftriaxone.

29) withdrawn

30) Mori Schwartzberg et al of New Jersey described three cases of Lyme disease presenting as a polymyalgia rheumatica-like (PMR) syndrome. Lyme borreliosis should be considered in the differential diagnosis of PMR in endemic areas so that antibiotic treatment can begin and the use of corticosteroids avoided.

31) Twelve (46.5%) of 26 patients with persistent fatigue and arthralgia following treated Lyme disease met objective criteria for fibromyalgia or chronic fatigue syndrome.

32) Sigal and Patella of New Jersey describe 30 young people with symptoms of fibromyalgia who had been treated with various regimens of antibiotics. Because the therapy did not resolve the symptoms, the authors concluded that the symptoms were not caused by Lyme disease, but should be considered to be fibromyalgia.

33) Italian researchers found a different pattern of arthritis in Italy and United States. 67 (40%) of 168 Italian patients with Lyme borreliosis developed Lyme arthritis. Of these, arthritis was the only symptom in 64%.

34) Another Italian study suggested that in certain patients, psoriatic arthritis, ankylosing spondylitis, and

Reiter's syndrome may be triggered by infection with Bb. Antibody response analysed by Western Blot suggests a reactivity to intracellular antigens that might be shared with other bacteria.

35) Of 164 Hungarian patients with rheumatic complaints, 82% of those treated in the early stages of Lyme disease recovered. 50% of patients treated in the late stages recovered. Some patients required up to 3 rounds of antibiotic treatment. Some developed chronic rheumatologic problems.

36) Reisinger et al of Graz, Austria, described two patients who presented with bilateral tinnitus as the sole manifestation of *B burgdorferi*. One developed tinnitus 5 months following ECM and was seronegative; the other, 1 year following ECM and was seropositive. IV antibiotic therapy resolved the symptoms.

37) Researchers at Stonybrook discovered MRI abnormalities in almost 27% of 41 children with all of the major neurologic syndromes which characterize pediatric Lyme disease, including headache, behavioural changes, facial nerve palsy, papilledema, and diploopia. CSF parameters were not abnormal in all cases (mild pleocytosis in 12%, mildly elevated protein in 26.8%)

38) Stonybrook researchers also tabulated frequency of manifestations associated with neurologic Lyme disease in children. Headache, behavioural changes, and facial nerve palsy were the most frequent, with syndromes frequently found in adults (e.g. painful radiculoneuropathy) being rare.

39) Screening of Swedish patients admitted to the hospital for symptoms of stroke revealed 9% with positive titres to Bb. Neuroborreliosis may cause symptoms imitating cerebral thrombosis or transient ischemic attacks.

40) A 35-year old Spanish patient presented with sudden onset of vertigo. Subsequently she developed weakness of the facial muscles, blepharospasm, and eye problems,

including blurred vision. Other symptoms followed. Researchers suggest that an encephalitic lesion produced the peripheral palsy.

41) Polyradiculitis was found in 84% of 19 Spanish patients with neuroborreliosis (NB). The neurologic triad: radiculoneuritis, facial palsy, and lymphocytic meningitis was present in 21%, and in the authors' opinion, is definitive for NB, even without positive serology.

42) Electromyographic testing showed abnormalities in Russian patients with various disturbances of peripheral nervous system. Axonal structures of motor and sensory nerves, spinal motoneurons, and subcortical structures, and EMG-data were affected by LB infection.

43) New York Univ. School of Medicine researchers used quantitative EEG (QEEG) and a series of evoked potentials (EPs) to document electrophysiologic abnormalities in patients with definite and possible central nervous system borreliosis (CNSLD). 12 of 14 definite CNSLD patients had normal MRIs, but abnormal QEEGs were found in 10. QEEG and EPs may be useful in identifying the organic basis of cortical dysfunction associated with CNSLD.

44) Spirochetes similar to American Bb strain B31 were recovered from the blood of 2 or 6 Chinese psychiatric patients. One patient fully recovered after IV penicillin therapy.

45) Austrian researchers found that, compared to viral meningitis, Lyme borreliosis, although treated by high dose IV penicillin, may cause long term encephalopathy with severe neuropsychological deficits, predominantly in memory.

46) Hungarian neuroborreliosis patients with abnormal mental function as measured by several psychological tests improved rapidly with antibiotic treatment, proving that encephalopathy is caused by active infection.

47) Brian Fallon compared patients with non-Lyme arthritides to patients

Continued on next page

with Lyme arthritis. 66% of the Lyme patients reported having had a major depression during their illness, compared to 23% of the non-Lyme patients. Antibiotics alone are effective in treating some cases of LB depression. Mental health professionals should include LB in the differential diagnosis of major depression.

48) Dr. Fallon found that panic attacks and panic disorder were reported more frequently in patients with Lyme arthritis than in non-Lyme arthritis patients, but the difference was not statistically significant in his sample of 81 patients. He is continuing work on 200 patients.

49) 13% of cardiac transplant patients at Univ. of Minnesota had serologic evidence of prior infection with Bb. Bb is implicated in the pathogenesis of chronic cardiomyopathy in patients from endemic areas.

50) A self-referred walk-in Lyme Diagnostic Center was begun in Westchester County, NY, where Lyme disease is epidemic. 74 of the 1000 patients in the study were diagnosed with erythema migrans. 16% of the study group were treated with antibiotics. The authors recommend a late afternoon/evening clinic as convenient and efficient.

51) Tufts Univ. School of Medicine researchers followed a group of 113 patients with EM 10 to 15 years after they had been seen at Yale. Although all had been treated, a small but significant percentage of the group still had occasional brief episodes of joint pain, neurologic and eye problems.

52) Leonard Sigal presented possible underlying mechanisms which could explain persisting symptoms of Lyme disease in treated patients: true persisting infection, permanent tissue damage, sterile inflammation caused by dead organism, slowly resolving LD, factors related to chronic illness, "post-Lyme disease", and misdiagnosis.

53) A British study showed the differences in clinical presentations of LB over a period of years, before and after serologic testing became

available. Poor awareness may contribute to the lack of findings of certain syndromes.

54) Dorin Stuart et al. discuss the problems of diagnosis when physicians are faced by patients who have, or think they have, a highly publicized disease. Patient history and symptoms were relatively unhelpful, as patients who were considered to have definite, probable, and unlikely LD had similar presentations.

55) Two cases of meningoradiculitis due to LB were discovered only after unsuccessful neurosurgical treatment for vertebral disc herniation. Physician suspicion and a careful history along with blood tests may reveal differences.

55A) Audrey Stein Goldings reported a case of a patient who was treated for LB, and who had recurrences preceded by malar rash. The rash and accompanying symptoms disappeared with repeated courses of antibiotics. A maternal history of SLE suggests immune factors play a role in determining disease presentation.

55B) Ken Liegner reported a case of global cerebellar atrophy in LB in a 28-year old woman who was wheelchair bound within a month of an initial flu-like illness. She had repeated positive Lyme titers. In spite of treatment with IV and oral antibiotics for over a year her status remains unchanged. An immune-mediated process is suspected, although the mechanism of injury is unknown.

55C) Five cases of Lyme disease without erythema migrans from an endemic rural area of northern California were described. Differential diagnoses are suggested.

55D) Russian patients with LB frequently have rheumatic syndromes and neuropathy. The authors recommend that special attention be paid to vascular manifestations of LB, including livedo reticularis, digital vasculitis, ulcerated-necrotic vasculitis, all of which they treated successfully with antibiotics.

55E) A Russian study in an endemic area revealed that LD can manifest as early form (mainly EM), late typical LD (ACA, chronic cardio-borreliosis, etc.) chronic atypical LD (nonspecific symptoms with positive Western blot) and latent form.

55F) The Borreliosis Study Group from the Univ. of Graz studied two patients in whom Bb infection apparently caused some alteration of the coronary artery which resulted in myocardial ischemia, possibly in form of a transient vasculitis.

56) Stonybrook researchers conducted a randomized, double-blind, double-dummy, multicenter, national trial on the relative value of azithromycin (AZ) and amoxicillin (AM) in treating early Lyme disease. A one week course of AZ appears to be as effective as a 3-week course of AM in patients with EM without the flu-like syndrome, however with the flu-like syndrome, 3 weeks with AM was better. Patients were evaluated up to 24 weeks post treatment.

