LYME TIMES

Fall 2008
Number 53

Patient's Issue:

Two Standards of Care
Drug-Supplement Interactions
Yeast
Probiotics
Insurance Denials
Prevention
Co-infections
Symptoms Checklist
Burrascano Guidelines
Lab tests

About the LDA

The national Lyme Disease Association has many accomplishments:

- Published 1st educational on-line Powerpoint module: **How A Tick Can Make You Sick** for grades 6 – adult. Free, downloadable, tests.
- Helped endow Lyme & Tick-Borne Diseases Research Center at Columbia University; gave grant toward NYU Neuromuscular Center.
- Funded research nationwide published in *Emerging Infectious Diseases, Neurology, Proceedings of Nat'l Academy of Science, JAMA, Journal of Clinical Microbiology, Infection, Psychiatric Clinics of North America, Journal of Psychiatry & Clinical Neuroscience (2), Infection & Immunity, Jrnl. of Internat'l Neuropsychological Soc., JSTBD.*
- Provided research monies initiating genome mapping of several *Borrelia* strains & identifying organisms in ticks coast-to-coast.
- Held 9 CME-certified Lyme & Tick-Borne Diseases scientific conferences for doctors, 7 jointly sponsored with Columbia University.
- Met with CDC Vector-Borne Disease Division, Ft. Collins, CO, to discuss Lyme/TBDs in '07.
- Selected for Combined Federal Campaign for 2008, again on federal approved charities list.
- Partners with the Environmental Protection Agency PESP program−LDA strategies to educate & develop tools for schools/ families & people who access public lands are on EPA website.
- Presented Lyme educational briefings 2008 (sponsor, US Senator Dodd) to the US Senate HELP Committee & 2 for US House (sponsor, LDA in cooperation with House Lyme Disease Caucus) in DC.
- Initiated in NJ first law in the country to mandate Lyme disease teacher in-services, formulated first State-adopted Lyme school curriculum, and is a NJ professional development provider (credits for teachers).
- Published first brochure devoted to children with Lyme disease, **The ABC's of Lyme Disease**; published first book for children with Lyme**, Lyme Disease Is No Fun: Let's Get Well!** and published first on impact of Lyme in schools in a state school board journal.
- Provides free online dr. referral link.
- Administers *LymeAid 4 Kids* for children without insurance, supported by author Amy Tan.
- Partners with IDEXX, bringing Lyme disease in pets and humans to the forefront.
- Works with celebrities−Literati with Lyme (authors) & actor Mary McDonnell, Battle Star Galactica, LDA national spokesperson.
- Distributed ~ 1.8M pieces of Lyme literature.
- Has free incidence/case number color maps on website www. LymeDiseaseAssociation.org
- Has free LymeR Primer brochures/Tickmarks.
- Has 32 associated groups under its umbrella.

About CALDA

The California Lyme Disease Association (CALDA) is a non-profit corporation that serves as the central voice for all tick-borne disease issues in California and a supporting voice for national issues. Through advocacy and education of the public and healthcare professionals, CALDA seeks to prevent tick-borne diseases, encourage early diagnosis, and improve the quality of healthcare provided to people with tick-borne diseases.

Activities:

- Collects and shares information through the Lyme Times and websites
- Shares best practices with other state and national organizations
- Acts as a central resource for patients, physicians, and support groups
- Supports physician education
- Provides technical support for local education and advocacy efforts
- Builds community through networking and state online support groups
- Advocates for patients through legislation and political action
- Supports Lyme disease research

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LYME TIMES

Journal of the California Lyme Disease Association

Contents

ILADS Guidelines

Share the International Lyme and Associated Diseases Society (ILADS) diagnostic and treatment guidelines with your healthcare professionals. Download them from the ILADS website: www.ilads.org.

Editorial

Dear Readers,

If you are reading this, you or a loved one likely have Lyme disease or know someone who does. Your doctor may have told you, "We don't have Lyme in this area," or "You can't have Lyme, your test is negative." You may have suffered for years with another diagnosis – fibromyalgia, chronic fatigue, arthritis, MS – or any one of a long list of "Lyme mimics." The average Lyme patient is misdiagnosed for more than four years!

People with Lyme have a *political* disease. Different interest groups publish contradictory information that misleads and confuses us all. No surprise that you may have questions about your Lyme diagnosis or treatment.

Four years ago we wondered how to bring a packet of materials to newly diagnosed people. CALDA volunteers – people like you, patients or moms and dads of children with Lyme – wanted to make sure no one else suffered like they had.

Inspiration struck and we decided to reproduce some of the best materials for beginners between two covers. Voilà! The first Special Patient Issue of the Lyme Times was born. Other "special issues" followed, including the Special Insurance Issue. The series has proven enormously popular and (we hope) helpful.

If you are dealing with Lyme or any of the tick-borne co-infections, this issue provides basic information you will need to make informed decisions about your healthcare. If you still have questions about insurance coverage…or children with Lyme disease…or alternative and integrative treatments…or other topics not included in this issue, we encourage you to browse the CALDA website, www.lymedisease.org, and order those issues addressing your special interests.

You may have heard people say how they have met the most wonderful people through Lyme. Over the years, special people in the Lyme community have supported many patients in need out of the goodness of their hearts. You will find some of these folks in this issue. We are grateful for their wisdom, dedication and generosity:

- Doug Fearn, a member of the Lyme Disease Association of Southeastern Pennsylvania, which has printed and distributed over 200,000 copies of *The Basics,* now in its sixth edition;
- Joseph Burrascano, Jr, MD, whose experience with successfully diagnosing and treating over 10,000 patients is summarized in our excerpt of his newly revised guidelines;
- Family therapist Sandy Berenbaum, our Children's and Mental Health Editor, whose devotion to families and children is legendary;
- Minnesota physician Betty Maloney, MD, who lays out the evidence against the CDC-recommended testing algorithm;
- Dr. Dan Kinderlehrer, who addresses some of the problems of long-term antibiotic treatment;
- Lorraine Johnson, JD, MBA, CALDA's CEO, who designed many charts in this issue and shares her expertise in the legal realm. She formulated the definitive "two standards of care" position. Patients continue to depend on her advice for handling insurance denials.
- Dr. Leo Galland and Polly Hattemer provide invaluable information on drug interactions and probiotics.

We need your help, too. Wherever you live, please join CALDA to receive the Lyme Times and support our educational mission. Visit our website, sign up for our electronic newsletter, and participate in the online support group for your state. Get involved and work with us to improve the quality of healthcare for people with Lyme and other tick-borne diseases. The life you save may be your own!

Phyllis Mervine, Editor-in-Chief

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Prevention Tips

by Doug Fearn

What is Lyme Disease?

Lyme disease is a bacterial infection caused by the bite of a tiny deer tick that carries the infection. If not properly diagnosed and treated promptly, it can become crippling and debilitating.

Who is at risk for Lyme disease?

Anyone who works or plays outdoors is at risk. Deer ticks like cool, moist environments, like tall grassy areas around the edge of yards or along roads. They also like moist garden areas, around shrubs and in wooded areas. Outdoor workers, gardeners, campers, hikers, people who hunt or fish, golfers who stray into the rough, people who live in the city but go for a picnic in a park are all at risk. The list is endless. You can be at risk right in your own back yard. You can be at risk when mowing the lawn or picking up leaves in the fall. Children are especially vulnerable since they tend to run and play without caution.

You are at risk anywhere you see deer. Deer bring the ticks to your yard; birds and other animals also help transport the ticks. But the principal culprits in spreading the actual disease are mice. A deer tick infected with the Lyme bacteria and seeking a blood meal will bite a mouse. The tick transmits the Lyme bacteria to the mouse while feeding. Deer ticks can also transmit other disease organisms at the same time including *Babesia, Ehrlichia, Bartonella,* Rocky Mountain spotted fever, and *Mycoplasma*. Ticks are often described as cesspools of diseases. Other deer ticks sucking on the infected mouse will become infected, thereby spreading the diseases. Mice have been found with many deer ticks attached to them. The spring and summer months are the "Pryme Tyme for Lyme," although you can be bitten any month of the year when the weather is mild. Ticks are active when the temperature gets above 40 degrees.

[*Editorial comment: recent research has implicated other small animals such as squirrels and shrews as reservoirs of Lyme disease bacteria*.]

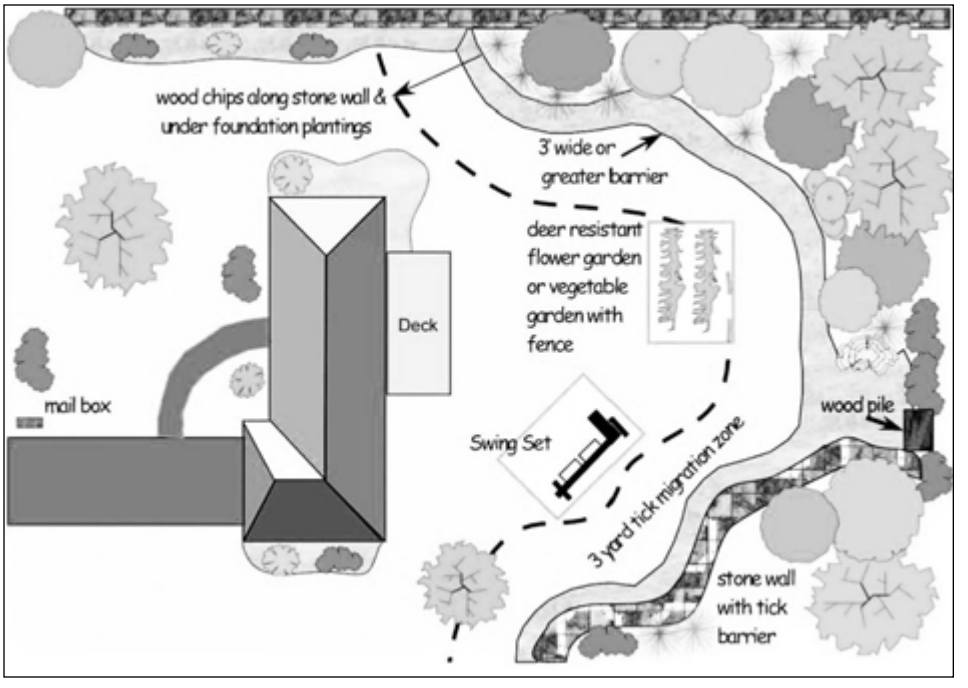
Prevention in your yard

- Keep your lawn mowed and cut down brushy areas. Remove enough trees so the lawn gets sunshine to create a less inviting environment for deer ticks. Remove brush and leaves around your house and the edge of the yard. Trim bushes away from your house. When working in your yard, avoid touching the ground with your bare hands. Avoid touching plants and bushes as much as possible.

- Modify your landscape to create Tick-Safe Zones. Ticks need moist environments; they die quickly where it's dry. So you can use a few tricks to keep them away from areas of the yard where you spend the most time. Laying down wood chips or gravel where lawns butt up against wooded areas can reduce the number of ticks on grassy areas by creating a drying barrier.

- Inspect pets closely before they come into your house as they are particularly vulnerable and frequently carry deer ticks. See your veterinarian for protective chemicals that will kill deer ticks.

- Use Damminix® tubes to kill the deer ticks.[1] Damminix® consists of biodegradable cardboard tubes with cotton balls inside that are treated with permethrin. Mice will carry the cotton back to their nest where the permethrin will kill the deer ticks but not the mice. It is highly targeted. Tests on Long Island, NY, have shown that Damminix® will reduce the number of infected deer ticks by more than 90% year after year. Maxforce® Tick Management System also targets mice and uses the insecticide fipronil.[2] Certified applicators are available in 13 states.



(Image courtesy Kirby Stafford III, Connecticut Agricultural Experiment Station)

- Have your yard sprayed with permethrin. This is a complement to the Damminix® tubes. Professionals spray only the tick habitat areas, edges of lawns, not the entire lawn, for example.

- Another prevention device is called a 4-poster. It is baited with corn and has four roller-applicators mounted on it. When deer eat the grain, they get dosed with an acaricide that kills the ticks on them.[3]

Other prevention tips

- Avoid tick-infested areas whenever possible. Avoid sitting directly on the ground or on fallen logs; use a blanket or other ground cover.

- When walking near bushes or trees, avoid touching them. Walk in the center of trails. Avoid sitting on stonewalls or woodpiles as these are places deer ticks are likely to be found.

Clothing

When outside, wear long sleeves, long pants, and closely-knitted socks. Look at the differences among various types of socks and make sure the fabric is tight enough so nymphal ticks cannot pass through them.

- Tuck your shirt into your pants and tuck your pants into your socks. This will help prevent a tick from crawling under your clothing and getting on to your skin. Wear light colored clothing and gloves. The light color makes it easier to see a tick crawling on your clothing or gloves. Wear a hat to protect your head from deer ticks especially when working around bushes.

- Consider wearing Rynoskin protective underwear.[4] It is made of a closely knitted but breathable stretch fabric that ticks apparently have difficulty penetrating. It is especially helpful for hunters and those outdoors when the weather is cooler. It is available in long-sleeved tops, long bottoms, socks, hoods and gloves.

- Spray your boots, socks, pants, sleeves, gloves, and hat with permethrin tick repellent spray.[5] Do not apply it to your skin and apply it outdoors. The permethrin spray has the same active ingredient as the Damminix® tubes mentioned above, only in a lower concentration. It not only repels deer ticks, but it will kill them. It is relatively long-lasting. Follow all label directions carefully.

What is permethrin?

Permethrin is a synthetic chemical developed to simulate the natural chemical pyrethrum that protects plants from insect attack. Permethrin is not a natural product. It is different from regular insect repellents in that it will kill insects and deer ticks as

The 4-Poster

Studies by Agricultural Research Service and cooperators have shown that after two to three years, use of the 4-poster technology will control from 92 to 98 percent of the free-living tick population around the devices. Depending on the size of the herd, each device will treat deer on approximately 40 to 50 acres.

[Photo by Scott Bauer, ARS]

well as repel them. Also, the labels state that one treatment lasts two weeks. It was developed in the 1970s by the Department of Agriculture and has been used successfully since then.

Skin protection

Avon makes Skin-So-Soft Bug Guard Plus IR3535®, but tests by Consumers Union and a group from the Mass General Hospital (published in the New England Journal of Medicine) showed this product not to be at all useful in repelling insects. DEET was reported to be the best repellent.[6] Insect repellents containing DEET are widely available and offered under many brand names. They can be used on skin or clothing. Many authorities suggest you use repellants with less than 10% DEET on the skin of children. All repellents should be applied to the skin carefully. Avoid getting the repellents in eyes. Adults should apply repellents to children. Follow label directions carefully. DEET repels insects by its vapors, so applying DEET to clothing can be effective.

After returning indoors...

After returning inside, do a careful tick check. Most deer ticks are tiny and may be hard to see. If possible, have someone else inspect you especially in the areas where it is difficult for you to see. Be sure to check your hairline. Parents should check their children whenever they have been outdoors and might have been exposed to ticks. Some parents give their boys a buzz haircut so it is easier to see a tick in the hair.

If you do find a deer tick attached, remove it carefully. Use fine pointed tweezers and grasp the tick as close to the mouth parts as possible. Pull gently straight out.
DO NOT put petroleum jelly, alcohol or any irritant on the tick or try to get the tick to release by putting a lit match on it. Any agitation might cause the tick to regurgitate the Lyme bacteria into you. Save the tick in a plastic bag or vial with a moistened cotton ball for identification and testing. After removing the tick, see your doctor promptly. If the tick is infected with the Lyme bacteria, early diagnosis and antibiotic treatment is the key to recovery. Delay will allow the Lyme bacteria to disseminate into tissue in the body where the antibiotics are less effective.

After returning inside, wash and dry your clothes immediately. Do not even let them lie on the floor since a deer tick might be attached and get loose in your house. Some people put the clothes in a trash bag then spray with permethrin and tie up the bag. This should kill the ticks or other insects before washing. Running the clothes through a timed 30-minute hot cycle in a dryer will also kill ticks. They cannot survive being dried out.

Have a great DEER TICK-FREE year outdoors!

Did you know?

DEET is an excellent mosquito repellent, but a very poor tick repellent. Permethrin causes ticks to curl and die on contact. In a field test conducted by the Minnesota Insect-Borne Disease Education Council in Jay Cook State Park in Northern Minnesota, they found that the permethrin products out-performed the DEET-containing tick repellents. A walking shoe was sprayed with Duranon 0.5% permethrin; three weeks later, it was tested against its matching mate that was sprayed with Deep Woods Off 35% DEET. The ticks that made contact with the Duranon shoe immediately rolled up and dropped off. The ticks on the soaking wet DEET saturated shoe continued to crawl unimpaired.

Tick Kit Sales Support Nonprofit

The Lyme Association of Greater Kansas City sells tick removal kits that include the Pro-Tick Remedy tick remover tool.

To order, send a check for $4 payable to Lyme Association to: Lyme Association, P.O. Box 25853, Overland Park, KS 66225.

Adapted with permission from the booklet "The Basics," published by the Lyme Disease Association of Southeastern Pennsylvania, www.lymepa.org.

References

1 Damminix is manufactured by EcoHealth, Inc., 110 Broad Street, Boston MA 02110; Tel: 617.742.2400.
2 Maxforce - See www.maxforcetms.com
3 The 4-poster can be obtained through the American Lyme Disease Foundation, Inc., Mill Pond Offices, 293 Route 100, Somers, New York 10589; Tel: 914.277.6970 Fax: 914.277.6974. For more information see www.aldf.com.
4 Rynoskin garments can be ordered from Har-Son, Inc., PO Box 10772, Midwest City, OK 73140 or by calling 866.934.7546, 405.737.2494, or fax 405.737.2478. For more information see www.rynoskin.com.
5 Permethrin spray is available under several brand names including Sawyer, Duranon, and Permanone. It can be found in retail stores such as REI and veterinarian offices. It is also available through the manufacturer's website www.tickinfo.com or call 800.749.8425.
6 Sprays containing DEET are widely available under many brand names including: OFF!, Deep Woods OFF!, Cutters, and Ben's. Most authorities suggest you use only sprays containing less than 10% DEET for application to children's skin.