57) Klaus Weber et al compared azithromycin (AZ) and penicillin V for the treatment of EM. EMs cleared sooner with AZ, but more AZ patients had minor symptoms 3 months after therapy.

58) Another German study compared AZ to doxycycline (D) for the treatment of EM. AZ was given for 5 days, D for 14. During the 6-month followup period, AZ was superior to D in preventing sequelae. Sequelae did occur in both groups, however.

59) Czechoslovakian patients with a variety of dermatological manifestations of LB were treated for 10 to 28 days with a variety of antibiotics. While skin lesions resolved or improved in all but one of 371 patients, extracutaneous manifestations were observed in 14 patients after therapy.

60) Russell Cancellieri of New York studied 181 patients who had reactions (urticaria, non-urticarial rash, joint pain, abdominal pain, muscle aches, fever) following antibiotic therapy for

See **International** on next page

Angiology Congress to focus on borreliosis

The International College of Angiology will hold its 35th Annual Congress in Copenhagen in July, 1993. According to Chairman Robert Gasser, MD, of Austria, the Congress will be specially devoted to Lyme borreliosis in general, covering not only vascular, but all aspects of the disorder, including diagnosis, manifestations, and treatment. Lyme borreliosis constitutes an important part of cardiovascular diseases,

according to Gasser, and may cause perivascular inflammation, trophic disturbances, and other vascular problems.

All members of the International College of Angiology and other physicians and scientists who intend to register are invited to submit their original and unpublished papers. Papers must be submitted according to certain instructions which may be obtained from Denise Rossignol,

Executive Director
International College of Angiology
5 Daremy Court
Nesconset, NY 11767, USA Tel 516-366-1429 FAX 516-366-3609

The time allotted for each oral presentation will be 15 minutes and poster presentations will be 10 minutes. There will be ample time provided for discussion of both oral and poster presentations.

Award Certificates will be presented to the poster presentations reflecting innovativeness, originality, and scientific merit. There will be a Young Investigators Award Competition to one or more young physicians and/or research fellows whose research reflects new and relevant work in either the basic or clinical sciences of vascular diseases.

All accepted papers will be published in full in a special issue of the official ICA journal, the International Journal of Angiology.

For more information contact Denise Rossignol at the address above, or Dr. Gasser at Dept of Medicine, University of Graz, A-8036, Graz, Austria, tel. 0043 (0) 316/385-2863 [See Calendar on back page]

International, cont.

Lyme disease. 85% of the patients did not have IgE mediated sensitivity, but may have been experiencing a Herxheimer type of reaction.

61) Austrian researchers discovered positive serology for Bb in 21% of 42 patients with dilated cardiomyopathy. The damage was reversed and left ventricular function improved in most patients treated with antibiotics.

62) They also treated a patient with cardiac and other manifestations of LB with roxithromycin. While the heart symptoms resolved, the others did not, giving rise to speculation about the action of macrolides *in vivo*.

63) Ken Liegner reported the first case of culture-confirmed treatment failure in a case of neuroborreliosis from the United States.

64) Robert Gasser et al. found a success rate of 76% in a study of 17 cases of LB treated with a combined roxithromycin plus co-trimoxazole. Further studies are needed.

65) Ed Masters described a case of spirochetemia two weeks post cessation of 6 months of continuous p.o. amoxicillin therapy. The patient relapsed and then responded a second time to antibiotics.

66) In a New York study of 34 patients with late LD, treatment failures were more frequent in patients with arthritis or mixed

presentations. The most common residual complaints were joint pain and cognitive deficits.

67) Combined antibiotic treatment on a group of Hungarian patients resulted in 78.9% success, 15.1% improvement. Several different PO and IV drugs were given for 4 to 6 weeks.

68) Austrian researchers reported that it was not known, whether formation of cysts and granules observed on Bb cultures treated with various antibiotics was due to degeneration or "protective encystment" seen under adverse growing conditions.

69) Clarithromycin and its metabolite 14-hydroxy-clarithromycin demonstrate excellent *in vitro* activity against midwestern United States isolates of Bb, compared to doxycycline, amoxicillin, and cefotaxime.

70) Spanish researchers observed pathologic changes as well as decreased motility of Bb spirochetes incubated with various concentrations (MIC and subMIC) of cefotaxime. Tetracycline and erythromycin at 2X MIC did not produce any ultrastructural change.

70A) Edmondo Mandac of Ohio treated one patient with cefotaxime one week per month until Jarisch-Herxheimer reactions no longer occurred.

70B) Victoria Malara and Daniel Cameron found oral antibiotics were

effective in 73% of patients presenting with late LD. Using IV antibiotics on treatment failures raised the success rate to 91%.

70C) In another group of treatment failures, 82% of patients were well at the end of retreatment, suggesting initial failure to eradicate the spirochete.

70D) While on high dose oral amoxil, a LD patient progressed from first degree heart block to third degree heart block. With the institution of IV cefotaxime he regressed to first degree AV block.

70E) In over half of 25 patients previously treated with long term antibiotics Bb antigen was detected. This may be due to persistent infection or lengthy clearance of dead spirochetal debris.

This summary will continue in the next issue of the Lyme Times

Bb now blamed for well known diseases

by W. Kristoferitsch

Neurological Manifestations of Lyme Borreliosis. Infection 4 vol 19 .© MMV Medizin Verlag GmbH München, München 1991. Reprinted by permission.

Summary: After the isolation of *Borrelia burgdorferi*, the previously unknown causative agent of Lyme disease, two neurological disorders, Bannwarth's syndrome and acrodermatitis chronica atrophicans-associated neuropathy, which have been known in Europe for decades, gained new interest. With the availability of serodiagnostic tests, a chronic debilitating disorder - progressive borrelia encephalomyelitis - was found to be caused by chronic infection with *B burgdorferi*. Beside these typical manifestations, a growing number of publications about various neurological phenomena appeared, which were thought to be caused by *B burgdorferi*. This assumption was based in many cases on the results of serodiagnostic tests only. Considerations for causal connections were frequently lacking. While prior to the availability of serodiagnostic tests neurological manifestations of Lyme borreliosis frequently remained undiagnosed, we now face a tendency for overdiagnosis. The great variety of neurological manifestations in Lyme borreliosis - most of them can also be attributed to other conditions - and the high rate of seropositivity for *B burgdorferi* amongst the population living in endemic areas require strict criteria for the correct diagnosis of new and atypical neurological manifestations.

Introduction

Decades ago European neurologists described two well-defined neurological disorders, Bannwarth's syndrome [1-4], a painful meningo-radicularitis, and a chronic neuropathy in patients with acrodermatitis chronica atrophicans [5]. Although

preceding tick bites and erythema migrans as well as the favourable influence of penicillin were known for both disorders, Bannwarth's syndrome and acrodermatitis chronica atrophicans-associated neuropathy were primarily described as separate entities. In 1983 a previously unknown *Borrelia*, *Borrelia burgdorferi*, was found to be the causative agent for tick transmitted Lyme disease, a multisystem disease in the USA, which showed neurological similarities to Bannwarth's syndrome [6,7]. From 1983 on, when serodiagnostic tests became available, a growing number of various neurological conditions were attributed to *B burgdorferi*. This was frequently based on the results of serodiagnostic tests, which have to be interpreted with some caution, since in *B burgdorferi* endemic areas 10-30% of the clinically healthy population has been found to be seropositive [8,9]. In atypical cases sound diagnostic criteria therefore seem to be mandatory. In the following review we will discuss the typical and atypical neurologic manifestations at the different stages of Lyme borreliosis and present diagnostic criteria.

Neurological Manifestations in Early Disseminated Lyme Borreliosis

Early disseminated Lyme borreliosis or early infection (stage 2)[10] occurs days or weeks after the inoculation of the infectious agent. In this stage spreading of *B burgdorferi* in the patients' blood [7] or lymph [11] takes place. There is also clinical evidence for borrelial migration along peripheral nerves towards nerve roots [12]. Usually neurological stage 2 manifesta-

tions show a self-limiting course after several weeks or a few months, while chronic disease occurs in late or persistent infection (stage 3). Sometimes the classification in stages seems to be arbitrary and overlapping of stages can be observed.