Know Your Tick Facts

American Dog Tick — ***Dermacentor variabilis***

The American dog tick can transmit Rocky Mountain spotted fever, Tularemia, Ehrlichiosis (anaplasmosis), and tick paralysis.

Soft Tick — ***Ornithodoros***

Soft ticks do not have the hard shell and are shaped like a large raisin. Soft ticks carry tick relapsing fever.

Ixodes pacificus — **Western Black Legged Tick**

The western black legged tick is prevalent on the West Coast. It transmits babesiosis, Lyme disease, bartonellosis and ehrlichiosis.

Ixodes scapularis — **Deer Tick**

The deer tick is prevalent on the East Coast and transmits Lyme disease, ehrlichiosis, babesiosis, and bartonellosis.

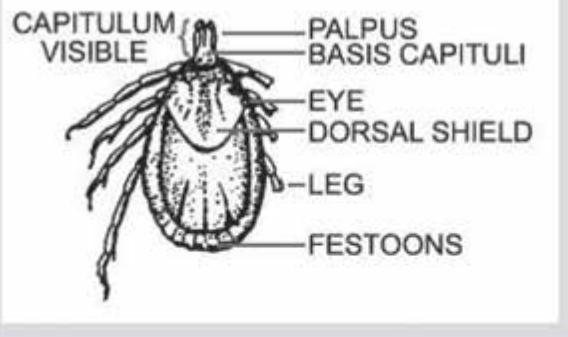
Brown Dog Tick — ***Rhipicephalus sanguineus***

The brown dog tick carries Q fever.

Rocky Mtn Wood Tick — ***Dermacentor andersoni***

The Rocky Mountain wood tick transmits tularemia, tick paralysis, Rocky Mountain spotted fever, Q fever, and Colorado tick fever.

Identifying features on Pacific Coast Tick
Dermacentor occidentalis



Lone Star Tick — ***Amblyomma americanum***

The lone star tick is prevalent in the Southwest and can transmit Rocky Mountain spotted fever, tularemia, ehrlichiosis, Q Fever and tick paralysis as well as *"STARI,"* an illness identical to Lyme disease, caused by *Borrelia lonestari.*

The Pacific Coast Tick is prevalent in the West and Southwest. It can transmit Colorado tick fever virus, the rickettsia of Q fever and Spotted fever as well as the bacterium that causes tularemia. It is known to cause tick paralysis in cattle, horses and deer. Bite wounds are commonly mistaken for wounds caused by biting insects and spiders.

The species of bacteria among the tick-borne pathogens are diverse. This complicates diagnosis because current antibody tests are species-specific. Fifteen tick-borne bacterial pathogens have been identified worldwide, including 3 species of ehrlichia, and 4 or 5 of *B. burgdorferi*. Scientists have not identified all of the pathogens that ticks may carry.

It's Lyme Time!

Be Tick Aware!

1 Walk in the middle of trails; avoid sitting on logs and leaning on trees.

2 Wear a hat,tuck in hair, if possible.

3 Wear a long-sleeved shirt fitted at the wrist.

4 Wear shoes, no bare feet or sandals.

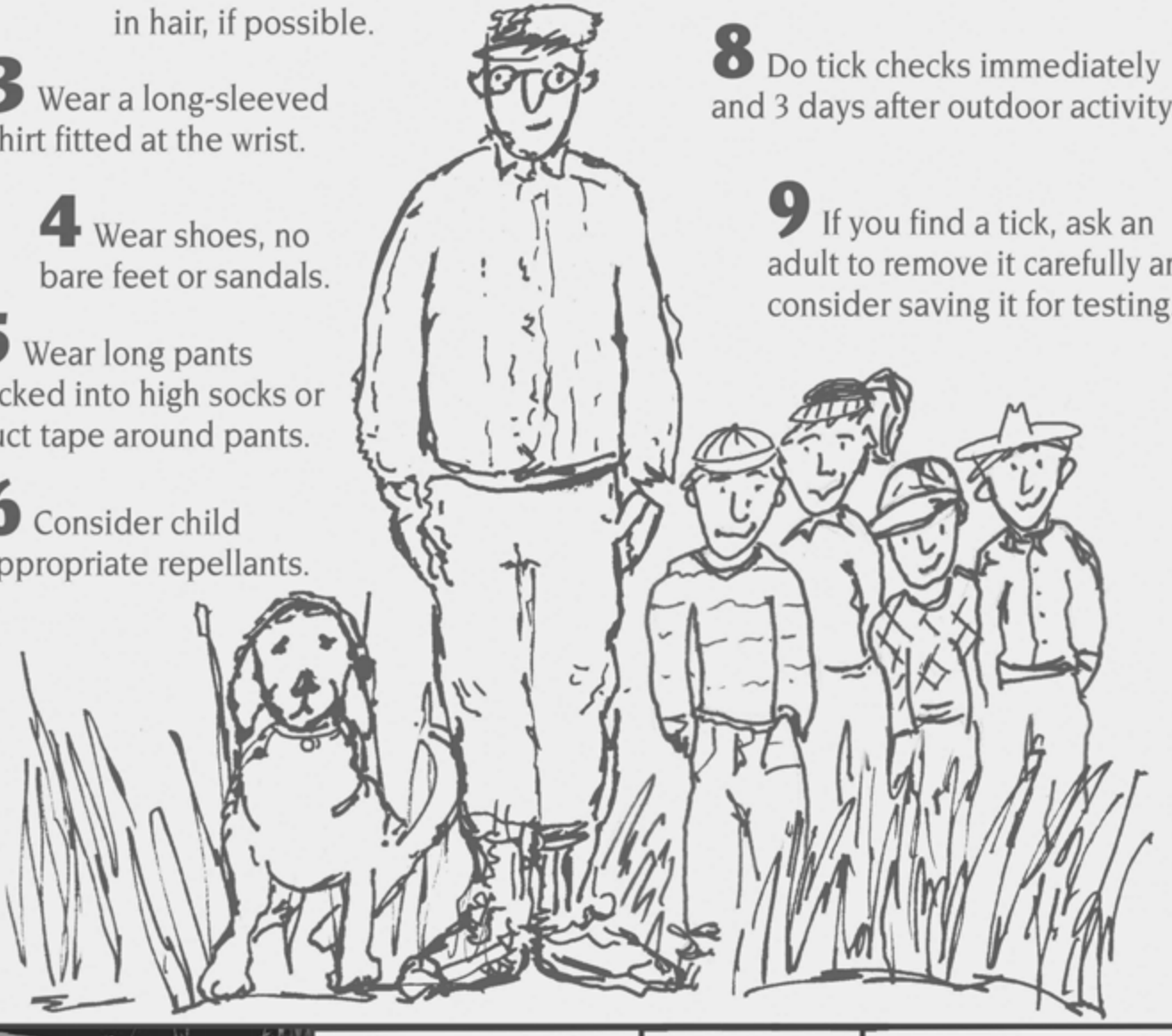
5 Wear long pants tucked into high socks or duct tape around pants.

6 Consider child appropriate repellants.

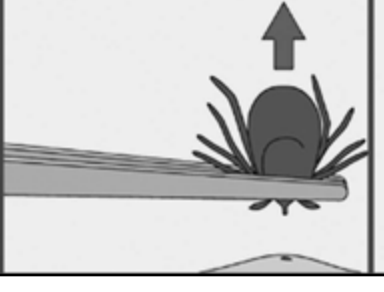
7 Wear white or light-colored clothing to make it easier to see ticks.

8 Do tick checks immediately and 3 days after outdoor activity.

9 If you find a tick, ask an adult to remove it carefully and consider saving it for testing.



Lyme Disease is transmitted by a tiny tick, most often the size of a poppy seed.



Remove tick with tweezers. Pull straight out as close to the skin as possible. Save tick in container and call doctor.

California Lyme Disease Association
www.lymedisease.org

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The Basics

by Doug Fearn

Answers to the most commonly-asked questions

Q. What is Lyme disease?

A. Lyme disease is a bacterial infection, most commonly contracted from a tick bite, that may initially cause a flu-like sickness. Untreated, or inadequately treated, it may cause long-term, persistent illness that can affect many systems of the body. Other tick-borne diseases are often contracted at the same time.

Q. How do you get it?

A. Lyme Disease (LD) is spread primarily through the bite of the deer tick in the eastern U.S., and the black-legged tick in the western U.S. The Lone Star tick, prevalent in the South and Midwest and spreading elsewhere, has also been associated with Lyme disease. Some researchers believe that other ticks and some biting insects such as mosquitoes, fleas, biting flies, and lice may also transmit LD. Babies may be born infected if the mother is infected, or possibly acquire it through breast milk. A blood transfusion with Lyme-infected blood may transmit the disease to the recipient. Some specialist medical researchers believe that Lyme, or other tick-borne diseases, can be sexually transmitted, although there has never been any research to confirm or deny it. Lyme spirochetes have been found in many bodily fluids.

Q. How do I know if I have Lyme disease?

A. This can be a problem because the symptoms of LD are very similar to those of many common infections, and mimic some of the symptoms of other diseases. One sign that is almost unmistakable is the development of a bull's eye rash around the site of a tick bite. If you have this rash, you have Lyme disease. The bull's eye rash varies considerably in different people, but it is typically centered on the tick bite and may range from a fraction of an inch to many inches in diameter. It may be colored anywhere from a mild red to a deep purple. It may appear in a few days or even several weeks after the bite. It may spread to other areas of the body, or there may be additional rashes far from the primary one. The classic rash has concentric areas of lighter and darker colors and expands with time, but the rash is not always in a bull's eye form. It is usually painless, but it may be warm to the touch and may itch. Typically it is flat, but some people have raised areas or bumps in the rash.

Unfortunately, not everyone develops a rash, and many people fail to notice it if it is in a hard-to-see location, such as the scalp. Fewer than half the people who develop LD recall a rash or a tick bite.

Other symptoms may appear at the same time. These often mimic a cold or flu, with fever, headache, muscle and joint pains, tingling or numbness, and/or general fatigue. Early Lyme can produce a wide range of symptoms, or no symptoms at all, and is different in each person. The varied symptoms may change rapidly, sometimes within hours.

The symptoms may disappear in a few days or a week (even without treatment), or may be so minor that the infected person barely notices them. Since flu season runs during the winter months, and most LD infections occur during the other seasons, any case of "flu" in warm weather should be considered suspect.

Even if these initial symptoms subside, the bacteria can remain in your body and may harm you later. In other cases, symptoms become increasingly severe, requiring prompt medical attention. In persistent Lyme disease, symptoms are most often severe fatigue, pains that seem to have no obvious cause, and neurological and/or psychiatric problems. The disease may involve multiple body systems and organs. Symptoms may be complicated by other tick-borne co-infections acquired from the same tick bite or another tick bite.

Doctors with experience in treating Lyme disease often prescribe no less than six weeks of antibiotic treatment for a tick bite with a bull's eye rash. If your doctor does not agree with this approach, it may be prudent to search for a doctor who will support extended treatment.

Q. Is there a test for LD?

A. According to many experts, there is no reliable test for Lyme disease at this time. Your doctor should base his or her diagnosis on your symptoms, medical history, and your exposure to ticks. Doctors should not rely solely on tests. There are several blood tests available, but all have problems. The blood test typically used by most family doctors, called an ELISA (or Lyme titer) test, means nothing if it is negative, and it rarely indicates infection if it is performed too early (2 to 6 weeks after the tick bite).

Patients with persistent LD seldom have a positive ELISA test, possibly because they have ceased to produce the antibodies the test looks for. Many experts believe that the ELISA test is only about 30-60% accurate. The ELISA test is not based on the specific Lyme bacteria strain that is most useful for accurate diagnosis. While a positive ELISA test is a reasonably reliable indication of infection, a negative test is useless.

There are other tests that may be more accurate. The Western blot test for Lyme disease often shows infection when an ELISA test does not. Unfortunately, the U.S. Centers for Disease Control (CDC) have set arbitrary criteria for considering a Western blot test as positive for LD. These criteria were established for statistical analysis of the spread of the disease and were not intended to guide doctors in their diagnosis and treatment. The CDC surveillance criteria are very strict and miss many people with LD. Doctors who use only the CDC guidelines to decide whether or not to treat leave many infected people without proper antibiotic treatment. Even if the test results are not positive by CDC standards, any positive Lyme-specific "bands" are useful indicators of infection.

Another test, PCR analysis, looks for the DNA of the Lyme bacteria in blood, urine, or tissue. Multiple tests are usually required before a sample is obtained that contains the bacteria. However, in recent years PCR testing has become extremely reliable when positive. Most doctors are unaware of this test.

Medical textbooks, the FDA, and the CDC emphasize that LD is a clinical diagnosis, which means that the doctor should examine the patient for typical LD signs, listen to the patient's history and description of his or her symptoms and use this information to make a determination. Blood tests are usually done at the same time, but should not be relied upon. According to ILADS (the International Lyme and Associated Diseases Society), if the doctor suspects LD, and sees little reason to believe the patient has some other disease, he or she should begin antibiotic treatment without delay. Of course, doctors should also perform general blood and other tests to rule out other diseases or conditions.

Q. Are all testing labs the same?

A. No, they are not. Some labs have made special efforts to focus on tickborne disease testing and they use procedures that make their tests more reliable and sensitive to LD. It is important to identify laboratories that utilize tests sensitive to tick-borne disease organisms, and urge your doctor to send your blood sample to one of the specialist laboratories. Test kit request forms may be available on the laboratory's web site.

Q. I had a bull's eye rash and other symptoms, but my doctor said my blood tests showed I didn't have LD, so it must have been something else, right?

A. Almost certainly not! This scenario has caused many people to needlessly suffer for months or years. Left untreated, LD can be a devastating disease. There are few conditions that mimic the LD rash. Lyme-literate doctors suggest starting immediate antibiotic treatment, regardless of the results of any tests.

Often a person suffering from chronic, unsuspected Lyme disease will be diagnosed as having something else, such as chronic fatigue syndrome, fibromyalgia, lupus, multiple sclerosis, Parkinson's disease, Alzheimer's disease, ALS, Crohn's disease, carpal tunnel syndrome, temporomandibular joint disorder (TMJ), and a wide variety of psychological or psychiatric disorders. Doctors often mistake tick bites for spider bites, but spider bites are actually uncommon. In areas where LD is prevalent, it should be seriously considered before a doctor denies antibiotic treatment.

Q. What happens if LD is not properly treated?

A. This varies tremendously among individuals. Some people may never have a recurrence of symptoms, while others may become seriously disabled from LD that is untreated or inadequately treated. Serious symptoms can appear immediately or they could take months or years to develop. The most common symptoms are unrelenting fatigue; joint or muscle pain (particularly in the neck, knee, back, or foot); vision or hearing abnormalities; numbness or tingling, particularly at the extremities; facial paralysis; heart damage; psychological disturbances; and stomach problems.

Untreated LD can result in neurological disorders, crippling arthritis, blindness, deafness, psychiatric or psychological disorders, or death.

Q. What is the proper treatment for Lyme disease?

A. Antibiotic treatment is the simple answer. But the detailed answer is unknown. If they are treated immediately after a tick bite, many patients seem to obtain elimination of all symptoms after a course of six weeks of an oral antibiotic like doxycycline. However, it is not known if this treatment permanently cures the disease. If you had a tick bite and a rash, knowledgeable physicians feel that you should be treated with antibiotics as long as symptoms persist. If there is any recurrence of symptoms after treatment, your doctor should put you on another course of antibiotics.

A patient who seems to be symptom-free should be vigilant in watching for any recurrence, and so should his or her doctor. Relapses do occur. At the other end of the spectrum, some patients find no relief at all from a short course of antibiotics, particularly if they have co-infections. Many long-term LD patients given the standard oral antibiotic treatment seem to do fine for years and then suddenly experience the same or new symptoms. Often a stressful life event such as a jarring accident, head injury, surgery, divorce, or a death in the family can trigger reemergence of symptoms mimicking a new infection. Some patients obtain relief with another course of oral antibiotics, while others require long-

term treatment with oral, intravenous (IV), or injected antibiotics. Because of the complexity of the Lyme bacteria's life cycle, combinations of antibiotics may be necessary.

In addition to medication, Lyme patients need to develop a good program of exercise and nutrition. Patients on antibiotics need to take acidophilus, which replaces the good bacteria (killed by antibiotics) that are necessary for the body's digestive system to function properly. Many patients also take supplements that help boost the immune system. Consult with your physician on all non-prescription treatments.

Q. How does my doctor know when I am cured?

A. Many doctors who treat LD patients avoid using the term "cured" because of the possibility of a relapse in the future. However, most Lyme literate doctors believe that treatment of persistent infection should continue for at least two months after all symptoms have disappeared. Both the patient and the doctor should be prepared to resume treatment if symptoms recur.

Q. Isn't there a vaccine for Lyme disease?

A. There was one, but the manufacturer took it off the market in 2002. Evidence indicated that people with a certain gene might develop an autoimmune arthritic disease from the vaccine. About 30% of the population has this gene, and taking the vaccine could result in severe arthritis. There is no known cure for this condition. Some doctors have seen cases where "cured" or previously undiagnosed LD is reactivated in patients who were vaccinated. The vaccine offered no protection against other tick-borne disease co-infections that frequently accompany LD. The vaccine was only about 80% effective and it was not known how long the partial immunity lasted.

Perhaps a safe and effective vaccine will be developed in the future, but for now, the only way to avoid contracting Lyme disease is to avoid ticks and the other possible sources of infection.

Q. Once you have had Lyme disease, you're immune, right?

A. No. You can get Lyme over and over from new tick bites. Each new tick bite can infect you with a new case of Lyme disease or other tickborne diseases. Some Lyme doctors believe that each subsequent infection makes symptoms more severe and treatment more difficult.

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Order your own "The Basics" booklets

You can print out "Lyme Disease and associated tick-borne diseases: The Basics" 5th Edition 2007 (15 pages) from The Lyme Disease Association of Southeastern Pennsylvania, Inc. website: www.lymepa.org

To obtain quantities of nicely printed, stapled booklets at cost, email Lymepa@Lymepa.org.

The booklet, written by Douglas W. Fearn, contains essential information about Lyme and other tick-borne diseases for anyone beginning to learn about these infectious illnesses. It is written in a non-technical question-and-answer format and was reviewed for accuracy by knowledgeable members of LDASEPA and by several prominent Lyme-literate physicians.

The booklet contains an excellent symptom checklist, organized around various body systems.

"Lyme Disease: The Basics" is a good starting point for learning about the tick-borne illnesses that are increasingly prevalent in Lyme-endemic Southeastern Pennsylvania as well as the rest of the United States.

Co-infections

by Doug Fearn

Q. What are these "co-infections" and "associated diseases"?

A. The ticks that carry the Lyme bacteria also often carry microorganisms that cause other diseases. The most common "co-infections" are anaplasmosis, ehrlichiosis, babesiosis, bartonellosis, and Rocky Mountain spotted fever. Anaplasmosis, ehrlichiosis, bartonellosis, and Rocky Mountain spotted fever may be cured by some of the same antibiotics that are prescribed for Lyme disease. But babesiosis is a different type of disease, caused by a blood parasite and not a bacterium. Antibiotics alone are not effective against babesiosis.

New organisms are being discovered in ticks all the time. Their role in human illness is not yet known.

Few doctors are familiar with these diseases. They may fail to recognize the symptoms or test for these diseases, so many people are suffering from untreated infections. The lab tests for these co-infections have many of the same problems as LD tests. Often, it is this combination of diseases that makes the patient so mystifyingly ill and unresponsive to treatment.

Q. What are the symptoms of anaplasmosis or ehrlichiosis?

A. Like Lyme disease, anaplasmosis and ehrlichiosis infections peak during May, June, and July and the symptoms typically appear from a week to a month after infection. The initial symptoms are flu-like and can include high fever, chills, headache, fatigue, and general achiness. Fewer than half of infected people report a rash. The rash is different from a Lyme disease rash; it is usually smaller and may have raised areas. The rash is more common in children than adults. Children may also suffer from swelling of the hands and feet. Other symptoms may develop later, including nausea, diarrhea or constipation, loss of appetite, cough, stiff neck, confusion, and weight loss. Untreated, the disease can sometimes be fatal in a few weeks, especially in children.

Q. How are anaplasmosis and ehrlichiosis diagnosed?

A. There are blood tests for anaplasmosis and ehrlichiosis, which vary in accuracy and reliability depending on when the test is performed. It is difficult to obtain an accurate test result during the first few weeks after infection.

Q. How are anaplasmosis and ehrlichiosis treated?

A. Anaplasmosis and Ehrlichiosis are usually treated with doxycycline. Most cases respond quickly when diagnosed and treated promptly. Like Lyme disease, you can get these diseases over and over again from new tick bites.

Q. What are the symptoms of babesiosis?

A. People with babesiosis sometimes have no symptoms at all. However, it can be life-threatening for someone with a suppressed immune system. It is also more serious for people over age 50. Symptoms are often the same as for Lyme disease but there may also be a very high fever of up to 104°F, and anemia. Night sweats, chills, severe headaches, fatigue, and sleep disturbances are common. You can get babesiosis from a blood transfusion from an infected donor.

Q. How is babesiosis diagnosed?

A. There are blood tests, but the test reliability declines after a few weeks of infection. These tests suffer from the same lack of sensitivity that plagues Lyme disease testing. PCR tests for babesiosis can be useful if positive, but a negative result does not rule out the disease. Examining the red blood cells under a microscope may reveal the parasites, but few diagnostic laboratories are skilled at the tedious job of carefully observing the blood cells.

Q. What is the treatment for babesiosis?

A. It is important to remember that babesiosis is caused by a protozoan parasite and not by a bacterium, so antibiotics alone will not cure this disease. Many people appear to recover without treatment, but the disease may flare-up later. Since babesiosis is closely related to malaria, anti-malarial drugs are used to treat it. Usually an atovoquone drug like Mepron or Malarone is used along with an antibiotic such as azithromycin; the combination increases the effectiveness of the treatment. As with most tick-borne diseases, you do not develop any immunity after infection and you can get babesiosis over and over.

Q. What are the symptoms of bartonellosis?

A. Bartonellosis usually starts with a rash and swollen glands. Often it is a mild disease and the symptoms subside on their own. But in some cases, bartonellosis may cause on-going fatigue, mental

symptoms, headaches, swollen glands, arthritis, generalized aches and pains similar to the other tick-borne diseases, seizures, neurological disorders, and even dementia. Vision loss and eye infections may occur. Symptoms tend to come and go.

Some areas have a very high rate of *Bartonella* organisms in ticks, sometimes much higher than the rate for Lyme bacteria.

Q. How is bartonellosis diagnosed?

A. There are blood tests, but as with other tick-borne diseases, the tests are often inaccurate. Some doctors report success with a series of PCR tests, but tick-borne bartonellosis has not been recognized long enough to have other reliable diagnostic testing procedures. Few doctors are familiar with tick-borne bartonellosis. The cause of tick-borne bartonellosis is the same bacterium that causes "cat scratch disease," which typically is far less serious and has different symptoms.

Q. What is the treatment for bartonellosis?

A. Antibiotics are used to treat bartonellosis. As with the other tick-borne diseases, treatment time can be lengthy. Since this disease has been recognized only recently, doctors are still learning which drugs are best.

Q. What are the symptoms of Rocky Mountain spotted fever?

A. Despite its name, Rocky Mountain spotted fever is far more prevalent in the South and East than it is in the Rocky Mountains. Like Lyme disease, it is caused by a bacterium. Untreated, it can sometimes be a fatal disease. It is spread by dog ticks as well as the deer tick. After two to fourteen days, most infected people suffer from a fever (sometimes 102°F or higher), headache, and achiness. Most people will develop a rash which may begin around the wrists and ankles, but it sometimes starts on the trunk. A classic symptom is a rash on the palms and soles of the feet, but fewer than half of the patients will have that. Untreated, half of the people infected with Rocky Mountain spotted fever will develop permanent neurological problems.

If you handle a tick while removing it, be sure to wash your hands thoroughly to minimize your risk of infection with RMSF. There are reports of infection simply from contact with an infected tick.

Q. How is Rocky Mountain spotted fever diagnosed?

A. Like Lyme disease, RMSF is a clinical diagnosis, which means that it is up to your doctor to evaluate your signs and symptoms to determine if you have the disease. Early blood tests are not accurate.

Q. How is Rocky Mountain spotted fever treated?

A. Doxycycline is the recommended antibiotic for RMSF.

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Lyme and Co-infections Chart

Coinfections	Vector	Causative Agent	Endemic Area	Symptoms
Lyme disease (also called STARI or Masters' Disease)	Deer tick Pacific black-legged tick Lone star tick	*Borrelia burgdorferi* *Borrelia lonestari* *Other Borrelia?*	Throughout US	Off season "flu" Rash (bull's-eye or other) Constitutional symptoms Musculoskeletal symptoms Wide range of neurologic symptoms, including Bell's palsy
Babesiosis	Deer tick Pacific black-legged tick	*Babesia microti WA-1* *New strain*	Northeast West Coast	Fever Hemolytic anemia Constitutional symptoms Possible death
Ehrlichiosis	Deer tick Pacific black-legged tick American dog tick Lone star tick	*Anaplasma phagocytophila*	Northeast Upper Midwest	Fever Headache Constitutional symptoms Possible death
Colorado tick fever	Rocky Mtn wood tick	Colorado tick fever virus	Western US	Fever with remission Second bout of fever
Tick-borne relapsing fever	Relapsing fever tick (*soft tick*)	*Borrelia hermsii* *Borrelia parkeri* *Borrelia turicata*	Western US	Sudden onset high fever, recurrent fevers Petechial rashes Joint and muscle aches
Q-fever	Brown dog tick Rocky Mtn wood tick Lone star tick	*Coxiella burnetii*	Throughout US	Acute fever Chills Sweats
Powassan viral encephalitis	Woodchuck tick	Flavivirus	Eastern and Western US	Fever Meningoencephalitis 10% fatality rate 50% neurologic sequelae
Rocky Mountain spotted fever	American dog tick Rocky Mtn wood tick Relapsing fever tick (*soft ticks*)	*Rickettsia*	Throughout US	Sudden fever Maculopapular rash on soles of hands and feet that spreads over the entire body 3 to 5% fatality rate
Tick paralysis	American dog tick Rocky Mtn wood tick Lone star tick	Neurotoxin excreted from tick's salivary gland	Throughout US	Fatigue Flaccid paralysis Tongue and facial paralysis Convulsions Death
Tularemia	American dog tick Rocky Mtn wood tick Lone star tick	*Francisella tularensis*	Throughout US	Indolent ulcers Swollen lymph nodes Deaths can occur
Bartonella	Cats Ticks Fleas	*Bartonella quintana* *Bartonella henselae*	Worldwide	Fever Mild neurologic signs Granulomatous lymphadenitis Red papular lesion

Boundaries 101 for Lyme Patients

by Sandy Berenbaum, LCSW, BCD

Pay close attention to boundaries. Look at what is and is not your business and the business of those around you, and act accordingly. Good boundaries protect you from negative interactions with those who don't understand, while keeping loved ones in your life.

When chronic Lyme patients are diagnosed, they enter a new and different world—a world that is not inhabited by their families or friends. It is hard to find medical professionals who understand Lyme disease, and those close to the patient are often reluctant to believe that someone who does not "look sick" is so ill.

Lyme patients often have difficulty reconciling the two worlds in which they live – the world of chronic Lyme and the world that they share with family and friends. Relationships can suffer greatly for those who are living with Lyme.

When the patient experiences a lack of empathy and understanding from close family or friends, he may react in a number of different ways. He might spend endless and futile hours trying to convince loved ones of the nature and consequences of his illness.

He might come to doubt his own decisions and withdraw from needed treatment. Or, he might cut himself off from family and friends, becoming further isolated at a time when he really needs a support network. None of these solutions is good for the Lyme patient or the family.

When I see a family in which there is chronic Lyme and those close to them don't understand, I suggest that the patient and family pay close attention to boundaries, protecting themselves from negative consequences of interaction with those who don't understand, yet keeping their loved ones in their lives.

We can look at what is and what is not our business, or the business of those around us, and act accordingly. With clear boundaries in place, adults and their siblings, parents and even grandparents can enjoy warm and healthy relationships while respecting each other's decisions, even if there are differences of opinion.

As secure adults, people can develop an understanding of appropriate boundaries between themselves and others – within marriages, extended families and other relationships. At times of crisis (and chronic Lyme disease in a family *is*, for many families, a crisis), we may certainly turn to our extended family members and close friends for help. As loved ones become involved with the details of our medical struggle, boundaries may become blurred.

Close friends or relatives might consider it their right or responsibility to question the patient's judgment regarding medical and mental health treatment. The patient might become defensive, feeling a need to justify her decisions and get others to "understand" what she is going through. When this happens, the cycle that evolves from not attending to boundary issues can be destructive to the Lyme patient as well as to her relationships.

When boundaries are understood and respected, however, the patient does better emotionally and is better able advocate for needed support. As with other life crises, struggling with Lyme disease can provide an opportunity for a patient to grow in unexpected ways. A person who normally does not seek help may begin to ask for and accept help from those around her.

Although a non-assertive Lyme patient may feel comfortable accepting help, he may have difficulty confronting someone who is crossing his boundaries. Where boundaries are concerned, consider the following strategies:

Be aware of times when you become defensive, realizing that your defensiveness is a signal that someone may be crossing a boundary and becoming involved in an issue that is not his or her business.

• Define what kind of help you need, and keep it concrete – cooking, cleaning and shopping, for example.

• Be aware of times when you become defensive, realizing that your defensiveness is a signal that someone may be crossing a boundary and becoming involved in an issue that is not his or her business. Learn phrases that re-establish the boundary, such as, "I know you care about me, but my medical decisions are not open for discussion," or "I appreciate your help with the children, but I am responsible for their discipline. Is there something you'd like me to know about their behavior?"

• Understand what information you wish to keep private. Wherever possible, hold such discussions behind closed doors. If, for example, you and your spouse are discussing choices of medical treatment for your children, avoid holding the discussion in front of the grandparents and others who have been helping out.

• In the event of conflict, identify the real issue. Are you concerned about your decision or is someone questioning a decision that is not his business?

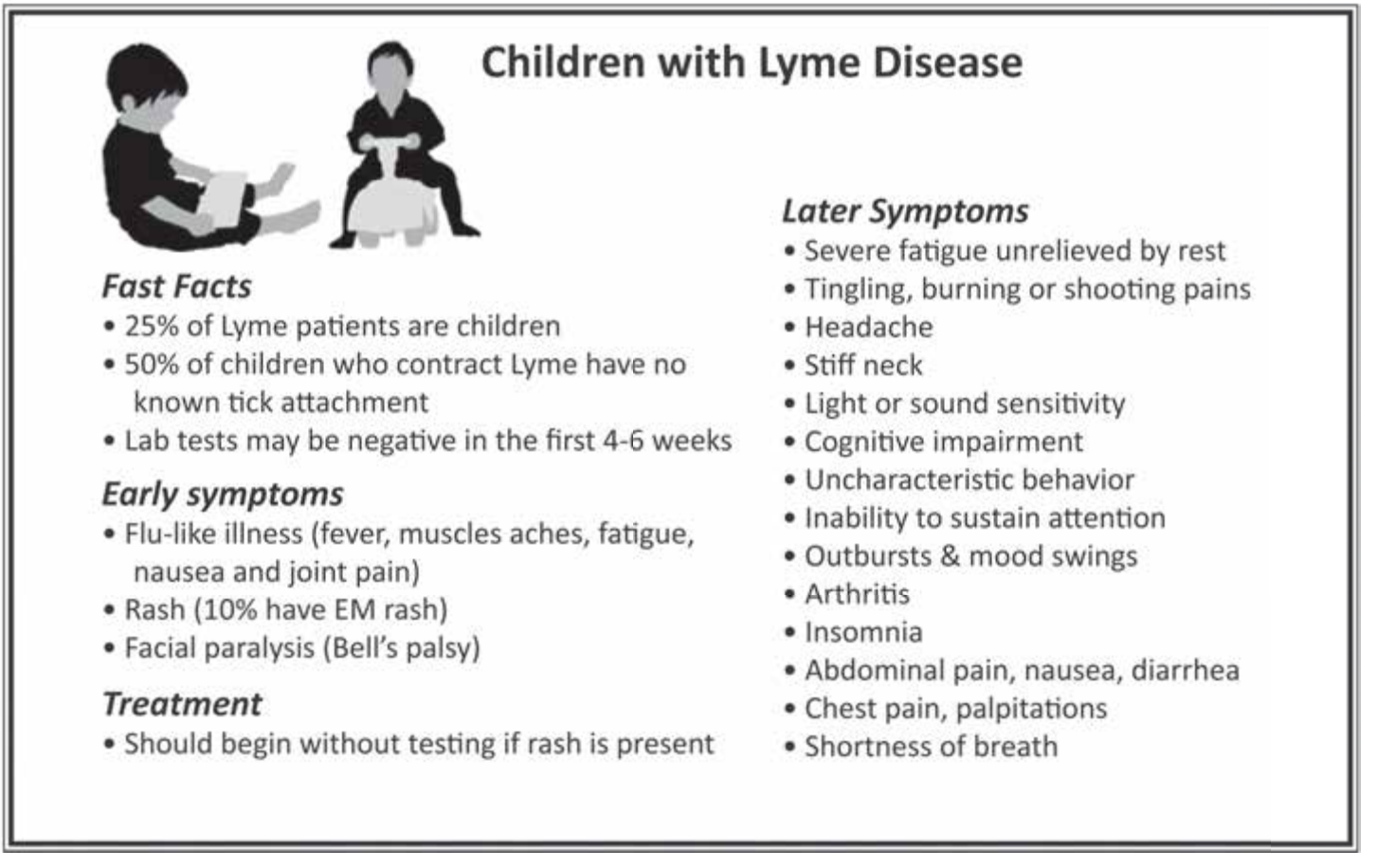
• Respectfully confront those who continue to cross boundaries. If they fail to respect your choices or to accept your decisions, perhaps you should keep their involvement with you during a time of crisis at a minimum.

• Take time to reflect on the interactions of each day. If there is unfinished business between you and another person, discuss it as soon as possible and re-establish the boundaries.

Psychotherapy and family therapy can be extremely helpful to Lyme patients tackling boundary issues. Understanding ourselves and our interactions with others can benefit us during our struggle with Lyme and far beyond.

Chronic Lyme disease is a minefield for a patient and family to negotiate. The process of recovery is lengthy and complex. When we seek support from others and keep our boundaries clear, our lives are enriched and our relationships have unexpected opportunities to grow.

Sandy Berenbaum, LCSW, BCD, is the Children's Editor and Mental Health Editor of the Lyme Times. She may be reached at Family Connections Center for Counseling in Southbury, CT. Tel. 203-240-7787.



Advanced Topics in Lyme Disease

Diagnostic Hints and Treatment Guidelines for Lyme and Other Tick-Borne Illnesses

by Joseph J. Burrascano, Jr., MD

DISCLAIMER: The information contained in this article is meant for informational purposes only. The management of tick-borne illnesses in any given patient must be approached on an individual basis using the practitioner's best judgment.