Bannwarth's Syndrome and Other Typical Stage 2 Manifestations

The leading symptom of Bannwarth's syndrome, is severe and migrating pain lasting weeks to several months. Erythema migrans preceding or accompanying the onset of neurological manifestations was seen in up to 60% of patients. Pain was found to be the sole clinical symptom in almost a fourth of patients without antibiotic therapy [13]. In the other patients the onset of pain in followed by peripheral pareses of extremities, most frequently appearing as polytopic radiculoneuritis. The onset of pain may also be followed by cranial nerve affection - in most cases facial palsy - with or without additional pareses of extremities. In about 50% of patients facial palsy will occur bilaterally. Agitation and sleeplessness frequently accompany Bannwarth's syndrome but pronounced fatigue has also been observed [4, 13-16]. CSF shows lymphocytic pleocytosis and plasma cells will be found frequently. Elevated CSF IgG and IgM index values and oligoclonal banding in CSF electrophoresis can regularly be shown over the course of the disease, but may be missing in the early stage [13, 17, 18]. Results of serodiagnostic tests are negative in 10-50% of cases depending on the disease's duration [13, 14, 19]. Seronegativity does not exclude Bannwarth's syndrome. Nerve biopsy studies showed prominent lymphocytic perivascular infiltration of epineurial vessels and axonal nerve fiber degeneration. Borreliae have not been detected in nerve specimens so far [20,21]. Prompt relief from pain after adequate antibiotic therapy is another characteristic of Bannwarth's

See **Neurologic** on next page

Neurologic, cont.

syndrome. Without antibiotics the disorder will cease in most cases within six months [13, 15, 22]. Only mild residual symptoms, but no late chronic manifestations could be observed in follow-up studies of untreated patients [13, 22], although *B burgdorferi* specific serum and CSF antibodies as well as CSF oligoclonal bands were found to persist in several patients [22, 23]. On the other hand, Bannwarth's syndrome presumably preceded several cases of chronic progressive borrelia encephalomyelitis [24] and a few cases of acrodermatitis chronica atrophicans [10, 13].

Although CNS involvement is not mentioned in the original publication of Bannwarth [3], cases with Bannwarth's syndrome and additional signs of CNS involvement should also be considered as typical neurological manifestations of early disseminated Lyme borreliosis [4, 14, 15, 25]. Bannwarth's syndrome is a rare disorder in children. Characteristic stage 2 neurological manifestation in children are frank meningitis or facial palsy with CSF pleocytosis without the otherwise typical migrating pain (see also *Miller*, Lyme Borreliosis of Central Nervous System in Children, *Infection* 14, #4, reprinted in the Lyme Times, Vol. 3, #1).

Atypical Stage 2 Manifestations

Soon after serodiagnostic tests became available, a growing number of various neurological conditions different from typical Bannwarth's syndrome were thought to represent early disseminated Lyme borreliosis. Meningitis, myelitis or encephalitis without additional symptoms of Bannwarth's syndrome [16, 25, 26], cranial nerve neuritis or plexitis without CSF alterations [16, 27], Guillain-Barré syndrome [28], a stroke-like disorder due to vasculitis [25, 29-31], acute ataxia [28], extrapyramidal syndrome [32], hydrocephalus internus [3, 25], stiff man syndrome [33], pseudotumor cerebri [34], and focal myositis [35, 36] were all associated with Lyme

Table 1: Criteria for diagnosis of early disseminated Lyme borreliosis (neurological manifestations).

Clinical picture	Onset within 4 months after tick bite and/or EM	Lymphocytic pleocytosis	Improvement following antibiotic therapy	Serodiagnosis
Typical	+	+	+	
Typical		+	+	-
Atypical	+		+	+
CNS and/or meninges involved	or concomitant other definite stage II disease			(intrathecal synthesis)
Atypical	+		+	+
CNS and/or meninges not involved	or concomitant other definite stage II disease			

Other possible causes not demonstrable.

borreliosis. This broad and unspecific spectrum of neurological phenomena and the fact that seropositivity does not prove active infection, require strict criteria for diagnosing definite early disseminated Lyme borreliosis. A proposal for such criteria, is shown in Table 1. Cases which do not fulfill all criteria should be considered as possible Lyme borreliosis.

CNS manifestations in late Lyme borreliosis

Progressive Borrelia Encephalomyelitis

Ackermann et al. were the first to find in several patients with chronic progressive encephalomyelitis intrathecal *B burgdorferi* specific antibody synthesis [37]. The neurological deficiencies improved markedly on parenteral antibiotic treatment. In a later report on 44 patients with this rather rare disorder, cases with predominant spinal symptoms, mimicking chronic spinal multiple sclerosis, were differentiated from cases with predominant cerebral manifestations, presenting as multifocal encephalitis [24]. Identical cases have also been observed by other European neurologists [25, 26, 38-40]. Spastic para- or tetrapareses, ataxia, organic mental disorder, lesions of the seventh or eighth cranial nerve, and bladder dysfunction were the predominant clinical symptoms. CSF alterations were characterized by lymphocytic

pleocytosis, elevated total protein content, intrathecal synthesis of IgG, IgM and IgA, and oligoclonal bands. Most patients did not remember preceding tick bite, erythema migrans or symptoms of Bannwarth's syndrome and were treated from multiple sclerosis, tuberculous meningitis, fungal meningitis or chronic viral encephalitis before the correct diagnosis was determined. The demonstration of intrathecal *B burgdorferi* specific antibody synthesis is mandatory to establish the diagnosis but on the other hand does not prove active disease. It was also found in clinically healthy persons and may in these cases represent former exposure to *B burgdorferi* [24]. The occurrence of intrathecal specific antibodies in healthy persons with former Bannwarth's syndrome was interpreted as "serum scar" [22, 23]. Progressive borrelia encephalomyelitis is well defined and can be considered as typical late CNS manifestation of Lyme borreliosis. Fortunately it does not occur frequently [13, 15].

Lyme Encephalopathy

Halperin et al. found in 485 of American patients with definite late Lyme borreliosis marked fatigue and evidence of impairment of memory and intellectual function. These symptoms were reversible after antibiotic therapy. Focal CNS disease

Continued on next page

could not be detected and in most cases CSF was normal with the exception of intrathecal *B burgdorferi* specific antibody synthesis, although in low ratios. The authors concluded that this condition reflects either a mild encephalomyelitis [41] or a non-specific encephalopathy without CNS infection [42]. Similar cases were also described by Logigian et al. Most of them showed mildly elevated CSF total protein levels or slight intrathecal specific antibody synthesis or both. Oligoclonal bands were not found and only one patient showed mild CSF pleocytosis. Logigian et al. reported no major improvement after antibiotic therapy [43] (*Ed.-2 g IV ceftriaxone/day for 14 days*). There is still no overall consensus on whether chronic encephalopathy represents active disease or just a residual symptom [23].

Other and Atypical Late CNS Manifestations

As in atypical stage 2 manifestations, a growing number of different clinical phenomena have also been associated with late Lyme borreliosis. In cases without demonstration of intrathecal specific antibody synthesis the diagnosis has to be regarded with some skepticism. The clinical spectrum covers such different conditions as MS-like cases [44], demyelinating encephalopathy [45], intracerebral vasculitis [25,31, 46-48], psychiatric disorders [44, 49], presenile dementia [50, 51], primary lateral sclerosis [52], and lower motor neuron disease [53]. Recurrent acute meningitis [54], focal encephalitis [55], or myelitis [56] have been interpreted as Lyme borreliosis. Sound diagnostic criteria for CNS manifestations of late Lyme borreliosis are necessary (Table 2).

Peripheral Nervous System Manifestations in Late Lyme Borreliosis

Acrodermatitis Chronica Atrophicans-Associated Neuropathy

In 1966 Hopf found in about 40% of patients with acrodermatitis chronica atrophicans signs and

symptoms of peripheral neuropathy [5]. In a more recent study, clinical and/or electroneurographical signs of neuropathy could be detected in even two thirds of patients with untreated acrodermatitis chronica atrophicans [13]. The clinical spectrum ranges from "patchlike" hyperthesia, over distal asymmetric to distal symmetric polyneuropathy. The patients complain about mild to moderate pain or paresthesia. Neurological deficits are predominantly sensory and distally located. Pareses do not occur frequently and are slight. The course of the disease is chronic but mild. Sural nerve biopsy findings show, as in Bannwarth's syndrome, mononuclear perivascular infiltration of epineurial vessels with disseminated loss of myelinated nerve fibers [57]. CSF usually shows no pathologic alterations [5, 13]. After antibiotic therapy the clinical symptoms improved but not the neurological signs and electroneurographic data [20].