GENERAL BACKGROUND

WHAT IS LYME DISEASE?

I take a broad view of what Lyme Disease actually is. Traditionally, Lyme is defined as an infectious illness caused by the spirochete, *Borrelia burgdorferi* (Bb). While this is certainly technically correct, clinically the illness often is much more than that, especially in the disseminated and chronic forms.

Instead, I think of Lyme as the illness that results from the bite of an infected tick. This includes infection not only with *B. burgdorferi,* but the many co-infections that may also result. Furthermore, in the chronic form of Lyme, other factors can take on an ever more significant role- immune dysfunction, opportunistic infections, co-infections, biological toxins, metabolic and hormonal imbalances, deconditioning, etc. I will refer to infection with *B. burgdorferi* as "Lyme Borreliosis" (LB), and use the designation "Lyme" and "Lyme Disease" to refer to the more broad definition I described above.

GENERAL PRINCIPLES

In general, you can think of LB as having three categories: acute, early disseminated, and chronic. The sooner treatment is begun after the start of the infection, the higher the success rate. However, since it is easiest to cure early disease, this category of LB must be taken VERY seriously. Undertreated infections will inevitably resurface, usually as chronic Lyme, with its tremendous problems of morbidity and difficulty with diagnosis and treatment and high cost in every sense of the word. So, while the bulk of this document focuses on the more problematic chronic patient, strong emphasis is also placed on earlier stages of this illness where closest attention and care must be made.

A very important issue is the definition of "Chronic Lyme Disease". Based on my clinical data and the latest published information, I offer the following definition. To be said to have chronic LB, these three criteria must be present:

1. Illness present for at least one year (this is approximately when immune breakdown attains clinically significant levels).
2. Have persistent major neurologic involvement (such as encephalitis/encephalopathy, meningitis, etc.) or active arthritic manifestations (active synovitis).
3. Still have active infection with *B. burgdorferi* (Bb), regardless of prior antibiotic therapy (if any).

Chronic Lyme is an altogether different illness than earlier stages, mainly because of the inhibitory effect on the immune system (Bb has been demonstrated *in vitro* to both inhibit and kill B- and T-cells, and will decrease the count of the CD-57 subset of the natural killer cells). As a result, not only is the infection with Bb perpetuated and allowed to advance, but the entire issue of co-infections arises. Ticks may contain and transmit to the host a multitude of potential pathogens. The clinical presentation of Lyme therefore reflects which pathogens are present and in what proportion. Apparently, in early infections, before extensive damage to the immune system has occurred, if the germ load of the co-infectors is low, and the Lyme is treated, many of the other tick-transmitted microbes can be contained and eliminated by the immune system. However, in the chronic patient, because of the inhibited defenses, the individual components of the co-infection are now active enough so that they too add to features of the illness and must be treated. In addition, many latent infections which may have pre-dated the tick bite, for example herpes viruses, can reactivate, thus adding to the illness.

An unfortunate corollary is that serologic tests can become *less* sensitive as the infections progress, obviously because of the decreased immune response upon which these tests are based. In addition, immune complexes form, trapping Bb antibodies. These complexed antibodies are not detected by serologic testing. Not surprisingly the seronegative patient will convert to seropositive 36% of the time after

The seronegative patient will convert to seropositive 36% of the time after antibiotic treatment has begun and a recovery is underway.

antibiotic treatment has begun and a recovery is underway. Similarly, the antibody titer may rise, and the number of bands on the western blot may increase as treatment progresses and the patient recovers. Only years after a successfully treated infection will the serologic response begin to diminish.

The severity of the clinical illness is directly proportional to the spirochete load, the duration of infection, and the presence of co-infections. These factors also are proportional to the intensity and duration of treatment needed for recovery. More severe illness also results from other causes of weakened defenses, such as from severe stress, immunosuppressant medications, and severe intercurrent illnesses. **This is why steroids and other immunosuppressive medications are absolutely contraindicated in Lyme. This also includes intra-articular steroids.**

Many collateral conditions result in those who have been chronically ill, so it is not surprising that damage to virtually all bodily systems can result. Therefore to fully recover not only do all of the active infections have to be treated, but all of these other issues must be addressed in a thorough and systematic manner. *No single treatment or medication will result in full recovery of the more ill patient. Only by addressing all of these issues and engineering treatments and solutions for all of them will we be able to restore full health to our patients.* Likewise, a patient will not recover unless s/he is completely compliant with every single aspect of the treatment plan. This must be emphasized to the patient, often on repeated occasions.

It is clear that in the great majority of patients, chronic Lyme is a disease affecting predominantly the nervous system. Thus, careful evaluation may include neuropsychiatric testing, SPECT and MRI brain scans, CSF analysis when appropriate, regular input from Lyme-aware neurologists and psychiatrists, pain clinics, and occasionally specialists in psychopharmacology.

HYPOTHALAMIC-PITUITARY AXIS

As an extension of the effect of chronic Lyme Disease on the central nervous system, there often is a deleterious effect on the hypothalamic-pituitary axis. Varying degrees of pituitary insufficiency are being seen in these patients, the correction of which has resulted in restoration of energy, stamina and libido, and resolution of persistent hypotension. Unfortunately, not all specialists recognize pituitary insufficiency, partly because of the difficulty in making the laboratory diagnosis. However, the potential benefits of diagnosing and treating this justify the effort needed for full evaluation. Interestingly, in a significant number of these patients, successful treatment of the infections can result in a reversal of the hormonal dysfunction, and hormone replacement therapies can be tapered off!

CO-INFECTION

A huge body of research and clinical experience has demonstrated the nearly universal phenomenon in chronic Lyme patients of co-infection with multiple tick-borne pathogens. These patients have been shown to potentially carry *Babesia* species, *Bartonella*-like organisms, *Ehrlichia, Anaplasma, Mycoplasma,* and viruses. Rarely, yeast forms have been detected in peripheral blood. At one point even nematodes were said to be a tick-borne pathogen. Studies have shown that co-infection results in a more severe clinical presentation, with more organ damage, and the pathogens become more difficult to eradicate. In addition, it is known that *Babesia* infections, like Lyme *Borreliosis*, are immunosuppressive.

There are changes in the clinical presentation of the co-infected patient as compared to when each infection is present individually. There may be different symptoms and atypical signs. There may be decreased reliability of standard diagnostic tests, and most importantly, there is recognition that chronic, persistent forms of each of these infections do indeed exist. As time goes by, I am convinced that even more pathogens will be found.

Steroids and other immunosuppressive medications are absolutely contraindicated in Lyme. This also includes intra-articular steroids.

Therefore, real, clinical Lyme as we have come to know it, especially the later and more severe presentations, probably represents a mixed infection with many complicating factors. I will leave to the reader the implications of how this may explain the discrepancy between laboratory study of pure *Borrelia* infections, and what frontline physicians have been seeing for years in real patients.

I must very strongly emphasize that all diagnoses of tick-borne infections remains clinical. Clinical clues will be presented later in this monograph, but testing information is briefly summarized below.

In **Lyme Borreliosis**, western blot is the preferred serologic test. Antigen detection tests (antigen capture and PCR), although insensitive, are very specific and are especially helpful in evaluating the seronegative patient and those still ill or relapsing after therapy. Often, these antigen detection tests are the only positive markers of Bb infection, as seronegativity has been reported to occur in as many as 30% to 50% of cases. Nevertheless, active LB can be present even if all of these tests are non-reactive! Clinical diagnosis is therefore required.

In **Babesiosis**, no single test is reliable enough to be used alone. Only in early infections (less than two weeks duration) can the standard blood smear be helpful. In later stages, one can use serology, PCR, and fluorescent in-situ hybridization ("FISH") assay. Unfortunately, many other protozoans can be found in ticks, most likely representing species other than *B. microti*, yet commercial tests for only *B. microti*

and *B duncani* (Formerly known as WA-1) are available at this time! In other words, the patient may have an infection that cannot be tested for. Here, as in *Borrelia*, clinical assessment is the primary diagnostic tool.

In **Ehrlichiosis** and **Anaplasmosis**, by definition you must test for both the monocytic and granulocytic forms. This may be accomplished by blood smear, PCR and serology. Many presently uncharacterized *Ehrlichia*-like organisms can be found in ticks and may not be picked up by currently available assays, so in this illness too, these tests are only an adjunct in making the diagnosis. Rarely, Rocky Mountain spotted fever can coexist, and even be chronic. Fortunately, treatment regimens are similar for all agents in this group.

In ***Bartonella***, use both serology and PCR. PCR can be performed not only on blood and CSF, but as in LB, can be performed on biopsy specimens. Unfortunately, in my experience, these tests, even when both types are done, will presently miss over half the cases diagnosed clinically.

Frequent exposures to ***Mycoplasmas*** are common, resulting in a high prevalence of seropositivity, so the best way to confirm active infection is by PCR.

Chronic viral infections may be active in the chronic patient, due to their weakened immune response. PCR testing, and not serologies, should be used for diagnosis. Commonly seen viruses include HHV-6, CMV, and EBV.

COLLATERAL CONDITIONS

Experience has shown that collateral conditions exist in those who have been ill a long time. The evaluation should include testing both for differential diagnosis and for uncovering other subtle abnormalities that may coexist.

Test **B12 levels**, and be prepared to aggressively treat with parenteral formulations. If neurologic involvement is severe, then consideration should be given to treatment with methylcobalamin (see website for details on nutritional support).

Magnesium deficiency is very often present and quite severe. Hyperreflexia, muscle twitches, myocardial irritability, poor stamina and recurrent tight muscle spasms are clues to this deficiency. Magnesium is predominantly an intracellular ion, so blood level testing is of little value. Oral preparations are acceptable for maintenance, but those with severe deficiencies need additional, parenteral dosing: 1 gram IV or IM at least once a week until neuromuscular irritability has cleared.

Pituitary and other endocrine abnormalities are far more common than generally realized. Evaluate fully, including growth hormone levels. Quite often, a full battery of provocative tests is in order to fully define the problem. When testing the thyroid, measure free T3 and free T4 levels and TSH, and nuclear scanning and testing for autoantibodies may be necessary.

Activation of the **inflammatory cascade** has been implicated in blockade of cellular hormone receptors. One example of this is insulin resistance; clinical hypothyroidism can result from receptor blockade and thus hypothyroidism can exist despite normal serum hormone levels. These may partly account for the dyslipidemia and weight gain that is noted in 80% of chronic Lyme patients. In addition to measuring free T3 and T4 levels, check basal A.M. body temperatures. If hypothyroidism is found, you may need to treat with both T3 and T4 preparations until blood levels of both are normalized. To ensure sustained levels, when T3 is prescribed, have it compounded in a time-release form.

Neurally mediated hypotension (NMH) is not uncommon. Symptoms can include palpitations, lightheadedness and shakiness especially after exertion and prolonged standing, heat intolerance, dizziness, fainting (or near fainting), *and an unavoidable need to sit or lie down*. It is often confused with hypoglycemia, which it mimics. NMH can result from autonomic neuropathy and endocrine dyscrasias. If NMH is present, treatment can dramatically lessen fatigue, palpitations and wooziness, and increase stamina. NMH is diagnosed by tilt table testing. This test should be done by a cardiologist and include Isuprel challenge. This will demonstrate not only if NMH is present, but also the relative contributions of hypovolemia and sympathetic dysfunction. Immediate supportive therapy is based on blood volume expansion (increased sodium and fluid intake and possibly Florinef plus potassium). If not sufficient, beta blockade may be added based on response to the Isuprel challenge. The long term solution involves restoring proper hormone levels and treating the Lyme to address this and the autonomic dysfunction.

SPECT scanning of the brain- Unlike MRI and CT scans, which show structure, SPECT scans show function. Therefore SPECT scans give us information unattainable through X-rays, CT scans, MRI's, or even spinal taps. In the majority of chronic Lyme Borreliosis patients, these scans are abnormal. Although not diagnostic of Lyme specifically, if the scan is abnormal, the scan can not only quantify the abnormalities, but the pattern can help to differentiate medical from psychiatric causes of these changes. Furthermore, repeat scans after a course of treatment can be used to assess treatment efficacy. Note that improvement in scans lag behind clinical improvement by many months.

If done by knowledgeable radiologists using high-resolution equipment, scanning will show characteristic abnormalities in Lyme encephalopathy- global hypoperfusion (may be homogenous or heterogeneous). What these scans demonstrate is neuronal dysfunction and/or varying degrees of cerebrovascular insufficiency. If necessary, to assess the relative contributions of these two processes, the SPECT scan can be done before and after acetazolamide. If the post acetazolamide scan shows significant reversibility of the abnormalities, then vasoconstriction is present, and can be treated with vasodilators, which may clear some cognitive symptoms. Therapy can include acetazolamide, serotonin agonists and even Ginkgo biloba, provided it is of pharmaceutical quality. Therapeutic trials of these may be needed.

Acetazolamide should not be given if there is severe kidney/liver disease, electrolyte abnormalities, pregnancy, sulfa allergy, recent stroke, or if the patient is taking high dose aspirin treatment.

LYME BORRELIOSIS

DIAGNOSTIC HINTS

Lyme Borreliosis (LB) is diagnosed clinically, as no currently available test, no matter the source or type, is definitive in ruling in or ruling out infection with these pathogens, or whether these infections are responsible for the patient's symptoms. The entire clinical picture must be taken into account, including a search for concurrent conditions and alternate diagnoses, and other reasons for some of the presenting complaints. Often, much of the diagnostic process in late, disseminated Lyme involves ruling out other illnesses and defining the extent of damage that might require separate evaluation and treatment.

Consideration should be given to tick exposure, rashes (even atypical ones), evolution of typical symptoms in a previously asymptomatic individual, and results of tests for tick-borne pathogens. Another very important factor is response to treatment- presence or absence of Jarisch Herxheimer-like reactions, the classic four-week cycle of waxing and waning of symptoms, and improvement with therapy.

> Erythema migrans (EM) is diagnostic of Bb infection, but is present in fewer than half. Even if present, it may go unnoticed by the patient.

ERYTHEMA MIGRANS

Erythema migrans (EM) is diagnostic of Bb infection, but is present in *fewer than half.* Even if present, it may go unnoticed by the patient. It is an erythematous, centrifugally expanding lesion that is raised and may be warm. Rarely there is mild stinging or pruritus. The EM rash will begin four days to several weeks after the bite, and may be associated with constitutional symptoms. Multiple lesions are present less than 10% of the time, but do represent disseminated disease. Some lesions have an atypical appearance and skin biopsy specimens may be helpful. When an ulcerated or vesicular center is seen, this may represent a mixed infection, involving other organisms besides *B. burgdorferi*.

After a tick bite, serologic tests (ELISA. IFA, western blots, etc.) are not expected to become positive until several weeks have passed. Therefore, if EM is present, treatment must begin immediately, and one should not wait for results of *Borrelia* tests. You should not miss the chance to treat early disease, for this is when the success rate is the highest. Indeed, many knowledgeable clinicians will not even order a *Borrelia* test in this circumstance.

LATER DISEASE

When reactive, serologies indicate exposure only and do not directly indicate whether the spirochete is now currently present. Because Bb serologies often give inconsistent results, test at well-known reference laboratories. The suggestion that two-tiered testing, utilizing an ELISA as a screening tool, be followed, if positive, by a confirmatory western blot, is illogical in this illness. The ELISA is not sensitive enough to serve as an adequate screen, and there are many patients with Lyme who test negative by ELISA yet have fully diagnostic western blots. I therefore recommend against using the ELISA. Order IgM and IgG western blots – but be aware that in late disease there may be repeatedly peaking IgM's and therefore a reactive IgM may not differentiate early from late disease, but it does suggest an active infection. When late cases of LB are seronegative, 36% will transiently become seropositive at the completion of successful therapy. In chronic Lyme Borreliosis, the CD-57 count is both useful and important (see below).

Western blots are reported by showing which bands are reactive. 41KD bands appear the earliest but can cross react with other spirochetes. The 18KD, 23-25KD (Osp C), 31KD (Osp A), 34KD (Osp B), 37KD, 39KD, 83KD and the 93KD bands are the species-specific ones, but appear later or may not appear at all. You should see at least the 41KD and one of the specific bands. 55KD, 60KD, 66KD, and 73KD are nonspecific and nondiagnostic.

PCR tests are now available, and although they are very specific, sensitivity remains poor, possibly less than 30%. This is because Bb causes a deep tissue infection and is only transiently found in body humors. Therefore, just as in routine blood culturing, multiple specimens must be collected to increase yield; a negative result does not rule out infection, but a positive one is significant. You can test whole blood, buffy coat, serum, urine, spinal and other body fluids, and tissue biopsies. Several blood PCRs can be done, or you can run PCRs on whole blood, serum and urine simultaneously at a time of active symptoms. The patient should be antibiotic-free for at least six weeks before testing to obtain the highest yield.

Antigen capture is becoming more widely available, and can be done on urine, CSF, and synovial fluid. Sensitivity is still low (on the order of 30%), but specificity is high (greater than 90%).

Spinal taps are not routinely recommended, as a negative tap does not rule out Lyme. Antibodies to Bb are mostly found in Lyme meningitis, and are rarely seen in non-meningitic CNS infection, including advanced encephalopathy. Even in meningitis, antibodies are detected in the CSF in less than 13% of patients with late disease! Therefore, spinal taps are only performed on patients with pronounced neurological manifestations in whom the diagnosis is uncertain, if they are seronegative, or are still significantly

> You should not miss the chance to treat early disease, for this is when the success rate is the highest.

symptomatic after completion of treatment. When done, the goal is to rule out other conditions, and to determine if Bb (and *Bartonella*) antigens or nucleic acids are present. It is especially important to look for elevated protein and white cells, which would dictate the need for more aggressive therapy, as well as the opening pressure, which can be elevated and add to headaches, especially in children.