Chronic neuropathy in Late Lyme Borreliosis without Acrodermatitis Chronica Atrophicans

Halperin et al. found in 36% of American patients with evidence of late disseminated Lyme disease electroneurographical alterations consistent with peripheral neuropathy [58]. Most of the patients had symptoms of intermittent paresthesia, although clinical signs were not evident. The results of electroneurographical examinations of of nerve biopsies were similar to those found in acrodermatitis chronica atrophicans

Table 2: Criteria for diagnosis of late, chronic Lyme borreliosis (CNS manifestations).

- Chronic progressive CNS disorder of no other cause
- CSF lymphocytic pleocytosis and intrathecal IgG synthesis
- Reliable demonstration of intrathecal specific antibody synthesis
- Clinical or CSF improvement following antibiotic therapy

cans-associated neuropathy. Similar results were found by Logigian et al. in 19 patients months to years after onset of typical Lyme disease [43]. Additional encephalopathy was observed by both authors. Signs of mild neuropathy were also seen in morphea and lichen sclerosus et atrophicus, disorders possibly caused by *B burgdorferi* [59]. Diagnostic criteria for peripheral nervous system involvement in late Lyme borreliosis are listed in Table 3.

Table 3: Criteria for diagnosis of late, chronic Lyme borreliosis (PNS manifestations)

- peripheral neuropathy of no other cause
- Consistent seropositivity
- At least two of the following criteria
 - Concomitant other stage III disease
 - Improvement following antibiotic

Other Non-CNS Manifestations in Late Lyme Borreliosis

Wokke et al. reported on a patient with painless chronic weakness of both lower extremities, which was probably caused by inflammation of ventral nerve roots. Serodiagnostic tests were positive for *B burgdorferi* and spirochetes could be demonstrated in CSF, which showed lymphocytic pleocytosis. Prior to the correct diagnosis, lower motor neuron disease was suspected [60]. A case of chronic neuromyopathy has been associated with Lyme borreliosis by Midgard and Hofstad [46]. Nodular myositis was found in a few patients with acrodermatitis chronica atrophicans and can therefore be regarded as a further neurological manifestation of late Lyme borreliosis [61].

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See **Neurologic** on next page

Neurologic, cont.

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Lab tests help diagnosis, but are not the last word

by G. Stanek

Laboratory Diagnosis and Seroepidemiology of Lyme Borreliosis. Infection 19 (1991) No. 4 © MMV Medizin Verlag GmbH München, München 1991.
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Summary: Laboratory diagnosis of Lyme borreliosis is performed by direct detection of *Borrelia burgdorferi* in body fluids and tissue samples. This can be achieved by cultivation of the organisms, staining techniques, or demonstration of parts of the genome. Although the best aetiological proof in case of positivity, these methods cannot yet serve as routine techniques: they are too time consuming and expensive. Currently, the usual method for establishing the diagnosis of Lyme borreliosis is serologic testing (indirect detection). Immunofluorescence, hemagglutination, ELISA tests with whole cell antigen should be considered as screening methods. Assays with selected fractions of *B. burgdorferi* antigens or tests using selected recombinant antigens should be considered as more specific. Immunoblotting (Western blotting) may be considered as a confirmatory test. However, the interpretation of test results requires an experienced investigator. Laboratory diagnosis of *B. burgdorferi* infections of the central nervous systems (CNS) is the most highly developed method. Demonstration of intrathecally produced specific oligoclonal bands may very well prove the actual infection of the CNS and/or nerve roots. Seroepidemiological investigations identify neurological manifestations as the most frequent ones among European cases of Lyme borreliosis. The true incidence and prevalence of Lyme borreliosis, however, cannot be determined with current diagnostic methods and must await the development of methods to identify actual infection.

Introduction

The predominantly tick-borne spirochetosis of Lyme borreliosis (or Lyme disease) shows all characteristics of a cyclic infectious disease. There are local manifestations such as erythema chronicum migrans, which usually spread out from the site of the arthropod bite days or weeks after it. Constitutional symptoms, e.g. headache, arthralgia, malaise, fever, lymphadenosis, may occur and indicate the hematogenous spread of the agent. Then, organ manifestations may affect the nervous system, the heart, and the musculoskeletal system.

Besides a self-limited course of the infection there are chronic conditions which may involve the skin, nervous system, joints and heart, e.g. acrodermatitis chronica atrophicans, chronic progressive meningoencephalomyelitis, chronic arthritis and chronic heart disease, respectively. Serologic testing is currently the usual method for establishing the diagnosis Lyme borreliosis. However, there is a remarkable background of seropositivity in the healthy population which is up to 10% on average. Further, there are certain manifestations of Lyme borreliosis which are clearly identified clinically, but are seronegative. Efforts were made to isolate spirochetal organisms from seronegative and seropositive patients as well as from antibioticly treated and untreated cases.

Thus, interpretation of serological results must be made with caution and needs the communication between an experienced researcher and the clinician or the practitioner. It

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Serologic, cont.

is not yet possible to identify an actual infection of *Borrelia burgdorferi* quickly and convincingly by laboratory procedures.

Laboratory Diagnosis

Laboratory diagnosis is direct by demonstration of the organisms in body fluids and tissue samples either by cultivation or by staining techniques, and indirect by demonstration of specific antibodies in the blood, cerebrospinal or synovial fluid of patients who are supposed to suffer from Lyme borreliosis.

Direct Detection of *Borrelia burgdorferi*

Direct detection focuses on the demonstration of the viable organism or the organism as a whole or on parts of it. It comprises culture techniques, staining techniques, or demonstration of parts of its genome.

Cultivation

Cultivation of *B. burgdorferi* was repeatedly successful from skin biopsies (erythema migrans, acrodermatitis chronica atrophicans), cerebrospinal fluid, blood, and in some cases from borrelia lymphocytoma, circumscribed scleroderma and endomyocardium [1-4]. The culture medium widely used is the complex BSK medium which was originally described by A.G. Barbour [5,6] and slightly modified by various researchers. Depending on the material incubated that may contain many or just a few spirochetal organisms, borreliae grow to countable numbers of organisms in dark field microscopy within five days to eight weeks.

Staining Techniques

Direct demonstration of borreliae in tissues was performed with various silver staining techniques. An overview on the pathohistology of Lyme disease describes the use of Warthin-Starry and a modified Dieterle stain [7]. In Europe, Bosma-Steiner technique was used successfully to demonstrate spirochetal organisms in skin and heart biopsies

of patients with erythema migrans and acute Lyme carditis, respectively [8]. The original Steiner technique served to demonstrate spirochetes in endomyocardial biopsies of a patient with longstanding, dilated cardiomyopathy [4]. The immunofluorescence technique was applied on tissue sections to detect spirochetes specifically [9]. In addition, immunohisto-stains were used to demonstrate borreliae specifically in skin biopsies of patients with circumscribed scleroderma and lichen sclerosus et atrophicans [10].

Polymerase Chain Reaction (PCR)

Currently, the PCR is being developed for the detection of *B. burgdorferi* in body fluids and tissue specimens. Although a convincing technique in animal models [11,12], PCR was inferior to the yield of long-lasting cultivation procedures of blood from patients with erythema migrans [13]. These results may be due to the low number of circulating spirochetes in humans and, possibly, due to preparation techniques not sufficiently developed for these specimens.

Value of direct detection: Cultivation of *B. burgdorferi* from biopsies and body fluids is the best proof of its etiologic role in the underlying disease. However, it is not the final proof. Although unlikely, Borrelia detection and clinical disorder may display a coincidence in time and not in cause. This should especially be considered when Borrelia are isolated from chronic disorders. For routine purposes, both culture and staining techniques are too time consuming, and, if direct detection is not possible, one cannot exclude an infection with *B. burgdorferi*.

The PCR method is currently not sufficiently evaluated on human specimens and needs further studies. However, this method is expected to be developed for the quick and safe identification of an actual *B. burgdorferi* infection.

Indirect Detection

The aim of this is to demonstrate

the antibody response to the infection with *B. burgdorferi* during the course of the disease.

Heterogeneity of Strains and Cross Reactivity

A strain of *B. burgdorferi* is utilized as antigen. There is, however, a marked variation in the protein pattern in SDS-PAGE as well as reactivity pattern with monoclonal antibodies of strains from different sources and countries compared to the original isolate *B. burgdorferi* B31. The two monoclonal antibodies H5332 and H3TS [14], raised against the outer surface protein A (OspA) of the *B. burgdorferi* B31 strain will recognize almost all isolates of North America, but less regularly strains of Europe [15,16]. Recognition of strains by these two monoclonals led to the differentiation of three main serogroups of *B. burgdorferi*. When introducing other monoclonals raised against European strains, seven subtypes were suggested [17]. It was observed that strains isolated from the skin of erythema migrans patients were more homogenous than those isolated from cerebrospinal fluid [17].

With respect to the heterogeneity of European strains the question arose whether different strains of *B. burgdorferi* will influence the serological test results. Detailed studies on this were undertaken and have shown that there are marked differences in individual specimens [18]. Furthermore, antibodies to *B. burgdorferi* recognize epitopes or oral treponemes as *Treponema denticola*, *Treponema pectinovorum*, *Treponema phagedenis*, or *Treponema vincentii*. Absorption of serum specimens with T phagedenis may avoid interspirochetal crossreactivity [19]. However, *B. burgdorferi* possesses common antigens in the 60 kD molecular weight range and antibodies to these proteins may crossreact with many different bacterial species [20].

Assays for Antibody Detection

Serological testing is currently the

Continued on next page

usual method for establishing a diagnosis of Lyme borreliosis. Techniques used for serologic studies are the indirect immunofluorescence assay (IFA), hemagglutination tests, which utilize whole *B burgdorferi* cells. Also ELISA techniques utilize sonicated whole cell preparations. All these tests should be considered as screening assays as they cannot differentiate crossreactivity.

More specific assays are ELISAs that utilize selected proteins of *B burgdorferi* as antigen. A flagella enriched ELISA has been developed which is superior in detecting specific antibodies in early localized or disseminated infections [21]. Selections of immunodominant antigens of *B burgdorferi* offer the advantage of reducing cross-reactivity and raising sensitivity and specificity. These antigens are obtained either by elution or recombination.

Immunoblotting (Western blot) allows the detection of the reactivity of antibodies with proteins of *B*

burgdorferi separated previously by electrophoresis. The immunoblot has been considered as a possible confirmatory test. However, its interpretation is difficult. Reactivity patterns are very variable. A recent study describes "significant discriminating capacities and relatively high specificities... for the 94K, 30K, and 21K bands." The 41K and 60K bands were found to be not discriminative and their specificity will hold only at high intensity values by densitometry [22].

Serum Antibodies

In specimens from patients with early localized (e.g. erythema migrans), early disseminated (e.g. meningo-radicleoneuritis), or chronic manifestations, IgG response ranges between 30-50%, 80-98%, and 100%, respectively. A peculiar problem in the interpretation of results is that seropositivity is present in the healthy population. Seroprevalence ranges from 2 to 10% and up to about 45% in studies on specimens from healthy

blood donors and forestry workers, respectively. Such figures, however, may vary greatly depending on the cut-off and threshold levels used by the individual researchers. The latter are especially responsible for the unacceptable differences found when comparing test kits offered commercially.

By immunoblotting, epitopes of the flagellar protein of *B burgdorferi* are recognized in the localized and the early disseminated stage of Lyme borreliosis. In chronic manifestations, several proteins of *B burgdorferi* will be recognized by the patients' sera. Results, however, cannot simply be compared with "typical" patterns of reactivity as they cannot inform about an actual or bygone infection.

Antibodies in the Cerebrospinal Fluid

Laboratory diagnosis of *B burgdorferi* infections of the central nervous system (CNS) and/or the nerve roots is the most highly developed and will serve as an important diagnostic aid. For the

Table 1: Specimens for the laboratory diagnosis of Lyme borreliosis.

Manifestation	Antibody detection	Method.	Direct detection
Erythema migrans, acrodermatitis chronica atrophicans, morphea, lichen sclerosus et atrophicans, <i>Borrelia</i> lymphocytoma	5 ml serum at first visit and 8 weeks thereafter	ELISA, immunoblot	Skin biopsy for <i>Borrelia</i> culture, silverstains, immunohistochemical investigation, (PCR?)*
Cranial neuritis, meningitis, meningopolyneuritis, meningoencephalitis, myelitis, radiculomyelitis, radicleoneuritis	5 ml serum and 3 ml CSF** 2 x in 4 weeks (if indicated clinically)	ELISA, specific intrathecal antibodies, specific oligoclonal bands	3 ml CSF** for <i>Borrelia</i> culture, (PCR?)*
Lyme carditis, cardiomyopathy	5 ml serum at first visit and 8 weeks thereafter	ELISA, immunoblot	Endomyocardial biopsy for <i>Borrelia</i> culture, silverstains, immunohistochemical investigation, (PCR?)*
Lyme arthritis	5 ml serum at and 8 weeks after first visit	ELISA, immunoblot	Synovial fluid for <i>Borrelia</i> culture (PCR?)*

* PCR = polymerase chain reaction: this method is being developed for the specific detection of nucleic acid components of *Borrelia burgdorferi* in human specimens.

** CSF = cerebrospinal fluid.

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Serologic, cont.

demonstration of intrathecally produced specific antibodies, it is necessary to use serum and CSF samples taken at the same time. After determination of total IgG, both samples are adjusted to the unit of 1 mg/dl total IgG. Specific antibodies in the equilibrated samples are then measured by ELISA. The ratio of CSF/serum ELISA optical density values is established and considered as positive if it is equal or exceeds the value of 2.0 (= CSF/serum index threshold; theoretically, an index of >1.0 indicates intrathecal production of specific antibodies. To avoid greater inaccuracy due to dilution of the specimens to the IgG unit, an index of ≥ 2.0 is voluntarily chosen). For this procedure a minimum of 3 ml of each specimen is needed. However, a disadvantage of index calculation is found in borderline index values.

The currently most sensitive and specific indicator of the infection is seen in the demonstration of specific oligoclonal bands (SOB). For their demonstration, CSF proteins first have to be separated in the electric field either by isoelectric focusing (IEF) or by reversed phase electrophoresis (RPE) in a native gel. The separated proteins are then transferred to nitrocellulose paper which was previously saturated with borrelia antigen. Specific reaction will be made visible by a chromogen. SOB demonstration is a qualitative test and, thus, threshold independent, and a minimum of 10ml CSF would be sufficient. Further, SOBs are detectable earlier.

Value of indirect detection: In the first weeks of *B burgdorferi* infection only a certain number of patients will become seropositive with IgM and IgG antibodies. The diagnosis has to rely on clinical findings. In early disseminated manifestations with affection of the central nervous system, demonstration of intrathecally produced antibodies of a CSF/serum index ≥ 2.0 nearly proves the

infection with *B burgdorferi*; demonstration of SOB is currently the best proof of it.

In suspected cases of chronic *B burgdorferi* infection, such as Lyme arthritis, chronic Lyme carditis, or acrodermatitis chronica atrophicans, high serum antibody levels are regularly found. These, however, should be controlled for specificity by immunoblotting. Table 1 comprises the patients' specimens which can be utilized for the laboratory diagnosis of Lyme borreliosis.

Seroepidemiology

In Europe and other parts of the world, Lyme borreliosis is being increasingly recognized by physicians and serodiagnostic laboratories. However, it is currently difficult to present conclusive epidemiologic data. There are no widely accepted case definitions for the numerous clinical features due to or supposedly linked to infection with *B burgdorferi*. Clinical diagnosis of suspected cases of Lyme borreliosis requires confirmation by the demonstration of the etiologic agent and the recognition of its causative role in the respective disorder. Data from different European laboratories that concern ranking of the most frequently registered manifestation show that neurological disorders rank first and erythema migrans second. From a clinical point of view, however, there is no doubt that erythema migrans ranks first. This disorder constitutes about two thirds of all clinical manifestations of Lyme borreliosis. Since serological test results are often not reliable, the true incidence and prevalence of this disease cannot be determined and must await the development of specific and dependable methods to identify actual infection.