I strongly urge you to **biopsy** all unexplained skin lesions/rashes and perform PCR and careful histology. You will need to alert the pathologist to look for spirochetes.

THE CD-57 TEST

Our ability to measure CD-57 counts represents a breakthrough in LB diagnosis and treatment.

Chronic LB infections are known to suppress the immune system and can decrease the quantity of the CD-57 subset of the natural killer cells. As in HIV infection, where abnormally low T-cell counts are routinely used as a marker of how active that infection is, in LB we can use the degree of decrease of the CD-57 count to indicate how active the Lyme infection is and whether, after treatment ends, a relapse is likely to occur. It can even be used as a simple, inexpensive screening test, because at this point we believe that only *Borrelia* will depress the CD-57. Thus, a sick patient with a high CD-57 is probably ill with something other than Lyme, such as a co-infection.

When this test is run by LabCorp (the currently preferred lab, as published studies were based on their assays), we want our Lyme patients to measure above 60; a normal count is above 200. There generally is some degree of fluctuation of this count over time, and the number does not progressively increase as treatment proceeds. Instead, it remains low until the LB infection is controlled, and then it will jump. If the CD-57 count is not in the normal range when a course of antibiotics is ended, then a relapse will almost certainly occur.

DIAGNOSTIC CHECKLIST

To aid the clinician, a workable set of diagnostic criteria were developed with the input of dozens of front line physicians. The resultant document, refined over the years, has proven to be extremely useful not only to the clinician, but it also can help clarify the diagnosis for third party payers and utilization review committees.

It is important to note that the CDC's published reporting criteria are for surveillance only, not for diagnosis. They should not be misused in an effort to diagnose Lyme or set guidelines for insurance company acceptance of the diagnosis, nor be used to determine eligibility for coverage.

LYME BORRELIOSIS DIAGNOSTIC CRITERIA RELATIVE VALUE

Tick exposure in an endemic region	1
Historical facts and evolution of symptoms over time consistent with Lyme	2
Systemic signs & symptoms consistent with Bb infection (other potential diagnoses excluded):	
Single system, e.g., monoarthritis	1
Two or more systems, e.g., monoarthritis and facial palsy	2
Erythema migrans, physician confirmed	7
Acrodermatitis Chronica Atrophicans, biopsy confirmed	7
Seropositivity	3
Seroconversion on paired sera	4
Tissue microscopy, silver stain	3
Tissue microscopy, monoclonal immunofluorescence	4
Culture positivity	4
B. burgdorferi antigen recovery	4
B. burgdorferi DNA/RNA recovery	4

DIAGNOSIS

Lyme Borreliosis Highly Likely.....	7 or above
Lyme Borreliosis Possible.....	5-6
Lyme Borreliosis Unlikely.....	4 or below

I suggest that when using these criteria, you state, “Lyme Borreliosis is ‘unlikely’, ‘possible’, or ‘highly likely’ based upon the following criteria.” Then list the criteria.

CHECK LIST OF ***CURRENT*** SYMPTOMS: This is not meant to be used as a diagnostic scheme, but is provided to streamline the office interview. Note the format- complaints referable to specific organ systems and specific co-infections are clustered to clarify diagnoses and to better display multisystem involvement.

Have you had any of the following in relation to this illness? (CIRCLE "NO" OR "YES")

Tick bite	*N Y*	*"EM" rash (discrete circle)*	*N Y*
Spotted rash over large area	*N Y*	*Linear, red streaks*	*N Y*

	CURRENT SEVERITY				CURRENT FREQUENCY				
SYMPTOM OR SIGN	**NONE**	**MILD**	**MODERATE**	**SEVERE**	**NA**	**NEVER**	**OCCASIONAL**	**OFTEN**	**CONSTANT**
Persistent swollen glands									
Sore throat									
Fevers									
Sore soles, esp. in the AM									
Joint pain									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									
Joint swelling									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									
Unexplained back pain									
Stiffness of the joints or back									
Muscle pain or cramps									
Obvious muscle weakness									
Twitching of the face or other muscles									
Confusion, difficulty thinking									
Difficulty with concentration, reading, problem absorbing new information									
Word search, name block									
Forgetfulness, poor short term memory, poor attention									
Disorientation: getting lost, going to wrong places									
Speech errors- wrong word, misspeaking									
Mood swings, irritability, depression									
Anxiety, panic attacks									
Psychosis (hallucinations, delusions, paranoia, bipolar)									
Tremor									
Seizures									
Headache									
Light sensitivity									
Sound sensitivity									
Vision: double, blurry, floaters									
Ear pain									

	CURRENT SEVERITY				CURRENT FREQUENCY				
SYMPTOM OR SIGN	NONE	MILD	MODERATE	SEVERE	NA	NEVER	OCCASIONAL	OFTEN	CONSTANT
Hearing: buzzing, ringing, decreased hearing									
Increased motion sickness, vertigo, spinning									
Off balance, “tippy” feeling									
Lightheadedness, wooziness, unavoidable need to sit or lie									
Tingling, numbness, burning or stabbing sensations, shooting pains, skin hypersensitivity									
Facial paralysis-Bell's Palsy									
Dental pain									
Neck creaks and cracks, stiffness, neck pain									
Fatigue, tired, poor stamina									
Insomnia, fractionated sleep, early awakening									
Excessive night time sleep									
Napping during the day									
Unexplained weight gain									
Unexplained weight loss									
Unexplained hair loss									
Pain in genital area									
Unexplained menstrual irregularity									
Unexplained milk production; breast pain									
Irritable bladder or bladder dysfunction									
Erectile dysfunction									
Loss of libido									
Queasy stomach or nausea									
Heartburn, stomach pain									
Constipation									
Diarrhea									
Low abdominal pain, cramps									
Heart murmur or valve prolapse?									
Heart palpitations or skips									
“Heart block” on EKG									
Chest wall pain or ribs sore									
Head congestion									
Breathlessness, “air hunger”, unexplained chronic cough									
Night sweats									
Exaggerated symptoms or worse hangover from alcohol									
Symptom flares every 4 wks.									
Degree of disability									

LYME DISEASE TREATMENT GUIDELINES

LYME BORRELIOSIS:

Background

After a tick bite, Bb undergoes rapid hematogenous dissemination, and for example, can be found within the central nervous system as soon as *twelve hours* after entering the bloodstream. This is why even early infections require full dose antibiotic therapy with an agent able to penetrate all tissues in concentrations known to be bactericidal to the organism.

It has been shown that the longer a patient had been ill with LB prior to first definitive therapy, the longer the duration of treatment must be, and the need for more aggressive treatment increases.

More evidence has accumulated indicating the severe detrimental effects of the concurrent use of immunosuppressants including steroids in the patient with active *B. burgdorferi* infection. **Never give steroids or any other immunosuppressant to any patient who may even remotely be suffering from Lyme, or serious, permanent damage may result, especially if given for anything greater than a short course.** If immunosuppressive therapy is absolutely necessary, then potent antibiotic treatment should begin at least 48 hours prior to the immunosuppressants.

TREATMENT RESISTANCE

Bb contains beta lactamases and cephalosporinases, which, with some strains, may confer resistance to cephalosporins and penicillins. This is apparently a slowly acting enzyme system, and may be overcome by higher or more continuous drug levels especially when maintained by continuous infusions (cefotaxime) and by depot preparations (benzathine penicillin). Nevertheless, some penicillin and cephalosporin treatment failures do occur and have responded to sulbactam/ampicillin, imipenem, and vancomycin, which act through different cell wall mechanisms than the penicillins and the cephalosporins.

Vegetative endocarditis has been associated with *Borrelia burgdorferi*, but the vegetations may be too small to detect with echocardiography. Keep this in mind when evaluating patients with murmurs, as this may explain why some patients seem to continually relapse after even long courses of antibiotics.

COMBINATION THERAPY

Treatment of chronic Lyme usually requires combinations of antibiotics. There are four reasons for this:

1. TWO COMPARTMENTS – Bb can be found in both the fluid and the tissue compartments, yet no single antibiotic currently used to treat Bb infections will be effective in both compartments. This is one reason for the need to use combination therapy in the more ill patient. A logical combination might use, for example, azithromycin plus a penicillin.

2. INTRACELLULAR NICHE – Another reason, discussed below, is the fact that Bb can penetrate and remain viable within cells and evade the effects of extracellular agents. Typical combinations include an extracellular antibiotic, plus an intracellular agent such as an erythromycin derivative or metronidazole. Note that some experts discourage the co-administration of bactericidal plus bacteriostatic agents, thus the recommendation to avoid a cell wall drug combined with a tetracycline.

3. L-FORMS (SPHEROPLAST) – It has been recognized that *B. burgdorferi* can exist in at least two, and possibly three different morphologic forms: spirochete, spheroplast (or L-form), and the recently discovered cystic form (presently, there is controversy whether the cyst is different from the L-form). L-forms and cystic forms do not contain cell walls, and thus beta lactam antibiotics will not affect them. Spheroplasts seem to be susceptible to tetracyclines and the advanced erythromycin derivatives. Apparently, Bb can shift among the three forms during the course of the infection. Because of this, it may be necessary to cycle different classes of antibiotics and/or prescribe a combination of dissimilar agents.

4. CYSTIC FORM- When present in a hostile environment, such as growth medium lacking some nutrients, spinal fluid, or serum with certain antibiotics added, Bb can change from the spiral form ("spirochete") into a cyst form. This cyst seems to be able to remain dormant, but when placed into an environment more favorable to its growth, Bb can revert into the spirochete form. The antibiotics commonly used for Lyme do not kill the cystic form of Bb. However, there is laboratory evidence that metronidazole and tinidazole will disrupt it. Therefore, the chronically infected patient who has resistant disease may need to have metronidazole (or tinidazole) added to the regimen. More details are provided in the section on treatment options.

BORRELIA NEUROTOXIN (With thanks to Dr. Shoemaker)
Two groups have reported evidence that *Borrelia*, like several other bacteria, produce neurotoxins. These compounds reportedly can cause many of the symptoms of encephalopathy, cause an ongoing inflammatory reaction manifested as some of the virus-like symptoms common in late Lyme, and also potentially interfere with hormone action by blocking hormone receptors. At this time, there is no assay available to detect whether this compound is present, nor can the amount of toxin be quantified. Indirect measures are currently employed, such as measures of cytokine activation and hormone resistance. A visual contrast sensitivity test (VCS test) reportedly is quite useful in documenting CNS effects of the neurotoxin, and to follow effects of treatment. This test is available at some centers and on the internet.

It has been said that the longer one is ill with Lyme, the more neurotoxin is present in the body. It probably is stored in fatty tissues, and once present, persists for a very long time. This may be because of enterohepatic circulation, where the toxin is excreted via the bile into the intestinal tract, but then is reabsorbed from the intestinal tract back into the blood stream. This forms the basis for treatment.

Two prescription medications that can bind these toxins include cholestyramine resin and Welchol pills. When taken orally in generous amounts, the neurotoxin present in the intestinal tract binds to the resin, is trapped, and then excreted. Thus, over several weeks, the level of neurotoxin is depleted and clinical improvement can be seen. Current experience is that improvement is first seen in three weeks, and treatment can continue for a month or more. Retreatment is always possible.

These medications may bind not only toxins but also many drugs and vitamin supplements. Therefore no other oral medications or supplements should be taken from a half hour before, to two hours after a dose of one of these fiber agents.

Cholestyramine should be taken two to four times daily, and Welchol is prescribed at three pills twice daily. While the latter is obviously much simpler to use, it is less effective than cholestyramine. The main side effects are bloating and constipation, best handled with increased fluid intake and gentle laxatives.

TREATING LYME BORRELIOSIS

LYME DISEASE TREATMENT INFORMATION

There is no universally effective antibiotic for treating LB. The choice of medication used and the dosage prescribed will vary for different people based on multiple factors. These include duration and severity of illness, presence of co-infections, immune deficiencies, prior significant immunosuppressant use while infected, age, weight, gastrointestinal function, blood levels achieved, and patient tolerance. Doses found to be effective clinically are often higher than those recommended in older texts. This is due to deep tissue penetration by Bb, its presence in the CNS including the eye, within cells, within tendons, and because very few of the many strains of this organism now known to exist have been studied for antibiotic susceptibility. In addition, all animal studies of susceptibility to date have only addressed early disease in models that behave differently than human hosts. Therefore, begin with a regimen appropriate to the setting, and if necessary, modify it over time based upon antibiotic blood level measurements and clinical response.

ANTIBIOTICS

There are four types of antibiotics in general use for Bb treatment. The TETRACYCLINES, including doxycycline and minocycline, are bacteriostatic unless given in high doses. If high blood levels are not attained, treatment failures in early and late disease are common. However, these high doses can be difficult to tolerate. For example, doxycycline can be very effective but only if adequate blood levels are achieved either by high oral doses (300 to 600 mg daily) or by parenteral administration. Kill kinetics indicate that a large spike in blood and tissue levels is more effective than sustained levels, which is why with doxycycline, oral doses of 200 mg bid are more effective than 100 mg qid. Likewise, this is why IV doses of 400 mg once a day are more effective than any oral regimen.

PENICILLINS are bactericidal. As would be expected in managing an infection with a gram negative organism such as Bb, amoxicillin has been shown to be more effective than oral penicillin V. With cell wall agents such as the penicillins, kill kinetics indicate that sustained bactericidal levels are needed for 72 hours to be effective. Thus the goal is to try to achieve sustained blood and tissue levels. However, since blood levels are extremely variable among patients, peak and trough levels should be measured (for details, refer to the antibiotic dosage table). Because of its short half-life and need for high levels, amoxicillin is usually administered along with probenecid. An extended release formulation of amoxicillin+clavulanate ("Augmentin XR") may also be considered if adequate trough levels are difficult to attain. An attractive alternative is benzathine penicillin ("Bicillin-LA"- see below). This is an intramuscular depot injection, and although doses are relatively small, the sustained blood and tissue levels are what make this preparation so effective.

CEPHALOSPORINS must be of advanced generation: first generation drugs are rarely effective and second generation drugs are comparable to amoxicillin and doxycycline both in-vitro and in-vivo. Third generation agents are currently the most effective of the cephalosporins because of their very low MBC's (0.06 for ceftriaxone), and relatively long half-life. Cephalosporins have been shown to be effective in penicillin and tetracycline failures. Cefuroxime axetil (Ceftin), a second generation agent, is also effective against staph and thus is useful in treating atypical erythema migrans that may represent a mixed infection that contains some of the more common skin pathogens in addition to Bb. Because of this agent's G.I. side effects and high cost, it is not often used as first line drug. As with the penicillins, try to achieve high, sustained blood and tissue levels by frequent dosing and/or the use of probenecid. Measure peak and trough blood levels when possible.

When choosing a third generation cephalosporin, there are several points to remember: Ceftriaxone is administered twice daily (an advantage for home therapy), but has 95% biliary excretion and can crystallize in the biliary tree with resultant colic and possible cholecystitis. GI excretion results in a large impact on gut flora. Biliary and super-infection problems with ceftriaxone can be lessened if this drug is given in interrupted courses (known commonly as "pulse therapy"- refer to chapter on this on page 20), so the current recommendation is to administer it four days in a row each week. Cefotaxime, which must be given at least every eight hours or as a continuous infusion, is less convenient, but as it has only 5% biliary excretion, it never causes biliary concretions, and may have less impact on gut flora.

ERYTHROMYCIN has been shown to be almost ineffective as monotherapy. The azalide azithromycin is somewhat more effective but only minimally so when given orally. As an IV drug, much better results are seen. Clarithromycin is more effective as an oral agent than azithromycin, but can be difficult to tolerate due to its tendency to promote yeast overgrowth, bad aftertaste, and poor GI tolerance at the high doses needed. These problems are much less severe with the ketolide telithromycin, which is generally well tolerated.

Erythromycins (and the advanced generation derivatives mentioned above) have impressively low MBCs and they do concentrate in tissues and penetrate cells, so they theoretically should be ideal agents. So why is it erythromycin is ineffective, and why have initial clinical results with azithromycin (and to a lesser degree, clarithromycin been disappointing? It has been suggested that when Bb is within a cell,

it is held within a vacuole and bathed in fluid of low pH, and this acidity may inactivate azithromycin and clarithromycin. Therefore, they are administered concurrently with hydroxychloroquine or amantadine, which raise vacuolar pH, rendering these antibiotics more effective. It is not known whether this same technique will make erythromycin a more effective antibiotic in LB. Another alternative is to administer azithromycin parenterally. Results are excellent, but expect to see abrupt Jarisch-Herxheimer reactions.

Telithromycin, on the other hand, is stable in the intracellular acid environment, which may be why this is currently by far the most effective drug of this class, and may replace the others in the majority of patients with LB. Likewise, there is no need to co-administer amantadine or hydroxychloroquine. This antibiotic has other advantages – it has been engineered to prevent drug resistance, has almost no negative impact on *E. coli* in the intestinal tract (hopefully minimizing the risk for diarrhea), and it can be taken with or without food.

However, there are disadvantages:

1. May interact with a wide variety of medications because it is an inhibitor of the cytochrome CYP3A4. It is vital that this be taken into account as many Lyme patients take a variety of medications concurrently, and often from several practitioners.
2. May lengthen the QT interval. This should be measured prior to prescribing this drug, and if borderline, rechecked after it is begun.
3. Can transiently cause blurry vision, delayed accommodation, and even double vision.
4. Liver enzymes may become elevated. Blood tests should be done regularly to monitor this.
5. The usual precautions of any antibiotic also still apply- risk for allergy, stomach upset, Herxheimer reactions, etc.

QTc INTERVAL

- QTc is the QT corrected for heart rate
- Measure the precordial lead that has the best T wave (usually V-2 or V-5)
- Measure from the start of the Q wave to the end of the T wave
- QT interval is inversely related to the heart rate (slow pulse results in a longer QT)
- QTc = QT ÷ √ RR interval
- Normals: Females <450 ms, Males < 470 ms
- Want K+ > 4.0, Mg++ > 2.0; avoid hypocalcemia

METRONIDAZOLE (Flagyl) When present in a hostile environment, such as a growth medium lacking some nutrients, spinal fluid, or serum with certain antibiotics added, Bb can change into a cyst form. This cyst seems to be able to remain dormant, but when placed into an environment more favorable to its growth, the cyst can revert into the spirochete form. The conventional antibiotics used for Lyme, such as the penicillins, cephalosporins, etc. do not kill the cystic form of Bb, yet there is laboratory evidence that metronidazole will kill it. Therefore, the trend now is to treat the chronically infected patient who has resistant disease by combining metronidazole with one or two other antibiotics to target all forms of Bb. Because there is laboratory evidence that tetracyclines may inhibit the effect of Flagyl, this class of medication should not be used in these two- and three-drug regimens. Some clinicians favor tinidazole as this may be equally effective but result in fewer side effects. However, this has yet to be documented.

Important precautions:

1. Pregnancy while on Flagyl is not advised, as there is a risk of birth defects.
2. No alcohol consumption! A severe, "Antabuse" reaction will occur, consisting of severe nausea, flushing, headache, and other symptoms.
3. Yeast overgrowth is especially common. A strict anti-yeast regimen must be followed.
4. Flagyl can be irritating to the nervous system- in the short term, it may cause irritability, "spacey" feelings, etc. Longer term, it can affect the peripheral nerves, causing tingles, numbness, etc. If mild, a change in dose may be required. Often, extra vitamin B can clear these symptoms. If the nerve symptoms persist or are strong, then metronidazole must be discontinued or these symptoms may become very long lasting.
5. Strong Herxheimer-like reactions are seen in almost everyone.

RIFAMPIN is a well-known antibiotic that has been in use for many decades. It is primarily used to treat tuberculosis, but also has been used in other conditions, such as prevention of meningitis in those exposed, for treating resistant Staph, etc. Potentially, rifampin may be effective in treating *Bartonella, Ehrlichia, Mycoplasma*, and *Borrelia*. There are as yet no formal clinical studies on the use of this medication in these illnesses, but many patients have been treated with rifampin and have had favorable results. When used, regular blood tests (CBC, liver enzymes) are usually performed to monitor for side effects. Rifampin can also discolor urine, tears and sweat (brownish-orange). It may also stain some types of water-permeable contact lenses. Taking rifampin during pregnancy is not advised. Finally, because this drug is an inducer of cytochromes (CYP3A4), co-administration with other medications may result in lower and briefer blood levels of the co-administered drug. Thus, be aware of these potential drug interactions.

BENZATHINE PENICILLIN Comparative studies published by Fallon et al. at Columbia University have shown that parenteral therapy [intravenous] is superior to oral therapy in chronic patients. Options include intramuscular long acting penicillin G (benzathine penicillin, or “Bicillin-LA”) or intravenous antibiotics.

For an antibiotic in the penicillin class to be effective, time-killing curves show that significant levels of antibiotic must be sustained for 72 hours. Bicillin LA is a sustained release formulation that meets these criteria.

Published studies in children and adults, combined with over a decade of experience with this therapy by front line, Lyme-treating physicians have established the efficacy, safety and usefulness of this medication. In many patients it is more effective than oral antibiotics for treating Lyme, and compares closely to intravenous therapy in terms of efficacy if the dose is high enough.

It is usually administered three or four times weekly for six to twelve months. It has the advantage of being relatively inexpensive, free of gastrointestinal side effects, unlikely to promote the overgrowth of yeast, and has an excellent safety record spanning many decades.

Finally, an added plus is that family members can be trained to administer this treatment at home.

CEFTRIAXONE TREATMENT A subset of patients who have severe, longstanding illness due to *Borrelia burgdorferi* carry persistent infection despite having previously received antibiotic treatments which have eliminated the disease in less ill individuals. The mechanism for such persistence has been the subject of many peer reviewed articles. They include persistence of *B. burgdorferi* in protective niches, inhibition and lysis of lymphocytes, survival in phagocytic vacuoles, antigenic shifts, slow growth, shifting into alternate forms, and dormancy and latency.

One successful approach in the more ill patient, published in the early 1990s, is to use higher doses of ceftriaxone in a pulsed-dose regimen. Since then, clinical experience has expanded upon this concept, and at the MLDA Lyme Congress in September, 2002, Cichon presented data on a pulsed, high dose regimen which supports and refines this concept. This regimen is now considered the current standard of care in the use of ceftriaxone.

Treatment with ceftriaxone is dosed at 4 grams daily- given either as 2 grams IV twice daily, or 4 grams slowly once a day, four days in a row each week, usually for 14 or more weeks. Such a regimen is not only more effective in the Chronic Lyme patient, but regular interruptions in treatment lessen the potential complications of intensive antibiotic therapy with ceftriaxone, such as biliary sludging and colitis. Hence a more effective, safer regimen that by virtue of the treatment breaks, is less costly and affords the patient a more acceptable lifestyle. IV access with a heparin lock becomes possible (and preferred).

COURSE DURING THERAPY

As the spirochete has a very long generation time (12 to 24 hours *in vitro* and possibly much longer in living systems) and may have periods of dormancy, during which time antibiotics will not kill the organism, treatment has to be continued for a long period of time to eradicate all the active symptoms and prevent a relapse, especially in late infections. If treatment is discontinued before all symptoms of active infection have cleared, the patient will remain ill and possibly relapse further. In general, early LB is treated for four to six weeks, and late LB usually requires a minimum of four to six months of continuous treatment. All patients respond differently and therapy must be individualized. It is not uncommon for a patient who has been ill for many years to require open ended treatment regimens; indeed, some patients will require ongoing maintenance therapy for years to remain well.

Several days after the onset of appropriate antibiotic therapy, symptoms often flare due to lysis of the spirochetes with release of increased amount of antigenic material and possibly bacterial toxins. This is referred to as a Jarisch Herxheimer-like reaction.

Several days after the onset of appropriate antibiotic therapy, symptoms often flare due to lysis of the spirochetes with release of increased amount of antigenic material and possibly bacterial toxins. This is referred to as a Jarisch Herxheimer-like reaction. Because it takes 48 to 72 hours of therapy to initiate bacterial killing, the Herxheimer reaction is therefore delayed. This is unlike syphilis, in which these reactions can occur within hours.

It has been observed that symptoms will flare in cycles every four weeks. It is thought that this reflects the organism's cell cycle, with the growth phase occurring once per month (intermittent growth is common in *Borrelia* species). As antibiotics will only kill bacteria during their growth phase, therapy is designed to bracket at least one whole generation cycle. This is why the minimum treatment duration should be at least four weeks. If the antibiotics are working, over time these flares will lessen in severity and duration. The very occurrence of ongoing monthly cycles indicates that living organisms are still present and that antibiotics should be continued.

With treatment, these monthly symptom flares are exaggerated and presumably represent recurrent Herxheimer-like reactions as Bb enters its vulnerable growth phase and then are lysed. For unknown reasons, the worst occurs at the fourth week of treatment. Observations suggest that the more severe this reaction, the higher the germ load, and the more ill the patient. In those with long-standing highly symptomatic disease who are on I.V. therapy, the week-four flare can be very severe, similar to a serum sickness reaction, and be associated with transient leucopenia and/or elevations in liver enzymes. If this happens, decrease the dose temporarily, or interrupt treatment for several days, then resume with a lower dose. If you are able to continue or resume therapy, then patients continue to improve. Those whose treatment is stopped and not restarted at this point usually will need retreatment in the future due to ongoing or recurrent symptoms because the infection was not eradicated. Patients on I.V. therapy who have a strong reaction at the fourth week will need to continue parenteral antibiotics for several months, for when this monthly reaction finally lessens in severity, then oral or IM medications can be substituted. Indeed, it is just this observation that guides the clinician in determining the endpoint of I.V. treatment. In general, I.V. therapy is given until there is a clear positive response, and then treatment is changed to IM or po until free of signs of active infection for 4 to 8 weeks. Some patients,

however, will not respond to IM or po treatment and I.V. therapy will have to be used throughout. As mentioned earlier, leucopenia may be a sign of persistent Ehrlichiosis, so be sure to look into this.

Repeated treatment failures should alert the clinician to the possibility of an otherwise inapparent immune deficiency, and a workup for this may be advised. Obviously, evaluation for co-infection should be performed, and a search for other or concurrent diagnoses needs to be entertained.

There are three things that will predict treatment failure regardless of which regimen is chosen: Non-compliance, alcohol use, and sleep deprivation. Advise them to take a break when (or ideally before) the inevitable mid afternoon fatigue sets in (napping is encouraged).

All patients must keep a carefully detailed daily diary of their symptoms to help us document the presence of the classic four-week cycle, judge the effects of treatment, and determine treatment endpoint. One must follow such diaries, temperature readings in late afternoon, physical findings, notes from physical therapists, and cognitive testing to best judge when to change or end antibiotics.

There are three things that will predict treatment failure regardless of which regimen is chosen: Non-compliance, alcohol use, and sleep deprivation. Advise them to take a break when (or ideally before) the inevitable mid afternoon fatigue sets in (napping is encouraged).

Remember- there currently is no test for cure, so this clinical follow-up assumes a major role in Lyme Disease care.

ANTIBIOTIC CHOICES AND DOSES

ORAL THERAPY: Always check blood levels when using agents marked with an *, and adjust dose to achieve a peak level above ten and a trough greater than three. Because of this, the doses listed below may have to be raised. Consider Doxycycline first in early Lyme due to concern for *Ehrlichia* co-infections.

*Amoxicillin- Adults: 1g q8h plus probenecid 500mg q8h; doses up to 6 grams daily are often needed
Pregnancy: 1g q6h and adjust.
Children: 50 mg/kg/day divided into q8h doses.

*Doxycycline- Adults: 200 mg bid with food; doses of up to 600 mg daily are often needed, as doxycycline is only effective at high blood levels. Not for children or in pregnancy.
If levels are too low at tolerated doses, give parenterally or change to another drug.

*Cefuroxime axetil- Oral alternative that may be effective in amoxicillin and doxycycline failures. Useful in EM rashes co-infected with common skin pathogens.
Adults and pregnancy: 1g q12h and adjust. Children: 125 to 500 mg q12h based on weight.

Tetracycline- Adults only, and not in pregnancy. 500 mg tid to qid

Erythromycin- Poor response and not recommended.

Azithromycin- Adults: 500 to 1200 mg/d. Adolescents: 250 to 500 mg/d
Add hydroxychloroquine, 200-400 mg/d, or amantadine 100-200 mg/d
Cannot be used in pregnancy or in younger children.
Overall, poor results when administered orally

Clarithromycin- Adults: 250 to 500 mg q6h plus hydroxychloroquine, 200-400 mg/d, or amantadine 100-200 mg/d. Cannot be used in pregnancy or in younger children.
Clinically more effective than azithromycin

Telithromycin- Adolescents and adults: 800 mg once daily
Do not need to use amantadine or hydroxychloroquine
So far, the most effective drug of this class, and possibly the best oral agent if tolerated. Expect strong and quite prolonged Herxheimer reactions.
Must watch for drug interactions (CYP3A-4 inhibitor), check the QTc interval, and monitor liver enzymes.
Not to be used in pregnancy.

*Augmentin- Standard Augmentin cannot exceed three tablets daily due to the clavulanate, thus is given with amoxicillin, so that the total dose of the amoxicillin component is as listed above for amoxicillin. This combination can be effective when Bb beta lactamase is felt to be significant.

*Augmentin XR 1000- This is a time-release formulation and thus is a better choice thanstandard Augmentin.
Dose- 1000 mg q 8 h, to 2000 mg q 12 h based on blood levels.

Chloramphenicol- Not recommended as not proven and potentially toxic.

Metronidazole: 500 to 1500 mg daily in divided doses. Non-pregnant adults only.

PARENTERAL [INTRAVENOUS] THERAPY

Ceftriaxone- Risk of biliary sludging (therefore often Actigall is co-administered- one to three tablets daily).
Adults and pregnancy: 2g q12 h, 4 days in a row each week
Children: 75 mg/kg/day up to 2g/day

Cefotaxime- Comparable efficacy to ceftriaxone; no biliary complications.
Adults and pregnancy: 6g to 12g daily. Can be given q 8 h as divided doses, but a continuous infusion may be more efficacious. When exceeding 6 g daily, use pulsed-dose schedule

Cefotaxime cont'd-
Children: 90 to 180 mg/kg/day dosed q6h (preferred) or q8h, not to exceed 12 g daily.

*Doxycycline- Requires central line as is caustic.
Surprisingly effective, probably because blood levels are higher when given parenterally and single large daily doses optimize kinetics of killing with this drug.
Always measure blood levels.
Adults: Start at 400 mg q24h and adjust based on levels.
Cannot be used in pregnancy or in younger children.

Azithromycin- Requires central line as is caustic.
Dose: 500 to 1000 mg daily in adolescents and adults.

Penicillin G- IV penicillin G is minimally effective and not recommended.

Benzathine penicillin- Surprisingly effective IM alternative to oral therapy. May need to begin at lower doses as strong, prolonged (6 or more week) Herxheimer-like reactions have been observed.
Adults: 1.2 million U- three to four doses weekly.
Adolescents: 1.2 to 3.6 million U weekly.
May be used in pregnancy.

Vancomycin- observed to be one of the best drugs in treating Lyme, but potential toxicity limits its use.
It is a perfect candidate for pulse therapy to minimize these concerns. Use standard doses and confirm levels.

Primaxin and Unisyn- similar in efficacy to cefotaxime, but often work when cephalosporins have failed.
Must be given q6 to q8 hours.

Cefuroxime- useful but not demonstrably better than ceftriaxone or cefotaxime.

*Ampicillin IV- more effective than penicillin G. Must be given q6 hours.

TREATMENT CATEGORIES

PROPHYLAXIS of high risk groups- education and preventive measures. Antibiotics are not given.

TICK BITES - Embedded Deer Tick
With No Signs or Symptoms of Lyme (see appendix):

Decide to treat based on the type of tick, whether it came from an endemic area, how it was removed, and length of attachment (anecdotally, as little as four hours of attachment can transmit pathogens). The risk of transmission is greater if the tick is engorged, or of it was removed improperly allowing the tick's contents to spill into the bite wound. High-risk bites are treated as follows (remember the possibility of co-infection!):

1) Adults: Oral therapy for 28 days.
2) Pregnancy: Amoxicillin 1000 mg q6h for 6 weeks.
Test for *Babesia, Bartonella* and *Ehrlichia*.
Alternative: Cefuroxime axetil 1000 mg q12h for 6 weeks.
3) Young Children: Oral therapy for 28 days.

EARLY LOCALIZED - Single erythema migrans with no constitutional symptoms:

1) Adults: oral therapy- must continue until symptom and sign free for at least one month, with a 6 week minimum.
2) Pregnancy: 1st and 2nd trimesters: I.V. X 30 days then oral X 6 weeks
3rd trimester: Oral therapy X 6+ weeks as above.
Any trimester- test for *Babesia* and *Ehrlichia*
3) Children: oral therapy for 6+ weeks.

DISSEMINATED DISEASE - Multiple lesions, constitutional symptoms, lymphadenopathy, or any other manifestations of dissemination.

EARLY DISSEMINATED: Milder symptoms present for less than one year and not complicated by immune deficiency or prior steroid treatment:

1) Adults: oral therapy until no active disease for 4 to 8 weeks (4-6 months typical)
2) Pregnancy: As in localized disease, but treat throughout pregnancy.
3) Children: Oral therapy with duration based upon clinical response.

PARENTERAL (I.V.) ALTERNATIVES for more ill patients and those unresponsive to or intolerant of oral medications:

1) Adults and children: I.V. therapy until clearly improved, with a 6 week minimum. Follow with oral therapy or IM benzathine penicillin until no active disease for 6-8 weeks. I.V. may have to be resumed if oral or IM therapy fails.
2) Pregnancy: IV then oral therapy as above.

LATE DISSEMINATED: present greater than one year, more severely ill patients, and those with prior significant steroid therapy or any other cause of impaired immunity:

1) Adults and pregnancy: extended I.V. therapy (14 or more weeks), then oral or IM, if effective, to same endpoint. Combination therapy with at least two dissimilar antibiotics almost always needed.
2) Children: IV therapy for 6 or more weeks, then oral or IM follow up as above. Combination therapy usually needed.

CHRONIC LYME DISEASE (PERSISTENT/RECURRENT INFECTION)

By definition, this category consists of patients with active infection, of a more prolonged duration, who are more likely to have higher spirochete loads, weaker defense mechanisms, possibly more virulent or resistant strains, and probably are significantly co-infected. Neurotoxins may also be significant in these patients. Search for and treat for all of these, and search for concurrent infections including viruses, chlamydias, and mycoplasmas. Be sure to do an endocrine workup if indicated. These patients require a full evaluation for all of these problems, and each abnormality must be addressed.

This group will most likely need parenteral therapy, especially high dose, pulsed therapy, and antibiotic combinations, including metronidazole. Antibiotic therapy will need to continue for many months, and the antibiotics may have to be changed periodically to break plateaus in recovery. Be vigilant for treatment-related problems

such as antibiotic-associated colitis, yeast overgrowth, intravenous catheter complications, and abnormalities in blood counts and chemistries.

If treatment can be continued long term, then a remarkable degree of recovery is possible. However, attention must be paid to all treatment modalities for such a recovery- not only antibiotics, but rehab and exercise programs, nutritional supplements, enforced rest, low carbohydrate, high fiber diets, attention to food sensitivities, avoidance of stress, abstinence from caffeine and alcohol, and absolutely no immunosuppressants, even local doses of steroids (intra-articular injections, for example).