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Continued on next page

Flyer depicts tragedy of children with Lyme

A flyer with pictures of two young disabled people was received at our office as we were preparing our pediatric issue (Summer, 1992). We didn't have room for it, but we felt it deserved some space. Here it is.

Lyme Ticks Suck the Life Out of Our Kids!

We presently reside at a children's rehabilitation hospital. We have Lyme disease and cannot walk. One of us cannot talk and is atrophied from head to toe. We suffer terrible due to the severe head pain we have to endure twenty four hours a day.

Jessica (15 years old) has had Lyme for four years. Evan (13 years old) has had Lyme for 1 1/2 years. They are missing their childhood years as a result of their affliction with Lyme disease. They are just two out of many; there are countless others. It touches our kids much more severely than is ever written about, talked about, or known about.

Please Can Someone Help!

We are pleading for RESEARCH and a CURE! This is an epidemic and will strike someone you know.

Someone out there Help Us!!

Nothing is working. We lie in bed most of every day in pain.

HELP! HELP!

Children are supposed to have fun! Everyone thinks children have fun. Children with Lyme DON'T... AND NOBODY CARES.

We are not homeless, don't live on the streets, and are not starving in a foreign country. But we need your help nevertheless. We are your neighbors, your friend's children, and we could be your children. Lyme is indiscriminate.

NOBODY HEARS OUR CRIES... AND WE CRY EVERY DAY!

PLEASE HEAR OUR CRIES!

To: Scientists, Researchers, Physicians, People Who Can Help

From: Us, Our Moms and Dads, Brothers and Sisters, Grandmas and Grandpas

Lyme Life News
60 Tranquility Road
Suffern, NY 10901

Lyme community urges more research

In a letter to Conference chair-people Drs. Schulman and Johnson, patient representatives of the national Lyme community at the V International Conference noted six papers which confirmed the notion of persistence of infection, as well as seronegative Lyme disease. These included:

PAPER 63 - Culture-confirmed treatment failure of cefotaxime and minocycline in a case of meningococcal meningitis in the United States. K. Liegner

PAPER 65 - Spirochetemia two weeks post-cessation of six months of continuous P.O. amoxicillin therapy. E. Masters

PAPER 94 - Neuroborreliosis in children: Direct demonstration of Bb in CSF of seronegative cases. M.M. Millner

PAPER 143 - The fate of Bb in mouse macrophages: Destruction, survival, recovery. R.R. Montgomery

PAPER 149 - Persistence of Bb in chronic LD: Altered immune regulation or evasion into immunologically privileged sites? T. Haupl

PAPER 164 - Invasion of human skin fibroblasts by the LD spirochete, Bb. M.S. Klempner

Spirochetes have been demonstrated post-treatment, in one case after 6 months of continuous antibiotics, and there are indications of the ability of Bb to sequester in immunologically privileged sites. In addition, spirochetes have been demonstrated in seronegative individuals.

In their letter, patient representatives asked for more research on pathogenesis, long-term antibiotics and innovative drug delivery systems. Letter signers offered their services as participants in an NIH-sponsored effort to find a cure for chronic Lyme disease.

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Support Groups

The LDRC does not recommend or screen any support groups or leaders, but we hope that you will use this list to find someone in your state, who can give you information and support..

Arkansas

Fairfield Bay LDSG
Mary Alice Beer 501-884-3502
123 Shorthaven Lane
Fairfield Bay, AR 72088

California

Mid-Peninsula LDSG
Linda Goffinet 415-493-6391
801 Allardice Way
Stanford, CA 94305

Sonoma Valley Hospital LDSG
Karen McDonald, RN 707-935-5073
347 Andrieux St
Sonoma, CA 95476

Trinity County LD Network
Nancy A. Brown 916-623-3227
P. O. Box 707
Weaverville, CA 96093

Plumas/ Lassen Co LDSG
Luana Phinney 916-257-7853
698-640 Monte Vista Way
Susanville, CA 96130

East Bay LDSG
Steve Potter 510-540-8414
3010 Sacramento Street
Berkeley, CA 94702

Santa Rosa LDSG
Betty Owens 707-539-9395
5609 Yerba Buena Rd.
Santa Rosa, CA 95409

Living with Lyme Support Group
Nancy Adams, MFCC, 707-463-1305
Ukiah Counseling Site
813 S. Dora St.
Ukiah, CA 95482

Colorado

Rocky Mountain LD Network
Jan Derby 303-689-1299
8775 E. Orchard Rd. Suite 814
Englewood, CO 80111

Connecticut

Newtown LDSG
Jay McMahan 203-438-5289
70 Ridgeforest Dr.
Ridgefield, CT 06877

Ridgefield LDSG
Cynthia Onorato 203-438-0682
1 Westmoreland Road
Ridgefield, CT 06877

New Canaan LDSG
Eileen Wade 203-336-4280
474 Pemburn Drive
Fairfield, CT 06430
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Ellicott City, MD 21042

Massachusetts

Mid Mass LDSG
Claire D. Andrea 508-524-6316
4 Oak Drive
Upton, MA 01568

Martha's Vineyard LD Action Comm.
Patricia M. Arnold 508-693-4996
P. O. Box 112
Vineyard Haven, MA 02568

Minnesota

LD Coalition of Minnesota
Dan/Laura Sawyer 612-483-2464
3032 Sandy Hook Dr.
Roseville, MN 55113

Duluth/Superior LDSG
Barb Jones, RN 218-729-8557
5739 Rose Rd.
Duluth, MN 55811

Willmar Support Group
Mr. Lynn D. Zimmer 612-967-4306
14250 90th St. S.W.
Raymond, MN 56282

LD Network
Carol Bolte 612-574-0231
4448 Jefferson St NE
Columbia Heights, MN 55421
Joyce Tessmer
6890 Channel Rd.
Fridley, MN 55432
Lynn McMichael
1629 132 Ave. NE
Blaine, MN 55434

Missouri

Midwest LDSG
Kathy Cavert 816-252-6159
P.O. Box 3135
Independence, MO 64055

Michigan

Michigan LD Association
Jane A. Huegel 517-792-7170
231 Lockwood St
Saginaw, MI 48602

LDSG of Southwest Michigan
Meredith Spencer Foster 313-need #
2115 Georgetown Blvd.
Ann Arbor, MI 48105

South Eastern Michigan LDSG
Laurie Eichstead 313-231-9462
7734 Bishop Rd.
Brighton, MI 48116

LDSG of Southeast Michigan
Margaret Currier 313-563-3182
27104 Timber Trail
Dearborn Heights, MI 48127

Range Area LDSG
Peg Sutherland 906-932-2525
Grand View Hospital
N10561 Grand View Lane
Ironwood, MI 49938

Continued on next page

New Mexico

New Mexico LDSG
Helen Ingoglia 505-891-8533
830 Uranium Dr.
Rio Rancho, NM 87124

New Jersey

Lyme Disease Assoc. of No. NJ, Inc.
Sallie Timpone 201-288-5249
Kim Uffleman 201-391-4495
P. O. Box 20
Hasbrouck Heights, NJ 07604

Northwest New Jersey Regional LDSG
Cindi/Mary Ellen Monahan
201-625-0798
38 Old Middletown Road
Rockaway, NJ 07866

Take Tyme for Lyme
Diane Haskell 908-269-1544
110 Floral Ave.
Bayville, NJ 08721

LDSG for Teens and Parents
Christine Hatfield 908-922-8462
9 Cedar Terrace
Neptune, NJ 07753

LDNetwork of New Jersey
Carol Stelow 908-390-5027
43 Winton Rd.
East Brunswick, NJ 08816

New Jersey LDSG
Carol Gabriel 908-462-9021
1 Virginia Terrace
Freehold, NJ 07728

New York

Long Island Lyme Association
Diane Leary 516-797-LYME
P. O. Box 97
Plainview, NY 11803

Westchester Children's LDSG
Barbara Goldklang 914-769-6243
P. O. Box 495
Armonk, NY 10504

Orange County LDSG
Eileen Secor Gould 914-534-9957
P. O. Box 614
Cornwall, NY 12518

Southern Tier of W.N.Y. LDSG
Linda Chisholm 716-933-6416
95 Portville Ceres Rd.
Portville, NY 14770

Westchester LDSG
Betty Gross 914-591-7023
P. O. Box 82
Irvington-On-Hudson, NY 10533

Northern Westchester LDSG
Jill Branch 914-621-1602
P. O. Box 509
Purdys, NY 10578

Ohio

Upper Ohio Valley LDSG
Sharon Mieczkowski 614-264-2519
152 Orchard St
Wintersville, OH 43952

Mahoning LDSG
Marge Helle 216-782-4528
2904 Julian St.
Youngstown, OH 44502

Warren County LDSG
Linda Hory 513-885-7880
9931 Bunnell Hill Rd.
Centerville, OH 45458

Tri-State Lyme Vine Support Group
Linda Von Hoene 513-561-5794
5815 Bramble Ave.
Cincinnati, OH 45227

Greater Cleveland LDSG
Ann Hirschberg 216-235-4163
7644 Main Street
Olmsted Falls, OH 44138

Pennsylvania

LDSG - Pittsburg
Rene Landis 412-963-9395
309 Oxbridge Court
Fox Hall
Pittsburg, PA 15238

LDSG of Erie Co, PA
Deborah Abbott 814-866-3452
4301 W. Hershey Rd.
Erie, PA 16506

First Capital Lyme Network - S.E. PA.
Rosemary Grove 717-244-9694
R.D. #1 Box 22A
Windsor, PA 17366

Western PA Lyme Coordinator
Ronda Bartholomew 412-981-5728
7229 East State St.
Sharon, PA 16146

LD Network
Dave/Sally Coates 814-489-3898
RD #3 - 89-B
Sugar Grove, PA 16350

Mercer County Lyme Borreliosis
Information & Support Group
Ann Vesonder 412-962-7553
3336 Lamor Rd.
Hermitage, PA 16148

Tennessee

Mid-South LDSG
Cheryl L Leventhal 901-386-5648
5015 Sequoia
Memphis, TN 38117

Virginia

Northern Virginia LDSG
Sally Rabenko 703-709-0890
3207 Lockgate Ct.
Herdon, VA 22071

Central Virginia LDSG
Patricia M Arnold 703-832-3049
P. O. Box 567
Gordonsville, VA 22942

Wisconsin

Madison Lyme Resource Group
Jeanette Wheat 608-244-6425
1301 Menamonie Lane
Madison, WI 53704

Fox Valley LDSG
Beckie Murdock 414-984-3213
201 Sycamore Dr.
Black Creek, WI 54106
Monica Johnson 414-833-6617
824 Woodside Drive
Seymour, WI 54165

St. Agnes LDSG
Kathryn Montgomery 414-921-5588
833 Sterling Drive
Fond du Lac, WI 54935

LDSG
Jackie Johnston 715-277-3664
P. O. Box 306
Lake Tomahawk, WI 54539

Canada

Lyme Borreliosis SG of Ontario
John D. Scott 519-843-3646
365 St. David St. S.
Fergus, Ontario, Canada
N1M2L7

Telephone Tree

The Telephone Tree is simply a list of people who want to talk to others about Lyme disease. These people do not necessarily have any special training or knowledge. They are not screened in any way by the Lyme Disease Resource Center. However, we do feel that some people may find it helpful to be able to talk to someone else who shares similar problems. In this spirit, we offer you the Telephone Tree. If you wish to have your name, address, and phone listed, please circle YES and sign your name when you return the form on page 55.

Laura Slater
1272 Longtail Beach Rd
Little Suamico WI 54141
414-434-9721

Janet Horne
Rt. 1 8400 Hwy HH
Hallsville, MO 65255
314-696-2291

Sally Shields
RD 3 Box 287
Altoona, PA 16601
814-914-7740

Delores Cooper-Vance
1208 Sycamore
Farmington, NM 87401
505-327-2555

Marge Helle
2904 Julian St.
Youngstown, OH 44502
216-782-4528

Emma Mora
890 N. Bush St.
Ukiah, CA 95482
707-463-4461

Ida Lewis
W5830 690 TH Ave
Beldenville, WI 54003
715-273-5161

Suzanne Colter
900 Jefferson St.
Chillicothe, MO 64601
816-646-1936

Rori Hitt
1044 Viewpoint Blvd.
Rodeo, CA 94572
510-799-1310

Amy M. Sliker
32 Jones St. Apt 1A
New York, NY 10014
212-727-7265

Alice Barnes
1422 Tindall Ave.
Trenton, MO 64683
816-359-2771

Eudora Sommers
14 Daisy Court
Farmingdale, NY 11735
516-293-3298

Barbara Mohan
18 Michael Drive
Saratoga Springs NY
12866
518-584-4767

Sue Coffee
10 Saunders Hollow Rd.
Old Lyme, CT 06371
203-434-5641

Kathy McKensie
8760 Pierpoint Cove
Germantown, TN 38139
901-756-6600

Eldon Guymon
Box 997
Del Norte CO 81132
816-359-2771

Mae E. Dodson Taylor
2308 Hillman Place
Bowie, MD 20716
301-262-6461

Marion Rapp
514 Friday Road
Pittsburg, PA 15209
412-821-7866

Resources

Research Initiative

The National Lyme Community Research Initiative (NLCRI) is a Lyme patient organization dedicated to finding a cure for Lyme borreliosis. Organized into several sections, NLCRI will conduct clinical trials of alternative therapies for Lyme borreliosis. Some of the studies (i.e. Deer Velvet Therapy) do not use FDA-classified drugs; they are nutritional products believed to help the immune system to work better in fighting infection. Other trials will use drugs currently not approved by the FDA, for instance Liposomal Clarithromycin. In this case, Clarithromycin is FDA-approved, but the drug delivery system (the liposomes) is not. In these cases, the NLCRI will submit formal Investigational New Drug (IND) applications with the FDA and NIH.

As in the AIDS community, funding for such projects will come from three sources: pharmaceutical companies, governmental grants, and funding from the Lyme community. The NLCRI is interested in hearing from individuals or organizations that are familiar with these types of fundraising.

The NLCRI newsletter, Lyme Treatment News, is available for \$20-30/year, with waivers available. Write or call: 17 Monroe Ave, Staten Island, NY 10301, Tel. 718-273-3740.

New Gov't. booklet

A new 20-page public education booklet - Lyme Disease: The Facts, The Challenge - produced jointly by NIAID and NIAMS has just been printed. To obtain a free copy write to: Lyme Disease Booklet, NIAMS, NIH, Box AMS, 9000 Rockville Pike, Bethesda, MD 20892.

For new CDC leaflet, see page 7.

Continued on next page

You can be counted, too

Kathy Cavert of the Midwest Lyme Disease Support Group is conducting a national symptoms survey. The 4-page questionnaire contains over 100 questions about symptoms relating to different organ systems. Cavert encourages everyone to obtain a copy of the questionnaire by sending a SASE to PO Box 3135, Independence, MO 64055. She hopes that patients with CFIDS, lupus, MS, Alzheimers,

fibromyalgia syndrome, cardiac disease, depression and psychosis, ALS will fill out the forms.

"This will help me show the commonality of symptom history and make for a stronger case that our government needs to look at bacteria for an etiology of all of these diseases, especially the elusive spirochete.

Resource books

Lyme Disease 1991, a compendium of articles from various Lyme disease newsletters, is being offered at a special rate of \$7.00 per copy to public libraries. The public may obtain the book for \$11.95.

Lyme Disease Education Project
PO Box 55412
Madison, WI 53705

Discounts are available for multiple copies.

"It's essential reading for all patients who have Lyme disease. I recommend it to all my patients. It covers the majority of concerns that patients have and addresses comprehensively issues not well reviewed elsewhere."

Audrey Stein Goldings, MD
Dallas, TX

Handbook on Lyme Borreliosis, 5th Edition, 1992: a 41-page manual on the diagnosis and treatment of human Lyme disease. A valuable source of current information for physicians and Lyme patients. Written by a veterinarian with Lyme disease. This edition has Dr. Burrascano's March, 1992, treatment guide with his rationale for long term treatment, the paper by Dr. Lavoie from Conn's Current Therapy, and the case presentation from Dr. Drulle from Drug Therapy. As in previous editions, there is a thorough discussion of symptoms and diagnostic tests. Mail \$5 to Dr. Wendy Feaga, 13151 Triadelphia Road, Ellicott City, MD 21042.