Unfortunately, not all patients with chronic Lyme disease will fully recover and treatment may not eradicate the active *Borrelia* infection. Such individuals may have to be maintained on open-ended, ongoing antibiotic therapy, for they repeatedly relapse after antibiotics are stopped. Maintenance antibiotic therapy in this select group is thus mandatory.

In patients who have chronic Lyme, who do not fully respond to antibiotics, one must search for an explanation. In many cases, these patients are found to have pituitary insufficiency of varying degrees. The abnormalities may be extremely subtle, and provocative testing must be done for full diagnosis. Persistent fatigue, limited stamina, hypotension, and loss of libido suggest this possibility.

Similarly, a small but significant number of these patients harbor toxic levels of heavy metals. Challenge testing by knowledgeable, experienced clinicians is necessary for evaluation. Treatment must be directed toward correcting the specific abnormalities found, and post-treatment retesting to assess efficacy of treatment and endpoint of therapy should be done. Suspect this when poor immune responsiveness and persistent neuropathic signs and symptoms are present.

INDICATORS FOR PARENTERAL (I.V.) THERAPY

(The following are guidelines only and are not meant to be absolute. It is based on retrospective study of over 600 patients with late Lyme disease.)

- Illness for greater than one year
- Prior immunosuppressive therapy while infected with Bb.
- Major neurological involvement
- Active synovitis with high sedimentation rate
- Elevated protein or cells in the CSF

ADVANCED TREATMENT OPTIONS

PULSE THERAPY consists of administering antibiotics (usually parenteral ones) two to four days in a row per week. This allows for several advantages:
Dosages are doubled (i.e. cefotaxime, 12 g daily), increasing efficacy
More toxic medications can be used with increased safety (ie: vancomycin)
May be effective when conventional, daily regimens have failed.
IV access may be easier or more tolerable
More agreeable lifestyle for the patient
Often less costly than daily regimens

Note that this type of treatment is expected to continue for a minimum of ten weeks, and often must continue beyond twenty weeks. The efficacy of this regimen is based on the fact that it takes 48 to 72 hours of continuous bactericidal antibiotic levels to kill the spirochete, yet it will take longer than the four to five days between pulses for the spirochetes to recover. As with all Lyme treatments, specific dosing and scheduling must be tailored to the individual patient's clinical picture based upon the treating physician's best clinical judgment.

COMBINATION THERAPY

This consists of using two or more dissimilar antibiotics simultaneously for antibiotic synergism, to better compensate for differing killing profiles and sites of action of the individual medications, and to cover the three known forms of Bb. A typical combination is the use of a cell wall agent plus a protein inhibitor (ie: amoxicillin plus clarithromycin). Note that GI intolerance and yeast superinfections are the biggest drawbacks to this type of treatment. However, these complications can often be prevented or easily treated, and the clinically observed benefits of this type of regimen clearly have outweighed these problems in selected patients.

LYME DISEASE AND PREGNANCY

It is well known that *B. burgdorferi* can cross the placenta and infect the fetus. In addition, breast milk from infected mothers has been shown to harbor spirochetes that can be detected by PCR and grown in culture.

The Lyme Disease Foundation in Hartford, CT kept a pregnancy registry for eleven years beginning in the late 1980s. They found that if patients were maintained on adequate doses of antibiotic therapy during gestation, then no babies were born with Lyme. My own experience over the last twenty years agrees with this.

The options for treating the mother include oral, intramuscular, and intravenous therapy as outlined above. It is vital that peak and trough antibiotic levels be measured if possible at the start of gestation and at least once more during treatment.

During pregnancy, symptoms generally are mild as the hormonal changes seem to mask many symptoms. However, post-partum, mothers have a rough time, with a sudden return of all their Lyme

symptoms including profound fatigue. Post partum depression can be particularly severe. I always advise help in the home for at least the first month, so adequate rest and time for needed treatments are assured.

I also advise against breast feeding for obvious reasons as mentioned above.

MONITORING THERAPY

Drug levels are measured, where possible, to confirm adequate dosing. Often, the regimen may have to be modified to optimize the dose. This may have to be repeated again at any time major changes in the treatment regimen occur, and serially during pregnancy. With parenteral therapy, CBC and chem/liver panels are done at least twice each month, especially during symptom flares, with urinalysis and pro-time monitored less frequently.

SAFETY

Over two decades of experience in treating thousands of patients with Lyme has proven that therapy as described above, although intense, is generally well tolerated. The most common adverse reaction seen is allergy to probenecid. In addition, yeast superinfections are seen, but these are generally easily recognized and managed. The induction of Clostridium difficile toxin production is seen most commonly with ceftriaxone, but can occur with any of the antibiotic regimens mentioned in this document. However, pulsed dose therapy and regular use of the lactobacillus preparations seems to be helpful in controlling yeast and antibiotic related colitis, as the number of cases of *C. difficile* in Lyme patients is low when these guidelines are followed. Be sure to test stool for both toxin A and toxin B when evaluating for C. difficile colitis.

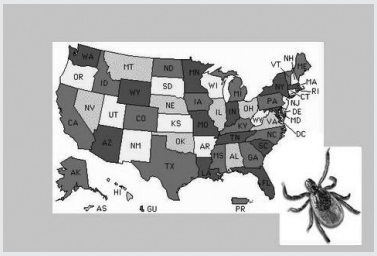
When using central intravenous lines including PICC lines (peripherally inserted central catheters), if ANY line problems arise, it is recommended that the line be pulled for patient safety. Salvage attempts (urokinase, repairing holes) are often ineffective and may not be safe.

Please advise all patients who take the tetracyclines of skin and eye sensitivity to sunlight and the proper precautions, and advise birth control if appropriate. When doxycycline is given parenterally, do not refreeze the solution prior to use!

Remember, years of experience with chronic antibiotic therapy in other conditions, including rheumatic fever, acne, gingivitis, recurrent otitis, recurrent cystitis, COPD, bronchiectasis, and others have not revealed any consistent dire consequences as a result of such medication use. Indeed, the very real consequences of untreated, chronic persistent infection by *B. burgdorferi* can be far worse than the potential consequences of this treatment.

The author serves on the Board of the International Lyme and Associated Diseases Society (ILADS). This article is excerpted by permission from the Sixteenth Edition of ***Advanced Topics in Lyme Disease,*** *Copyright 2008. Please visit the Dr. Burrascano's website for complete guidelines and details on co-infections.*

Online State Support Groups



Join with others in your own state to bring change through education, advocacy and activism. Here's how to find your own online state group:

Go to http://health.groups.yahoo.com/group/STATENAMELyme for instructions.

There are groups for each state and Washington DC. There is also a "militarylyme" for service people and a "lyme-espanol" for Spanish speakers.

All the state sites are moderated, mostly by volunteers within the state. They can help you find resources, answer your questions, and let you know about local events. CALDA makes sure the state groups receive action alerts and updates on national issues.

Help Spread the Word about Lyme Disease

Lyme Bumper Stickers!

Let's bring awareness to our cause! These bright green bumper stickers are easily removed by just peeling them off. They say,"Lyme Disease, A National Health Crisis." They are available for a suggested donation of $3 each.

Free shipping with your donation. Items can be ordered at www.LymeDisease.org or send a check to: CALDA, 1026 Mangrove Ave, Suite 10, Chico CA 95926. Need more information? Please contact Marisa at mnayfach@yahoo.com or call her at 415-499-3172.

Principles of Laboratory Testing for Lyme Disease

by Elizabeth Maloney, MD

Perhaps the most important diagnostic concept in Lyme disease is that Lyme is a clinical diagnosis, not a laboratory one. Yet this very concept seems to be one of the hardest for patients and physicians to truly grasp. While I don't know why this is the case, here are my thoughts on the matter.

Most cases of late Lyme are not diagnosed right off the bat. Several studies have shown that patients usually see multiple physicians before being diagnosed and delays in diagnosis are often greater than a year. Those delays, to put it bluntly, represent physician error. It is not surprising then, that patients might question a clinical diagnosis of Lyme without "proof" in the form of a test result. Busy physicians, with little experience in late Lyme disease, may find it difficult to reach a clinical diagnosis. Patients present in a myriad of ways and the variety defies clinical logic; how could a single infectious agent cause such divergent symptoms? Colleagues may quibble over which part of a history is most important or disagree with exam findings but it's hard for them to argue with a lab result. Plus, it's easier to take a two-minute history and order a blood test then it is to do a complete review of systems in a patient who has many, many symptoms. So physicians, too, want proof.

Enter lab testing. Everybody wants it, and the CDC won't recognize late Lyme without it, but what are they getting and, if they looked a little closer, would they still want it? Before getting into the specifics of Lyme disease testing, a review of some basic lab principles is in order.

Sensitivity and Specificity

When people talk about testing of any sort, one question that always comes up is, "Is the test accurate?" People want to know that the result is a true one, that it's right. Accuracy in lab testing is determined by a test's sensitivity and specificity. The ideal test would identify every patient who has the illness being tested for yet not indicate a patient had the disease when they don't. There are precious few ideal tests.

This grid shows the relationship between a disease and its test.

	Disease Positive	Disease Negative
Test Positive	True Positive	False Positive
Test Negative	False Negative	True Negative

Sensitivity is the ability of a test to find all of the ill. It can be expressed as:

Sensitivity = True Positives_
True Positives + False Negatives

From the perspective of sensitivity, false negatives are a bad thing. When dealing with a significant illness we don't want to tell a patient they don't have the disease (and don't need treatment) when they do.

Specificity is the ability of a test to only identify those who are ill. It can be expressed as:

Specificity = True Negatives
True Negatives + False Positives

From the perspective of specificity, false positives are a bad thing. We don't want to tell people they have a condition that requires treatment when they don't.

Sensitivity and specificity to not go hand-in-hand, in fact they vary inversely with each other. A highly sensitive test will have few false negative results but is likely to have several false positives. A highly specific test will have few false positives but it also yields many false negatives.

Most lab tests are not reported as being simply positive or negative but rather give a specific value. By manipulating the "normal" cut-off point for a test you can increase its sensitivity or specificity. But increasing the value of one comes at the cost of the other.

If failure to identify a condition leads to significant consequences and treating it is safe and easy you would be willing to sacrifice specificity to gain sensitivity. But if a disease is nonfatal and the treatment kills those who receive it when they don't have the disease then you would desire a highly specific test.

There are situations where you want to identify all patients who have an illness while at the same time treating only those who truly have it. Here it makes sense to run a sequence of tests. The first test should be highly sensitive so that you will have very few false negatives. In doing this you will pick up some false positives so the second test (run only on those who were positive on test 1) should be highly specific, finding only those who truly have the illness. If you mistakenly reversed the order of these tests the result would be disastrous.

Applying this to serologic testing for Lyme disease

The earlier that Lyme is diagnosed, the easier it is to treat. Missing the diagnosis can lead to significant morbidity so it is important that all potential Lyme patients be identified; to do this we want a highly sensitive test. Yet, the inappropriate use of antibiotics can also be harmful so it is important to only treat patients who have Lyme; here we would want a very specific test. Thus, Lyme is an illness where sequential testing makes sense and that's the reason for the CDC's two-tier protocol.

What looks good in theory falls apart in practice. This happens because the first step in the protocol lacks sufficient sensitivity. Most patients are first tested with the C6 ELISA by Immunetics, Inc. The following appears in the CDC's publication entitled Laboratory Management of Lyme disease Using a C6 Peptide Based ELISA Assay.

"The diagnosis of Lyme disease is based on clinical symptoms including potential exposure in a tick habitat and laboratory testing. Clinical symptoms include EM or a late stage manifestation of Lyme. EM appears in only 60-80% of infected patients. Laboratory diagnosis utilizes a two-tier protocol recommended in 1994 by the CDC and other groups.[3] In 1999 a novel peptide based assay for Lyme was first published using a 26 amino acid peptide (C6) which was determined to be conserved and immunodominant.[4] In a 2003 study by the CDC[5] comparing a C-6 peptide ELISA assay to the two-tiered testing protocol using a whole cell lysate ELISA and the western blot confirmatory test, showed, "overall sensitivities for detecting IgG antibodies to VlsE1 or C6 in samples from patients with diverse manifestations of Lyme disease were equivalent to that of 2-tiered testing." Data presented in the CDC paper showed that the ***sensitivity of the two tiered protocol for Acute Lyme (EM and early disseminated) was 38% (62% false negatives) while for the C6 assay alone the sensitivity was 44% (56% false negatives). For early convalescent patients, sensitivity was 65% for the two-tier method and 70% for the C6 ELISA method.*** *Clearly the single C6 Assay stands as equal to the two-tier test protocol in performance while improving significantly on cost per test turn around time and simplicity of testing."*

Look again at the sensitivity and specificity numbers. In a paper by Bacon et al.1, C6 could obtain a sensitivity of only 70%. This is a far cry from the sensitivity values we need to have in the first test of a two-step sequence and I suspect it's much lower than you were led to believe. When this test first hit the market the company claimed it had sensitivities close to 100% but that didn't pan out in real patients. Several papers have looked into why this happened and much of it comes down to differences between *Borrelia burgdorferi* species and strains and differences between the specimens used to develop the test and the specimens obtained from typical patients.

Given the poor sensitivity, a negative test has little value; it certainly does not rule out the infection."

Since step 1 is not sensitive enough, missing 30 – 56% of patients tested, it seems best to go back to making the diagnosis on clinical grounds. A physician may decide to use a positive result as a confirmatory test but given the poor sensitivity, a negative test has little value; it certainly does not rule out the infection.

If you decide to do serologic testing anyway, it makes sense to skip the ELISA. That's because a negative test has no usefulness and a positive test requires a confirmatory western blot. The sensitivity of western blots is dependent on the source of the test. There are pre-made kits with variable sensitivity and there are some specialized labs which do theirs tests from scratch. Either way, the sensitivity remains low, generally no more than 65%. If you do skip the ELISA and order a western blot, make it clear to your lab personnel that this is what you want. Many labs have an automatic over-ride for Lyme testing. This means that when you order a western blot they start

with the ELISA anyway and cancel the western blot if the ELISA is negative. Some physician orders apparently don't count for much; make sure yours do.

Most labs use FDA-licensed kits for doing western blots. This is because the test is very labor-dependent. Using a kit cuts down on the work but a lab tech still needs to "read" the bands and grade them based on the intensity of the signal. That is a subjective measure and it is reasonable to assume that techs who read lots of blots are better at it than those who rarely read them. When using a kit, a lab tech can only comment on the 10 CDC-designated bands. Even if a *Borrelia burgdorferi*-specific band were present, such as 31 or 34, the physician would not be notified of the occurrence. Labs which perform their western blots from scratch are free to report on any band that shows up. To create their own in-house western blot, a lab must jump through several regulatory hoops to prove that their tests are valid. To me it's like baking a cake – Betty Crocker might be quicker and easier but cakes made from scratch do taste better.

As stated above, western blots are insufficiently sensitive but they are highly specific, usually 95% or greater. Therefore a positive result truly does confirm a clinical diagnosis. One always has to keep in mind that western blots may remain positive after treatment. In asymptomatic patients you would expect them to eventually be clear of antibodies but we don't know when that event occurs in an individual patient. In symptomatic patients, it would seem prudent to consider a positive western blot as a sign of ongoing infection.

The sensitivity and specificity of western blots can be manipulated by changing the band criteria for what constitutes a positive test. The criteria adopted by the CDC were chosen on the basis of specificity. Recall that these were supposed to be criteria for establishing a surveillance group of Lyme patients. Surveillance groups are very select – every effort is made not to include someone in the group who does not have the illness. Epidemiologists want to follow an illness over time and geographic region and by treatment outcome; surveillance groups make this possible. But a patient can still have Lyme without meeting surveillance diagnostic criteria. Failing to recognize this possibility has been a common mistake made by most clinicians across the country.

To summarize: current ELISA tests, including the C6, are too insensitive to be used as a step 1 test in a sequential test scheme. Western blots have low sensitivity but high specificity. There is no compelling reason to deviate from the previously held position which acknowledged that Lyme disease should be diagnosed on clinical grounds.

References

1. Bacon, RM, et al. Serodiagnosis of Lyme disease by kinetic enzyme-linked immunosorbent assay using recombinant VlsE1 or peptide antigens of *Borrelia burgdorferi* compared with 2-tiered testing using whole-cell lysates. J Infect Dis. 2003 Apr 15;187(8):1187-99.