See **Resources** on back page

Book Review

by Jonathan Marmelzat

Protect Yourself from Lyme Disease - The New York Medical College Guide to Prevention, Diagnosis, and Treatment

By Diana Benzaia

Dell Publishing 1989
Bantam Doubleday Dell
Publishing
666 Fifth Avenue
New York, New York 10103

Here is a book which has essential information needed to understand Lyme Disease. Its organization and readability set it apart from other commercial books on the subject. This book carefully explains some history of the "discovery" of Lyme Disease, and then clearly describes the illness and its many aspects. Dealing in depth with the issues of infection, symptoms, complications, diagnosis, and treatment, this book takes the mystery out of medical jargon. It defines all medical terms in plain understandable English. I am certain anyone will be better able to communicate with medical professionals after reading this book. There

is sincere emphasis on the need for prevention and early diagnosis, with information to help achieve these goals. It also addresses the issues relevant to late stage chronic Lyme sufferers, and gives valuable suggestions to these patients. Although it was published in 1989, most of the information seems to be up to date. At the end of the book, there is a useful list of medical research centers and government agencies which can be contacted for more current information. This book was compiled by the author from information gathered at the New York Medical College, Center for the Study and Treatment of Lyme Disease. It is reassuring to know that a medical institution is so thoroughly aware and involved in the study of this complicated and often baffling illness. I would highly recommend this book to anyone wanting to gain a better understanding of Lyme Disease. It is an excellent basic reference text for any library, and worth the \$4.50 retail price in paper back form.

Protect Yourself From Lyme Disease is available from LDRC mail order. See order form on page 54.

Missouri, cont. from page 33

basically the same proposal that the CDC and the Missouri Dept. of Health wanted to do, only they wanted to do it. For my patients' sake and to further knowledge, I cooperated fully with them. However, rightfully or wrongfully, I felt that they 'stole' my research idea."

Dr. Masters has had numerous patients who have symptoms consistent with a diagnosis of Lyme borreliosis, who have positive serologic tests for antibodies to *Borrelia burgdorferi*, who experience Jarisch-Herxheimer reactions to antibiotic therapy, and who respond favorably to antibiotic treatment. Ticks in his state been proven to carry

Borrelia burgdorferi, and they do bite humans. The only missing link appears to be whether these ticks are capable of transmitting Bb spirochetes to their human victims. The answer seems obvious, but in the meantime, until the controversy is resolved, people in Missouri would do well to avoid tick bites, and not get either Lyme or "Lyme-like" disease. The additional question must be asked: Is it the mission of the CDC to establish microbiological standards? How CDC officials are tacitly answering this question has grave implications for public health on the national level.

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Quantity	Description	Unit Price	Amount
	Lyme Disease, The Great Imitator How to Prevent & Cure It by Dr. Alvin Silverstein, et al.	5.95	
	Protect Yourself from Lyme Disease by Diana Benzaia	4.50	
	When You're Sick and Don't Know Why by Linda Hanner and J. Witek, MD	9.95	
	Lyme Disease My Search For a Diagnosis by Linda Hanner	8.95	
	Ticks and What You Can Do About Them by Roger Drummond, Ph.D.	4.95	
	Common Sense Pest Control Quarterly Managing Ticks - The Least Toxic Way by Bio-Intergal Resource Center	6.00	
	Learning About Lyme Disease by Jo Ann Heltzel, Ph.D.	3.75	
	Natural Health, Natural Medicine by Andrew Weil, M.D.	10.95	
	Stretching by Bob Anderson	9.95	

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Thank you

For helping us to attend the International Conference in Arlington last May, we thank:

- Stewart-Cole Travel
- Mary E. C. Crossley♥
- Jacques Jehly
- Option Care
- Pat Arnold♥
- Walter Prehn, MD
- Susan Harryman
- Kaiser Permanente
- Fairfield American
- Joan Meek

Thanks also to United Way of Sonoma-Mendocino-Lake for funds for new screens and photographs for our educational display. Since their debut at the conference, the display screens have been used several times for local presentations.

Editor's message

We appreciate all the support we have received. Our single, biggest frustration is not being able to do more. We are trying to set up workable systems before the demand gets any more overwhelming. We have recently completed a rudimentary mailing list database which should be sustainable by people with very little energy (I feel like saying, like Pooh, "by a bear with very little brain.") There is so much more to be done, if only there were more of us who were able to be active. Anyone who has access to a computer and can type, we can put to work. Do join us, even on an occasional basis. It is fun! We will continue to do this work as long as possible. However, our health and our families should remain our priorities.

This summer was a difficult one for one of our active boardmembers, who was hospitalized twice with pul-

monary embolisms, cause unknown. She has had difficulties with medications. Since she is also a major contributor to *the Lyme Times*, and is solely responsible for the support group leader publication, *Lyme Connection*, our accomplishments have consequently lagged sadly behind our ambitions. Our current major goal is to obtain another computer, monitor, and printer to make her work easier. Having my own computer has made so much difference in when I can work, and how much, and how conveniently.

A second glitch in this Fall's schedule was the dearth of electricity in the Mervine household. We have a solar-powered system with a hydro-generator for the rainy season. When the days grow short in a year of drought, our batteries get too low to permit us to run computers. Finally I moved my computer to town and ignored the demands of the household for a couple of weeks to get this issue out to you. We hope you enjoy it.

Clip and Mail Subscription Coupon

**PEOPLE MAKING A DONATION OF \$25 (IN US) OR \$35 (OUTSIDE US) WILL RECEIVE A YEAR'S SUBSCRIPTION TO THE LYME TIMES. MAIL TO: Lyme Disease Resource Center
PO Box 9510
Santa Rosa, CA 95405**

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How did you find out about the Lyme Times and/or the Lyme Disease Resource Center?

The Lyme Disease Resource Center is a tax-exempt organization. Your contribution is tax-deductible.

WAIVER

I am a person with Lyme disease. I would like to receive the Lyme Times but at this time am unable to make a donation because of extreme financial hardship.

Signed _____

Calendar

35th Annual Congress of the International College of Angiology

July 3 - 10, 1993
Sheraton Hotel
Copenhagen, Denmark

This conference will be devoted to Lyme borreliosis (see article page xx) All presentations must be in English.

For Call for Papers and Abstract Form or information contact:

Denise Rossingnol, Executive Director
International College of Angiology, Inc
5 Daremy Court
Nesconset, NY 11767, USA
Tel 516-366-1429
FAX 516-366-3609
OR

Robert Gasser, MD, PhD, FICA
Head, Borrelia Study Group
Universitätsklinik Graz
Dept. of Medicine
Auenbruggerplatz 15
Graz, A-8036 Austria
Tel. 0043 (0) 316/385-2863

First International Congress of Vector Ecology

October 3-8, 1993

Hanalei Hotel
San Diego, California
For information contact:
Society for Vector Ecology
PO Box 87
Santa Ana CA 92702

Resources, cont.

Lyme newsletters

Lyme Disease Surveillance Summary
Public Health Service
CDC
PO Box 2087
Fort Collins CO 80522

Lyme Disease Update Monthly
Mrs. Charlene Glover
1511 N Stockwell Rd
Evansville, IN 47715
Home Office Phone: 618-382-5293

Lyme Life Lines
Westchester County LDSG
PO Box 82
Irvington-on-Hudson, NY 10533

Lyme Lines
Building 31, Room 7A32
9000 Rockville Pike
Bethesda MD 20892

Lyme Report
c/o Home Nutritional Support
600 Lanidex Plaza
PO Box 243
Parsippany NJ 07045

Lyme Treatment News
17 Monroe Ave
Staten Island NY 10301
Tel. 718-273-3740

Lymelight
Lyme Borrelia Foundation
PO Box 462
Tolland CT 06084-0462

Midwest LymeAid
Midwest Lyme Disease Support Group
PO Box 3135
Independence, MO 64055

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Ames to Please Publications
325 Fresno Street
Coalinga CA 93210
209-935-0914

Vector Ecology Newsletter
Published by the Society for Vector Ecology
PO Box 87
Santa Ana CA 92702

Please send conference and other announcements for the Calendar to:

Editor
the Lyme Times
PO Box 1423
Ukiah CA 95482

Life is short, the art long, opportunity fleeting, experience treacherous, judgment difficult.

Hippocrates