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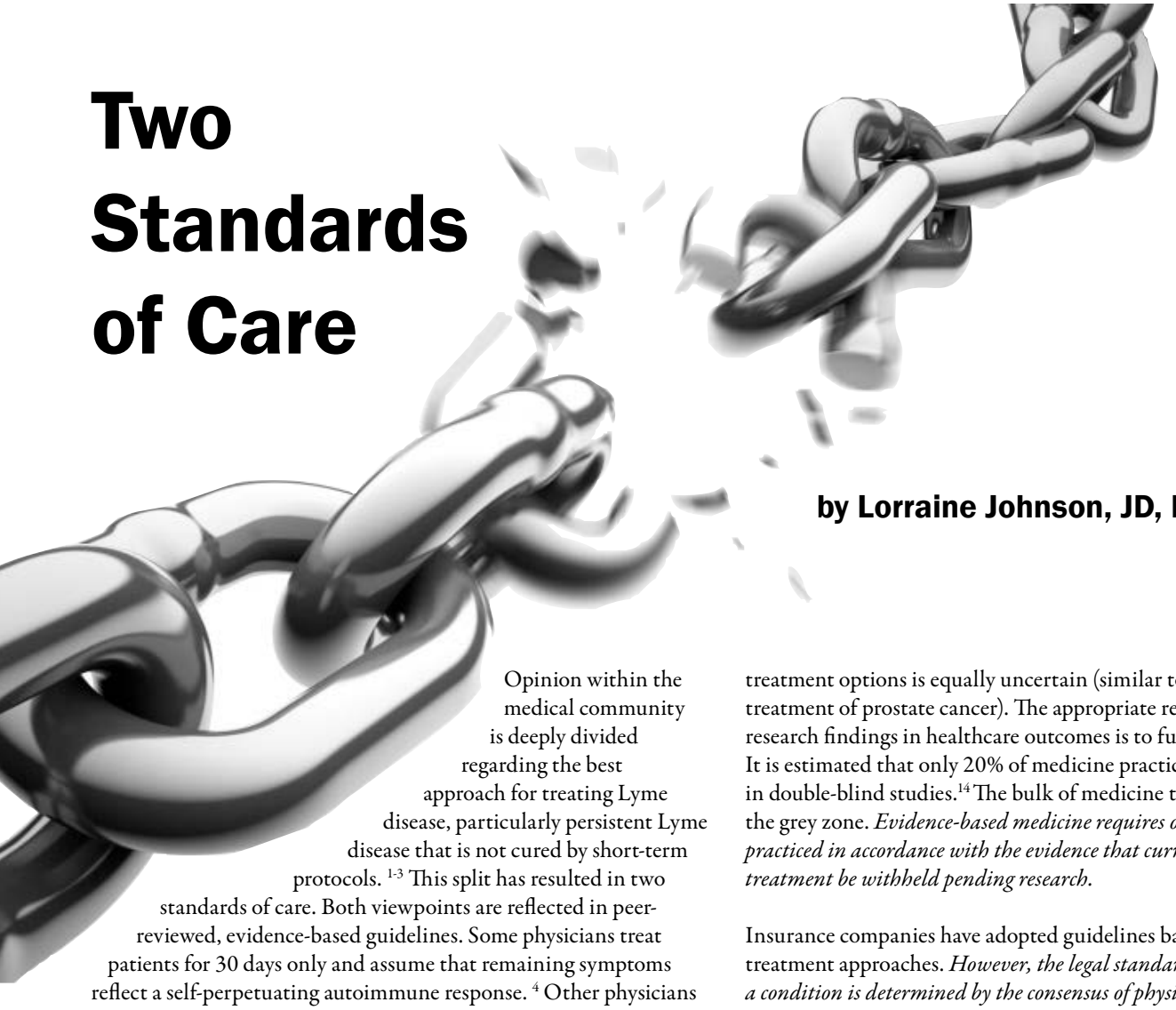
Two Standards of Care



by Lorraine Johnson, JD, MBA

Opinion within the medical community is deeply divided regarding the best approach for treating Lyme disease, particularly persistent Lyme disease that is not cured by short-term protocols. [1-3] This split has resulted in two standards of care. Both viewpoints are reflected in peer-reviewed, evidence-based guidelines. Some physicians treat patients for 30 days only and assume that remaining symptoms reflect a self-perpetuating autoimmune response. [4] Other physicians assume that the persistent symptoms reflect on-going infection and gauge the duration of treatment by the patient's individual clinical response. These physicians believe that there is insufficient evidence at this point to adopt standardized treatment protocols. [5]

While each viewpoint has a strong underlying hypothesis, the scientific evidence supporting either viewpoint is equivocal. Outcomes research is limited and conflicting. The National Institute for Allergy and Infectious Diseases (NIAID) has only funded three double-blind, placebo-controlled treatment outcome studies for long-term treatment of persistent Lyme disease. The findings of two studies (Klempner and Krupp) are contradictory, with one indicating that continued treatment is beneficial for treating fatigue and the other indicating that it is not.[6-8] The third NIAID-funded study has recently been completed and preliminary results support continued antibiotic treatment for patients with persistent Lyme disease.[9] The findings of five non-controlled studies support continued treatment.[1, 10-13] The existence of limited or conflicting controlled studies is not uncommon in the practice of medicine. When this is the case, of necessity the unique clinical course of the patient bears the laboring oar in treatment decisions.

Insurance companies have placed the full weight of their economic clout behind less expensive, short-term treatment protocols. More expensive longer-term treatment options are discredited as "experimental" or "not evidence-based." The point, of course, is that the science underlying both the short-term and the longer-term treatment options is equally uncertain (similar to the situation with treatment of prostate cancer). The appropriate response to equivocal research findings in healthcare outcomes is to fund more research. It is estimated that only 20% of medicine practiced today is rooted in double-blind studies.[14] The bulk of medicine today is practiced in the grey zone. *Evidence-based medicine requires only that medicine be practiced in accordance with the evidence that currently exists, not that treatment be withheld pending research.*

Insurance companies have adopted guidelines based on short-term treatment approaches. *However, the legal standard of care for treating a condition is determined by the consensus of physicians who actually treat patients, not by treatment guidelines.*[15] Moreover, more than one standard of care may exist. A number of surveys have found a fairly even split among treating physicians in the case of Lyme disease: One survey found that 57% of responding physicians treat persistent Lyme disease for three months or more.[16] In another survey, "50% of the responders considered using antibiotics for a time greater than one year in a symptomatic seropositive Lyme disease patient. Almost that same number would extend therapy to 18 months if needed."[17] For treating early Lyme disease, there is conflicting evidence. Most physicians responding to one survey specified short-term treatment [18], while 43% of those responding to another survey would treat erythema migrans-positive Lyme disease for three months or more.[16]

When more than one standard of care exists, the critical question becomes *who* decides the appropriate course of treatment for the patient. Under the medical ethical principle of autonomy, the treatment decision belongs to the patient. Hence, the American Medical Association requires that the physician disclose and discuss with the patient not only the risks and benefits of the proposed treatment, but also the risks and benefits of available alternative treatments (regardless of their cost or the extent to which the treatment options are covered by health insurance).[19] For example, patients with prostate cancer (where significant uncertainty exists regarding long-term treatment outcomes) must elect between watchful waiting, radiation and surgery. The legal doctrine of informed consent also requires that patients be advised of material treatment options. Treatment choices involve trade-offs between the

risks and benefits of treatment options that only patients—who know the kinds of risks they are willing to run and the types of quality of life outcomes that matter to them—are uniquely suited to make. [20]

Respect for the basic autonomy of the patient is a fundamental principle of medical ethics. Without adequate information about treatment options, their probable outcomes, and the risks and benefits associated with each, patients cannot act autonomously. Today, however, many patients are either denied treatment by their HMO physicians who follow actuarial treatment protocols generated to keep treatment costs down, or they must find an independent physician to treat them, with the all but foregone conclusion that coverage for this treatment will be denied by their insurer based on cherry-picked (economically favorable) guidelines. Moreover, HMO physicians generally do not advise their patients that treatment alternatives exist.

Scientific uncertainty about Lyme disease has resulted in more than one treatment approach (like prostate cancer). We agree with the AMA, ACP and other professional medical organizations interested in promoting informed patient consent and want to make sure that:

- Physicians, insurers, patients and governmental agencies are educated that two treatment approaches exist;
- Physicians give patients sufficient information about treatment options to enable patients to make a meaningfully informed choice and respect the autonomy of that choice;
- Insurance reimbursement be provided for treatment rendered in accordance with either standard of care; and
- Government agencies provide unbiased information and remain neutral regarding both standards of care and treatment approaches.

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Speciality Bias

Significant speciality bias exists in the treatment of persistent Lyme disease. A study by Ziska et al. shows that the majority of infectious disease physicians treat for four weeks or less, while the majority of internal medicine physicians treat for greater than six months:

Treatment Duration	Infectious Disease Specialists	Internal Medicine Specialists
2-4 weeks	43%	0%
3-6 months	7%	45%
>6 months	29%	55%

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Anti-fungal Agents

Prescription:

Fluconazole (Diflucan) – may have anti-Lyme activity; need to monitor liver tests

Itraconazole (Sporanox) – need to monitor liver tests

Ketaconazole (Nizoral) – need to monitor liver tests

Nystatin (Mycostatin) – non-absorbable, non-toxic

Amphotericin – intravenous med that can be given orally. Not absorbed

Non-Prescription:

Capryllic acid – derived from coconut oil

Citrus extract – may interfere with antibiotics

Oregano oil – can cause GI irritation

Olive leaf extract – well tolerated, may have activity against Lyme

Undecylinic acid – well tolerated

Gentian – very powerful but can be toxic to the liver

Taheebo tea – well tolerated but weak

Garlic – need to take high amounts to be effective

Hydrogen peroxide – potent but potentially toxic to the GI tract

Colloidal silver – short courses may be effective, but long-term administration may lead to toxic build-up of silver

Problems with Yeast

by Daniel A. Kinderlehrer, MD

Candida and other yeast are normal colonizers of our mucous membranes, including the mouth, intestines and vagina. Under normal circumstances, they don't bother us and we don't bother them. Their numbers are kept down by our immune systems and the presence of beneficial bacteria, which inhibit their growth. However, under certain circumstances, yeast can overgrow and cause problems. Lyme patients are particularly prone to these problems because of their long courses of antibiotics.

Yeast overgrowth can lead to local problems such as vaginitis, intestinal bloating and gas, as well as oral thrush. But it can also lead to systemic issues that overlap with Lyme, and can make problems associated with tick-borne diseases (TBDs) much worse. The mechanism is probably multifactorial, including the release of endotoxins from the yeast, as well as allergic reactions, since people with yeast problems feel worse when they eat yeast-containing foods as well as sugar, which feeds the yeast residing on their intestinal linings.

Common symptoms of yeast problems, often referred to as Candida Sensitivity Syndrome (CSS), include fatigue, brain fog, mood swings, intestinal pain, sugar and carbohydrate cravings, bloating and gas, headaches, unexplained pain syndromes, and recurrent yeast infections—of the vagina, the mouth and the skin. People with CSS often have hormonal abnormalities such as autoimmune thyroiditis and severe PMS. CSS can trigger autoimmune phenomena, and I have seen many patients with multiple sclerosis, rheumatoid arthritis and lupus go into sustained remission when their yeast problems were properly treated.

Testing for yeast is not particularly rewarding. The diagnosis is made by taking a good history and going on a trial diet of yeast-free foods, often with an antiyeast agent. There is typically a die-off period similar to the Herxheimer reactions experienced with Lyme, and then subsequent improvement, with exacerbation of symptoms when you eat that chocolate ice cream you were lusting after.

I often see patients who have already been treated with long courses of antibiotics, and I start out just treating their yeast problems. It is not unusual for more than half their symptoms to respond. Anyone on antibiotics should be on antifungal agents and probiotics, and off sugar, to prevent yeast overgrowth.

Dr. Daniel A. Kinderlehrer is an internist with a background in Complementary and Alternative Medicine, whose practice in Santa Fe, NM, is devoted to treating patients with tick-borne disease. He can be reached at dankinderlehrer@gmail.com.

Yeast-free Diets

Avoid foods with yeast in all forms—breads, rolls, pastries, mushrooms [hint: no yeast breads are available in the health food store].

Condiments—pickles, mustard, soy, ketchup, olives, sauerkraut, vinegar, salad dressings [hint: substitute lemon juice for vinegar on your salads].

Fermented beverages, alcohol, apple cider, root beer.

Sugar—sucrose, fructose, maltose, lactose, glycogen, glucose, mannitol, sorbitol, honey, maple syrup, date sugar, rice syrup.

Cheese, peanuts and peanut butter [Hint: almond butter on rice cakes with a slice of apple or banana makes a good snack.]

Fruits—avoid dried and candied fruits, fruit juices, berries, melons and grapes, and limit other fruits to one or less per day.

Gastrointestinal Lyme

by Martin D. Fried, MD

Lyme disease has been reported in the gastrointestinal (GI) tract of children and adolescents. Pediatric gastrointestinal Lyme disease may present as abdominal pain, vomiting, diarrhea, heartburn, blood in the stool, and it may mimic Crohn's disease or colitis. Blood tests for diagnosing Lyme disease may be negative while gastrointestinal and other Lyme disease symptoms persist. The diagnosis is made clinically on the basis of symptoms and by excluding other possible etiologies. Once treatment has begun with antibiotics, most patients reported a decrease in the frequency and severity of their abdominal pain. In addition to antibiotics, a low fat diet further alleviated some of the abdominal symptoms associated with Lyme disease. In patients who reported having a crampy, colicky, below the belly button pain, treatment also included antispasmodic and anticholinergic medications. After treatment is completed, some residual abdominal pain may persist for a couple of months at a markedly reduced level of severity. This diminished pain usually represents the activation and persistence of the immune system to fighting the infection even long after the infection is gone. In addition to Lyme disease, other coinfections such as Bartonella, mycoplasma, H. pylori and babesia have been confirmed to occur in the GI tract.

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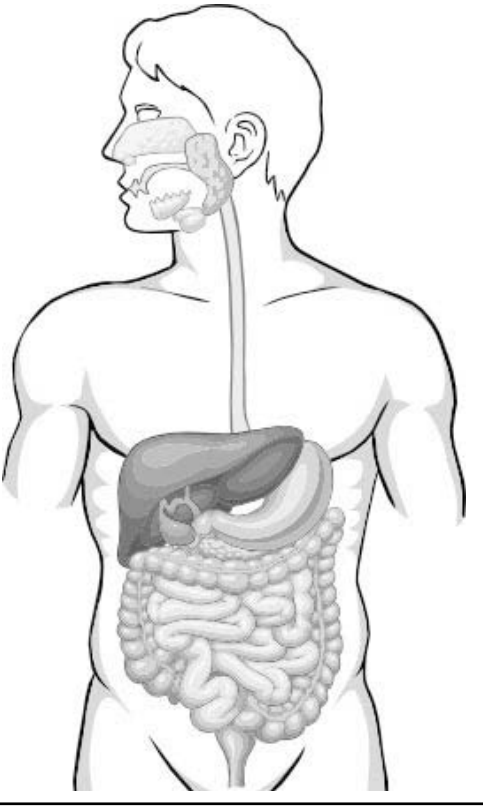
Common GI Symptoms Due to Lyme Disease

- Gastroparesis
- Small intestinal bacteria overgrowth (SIBO)
- May mimic Crohn's disease or colitis



- Abdominal pain
- Vomiting
- Diarrhea
- Heartburn
- Blood in the stool

For further information, see Fried, M.D., M.E. Adelson, and E. Mordechai, *Simultaneous gastrointestinal infections in children and adolescents*. Practical Gastroenterology, Nov. 2004: p. 78. Fried, M.D., M.P. Abel, D., and A. Bal, *The spectrum of gastrointestinal manifestations in Lyme disease*. J Pediatr Gastroenterology & Nutrition, 1999. 29(4): p. 495.

Flagyl Fights Spirochetes

by Martin Atkinson-Barr, PhD

The potential of a miracle drug from the 1950s

Adapted from an article by Martin Atkinson-Barr, PhD, which originally appeared in the Lyme Times #41, Spring 2005.

Back in 1974, when Dr. Atkinson-Barr first learned about metronidazole (Flagyl), he knew it was something special. Having joined the French drug firm Rhône-Poulenc, he found that his colleagues were excited about this compound even though it had been on the market with other nitroheterocyclic drugs since they were introduced in the late 1950's and 1960's. Unfortunately, since the patent had expired, the company accountants were not as enthusiastic.

Metronidazole, the first of a class of antimicrobials called the 5-nitroimidazoles, was followed by tinidazole (Fasigny), secnidazole, and ornidazole (Tiberal). Although metronidazole was originally the only one marketed in the US, tinidazole eventually became available. Elsewhere in the world, these drugs are mainstays of tropical medicine.

Initially, metronidazole was used against *Trichomonas vaginalis*, a sexually transmitted protozoal parasite. Trichomonas moves using a whip-like propeller of flagellar protein attached to its rear. Add a few drops of metronidazole to some *Trichomonas* and those propellers stop whirling within minutes. That's how metronidazole got the brand name *Flagyl.*

In 1967, a published paper described the successful use of metronidazole in treating syphilis. It concluded that penicillin was so effective that metronidazole was only of passing interest. A subsequent paper described how metronidazole impaired the mobility of *Treponema pallidum,* the spirochete that causes syphilis*,* in a gel medium.

In 1985, in the biggest medical upset in memory, Barry Marshall published his discovery that stomach ulcers were due to infection by a corkscrew-shaped bacterium, *Helicobacter pylori,* that lives in the mucous layer of the stomach. Eventually, doctors devised a triple therapy of metronidazole, tetracycline and Pepto-Bismol to eradicate the infection and cure the ulcer.

Because the typical spirochete is so small, viscosity is everything: there is no up and down, only variations within a gooey environment. With its spiral shape, a spirochete is especially well designed to move in gelled or fatty conditions and does less well in "thin" liquids like water.

In 1997, when Dr. Atkinson-Barr began to study Lyme, it struck him that the 41kDa line on the western blot was flagellar protein. Where was this protein? It turns out that it is the material of the axial filaments, literally the backbone of *Borrelia.* Flagellar protein is what makes many spirochetes spiral and provides the mechanism of motion. He called such spirochetes "internally flagellated" in contrast to "external flagellates" like *Trichomonas*. When you see a corkscrew or spiral organism, flagellar protein is likely present. Metronidazole can stop it from moving.

All *Borrelia burgdorferi* are not spiral-shaped at any one time, however. In fact, it seems to be quite a rare form. Most of the bacteria seem to be in round forms, either granules or cysts. When a spiral form converts to a cyst, the flagellar protein does not disappear but rather forms a layer beneath the cell wall, giving the wall three layers rather than two. In 1999, Norwegian researchers Øystein and Sverre-Henning Brorson demonstrated that metronidazole, unlike commonly used antibiotics, kills the Bb cysts *in vitro*. Dr. Atkinson-Barr and Richard Horowitz, MD, conducted a pilot study that demonstrated the effectiveness of metronidazole in a group of 144 patients previously treated aggressively with other antibiotics.

All 5-nitroimidazoles have some notable advantages: they are very small molecules (one-third the size of conventional antibiotics) and dissolve well in fats. They can reach everywhere in the body, especially the central nervous system, and cross easily into the interior of pathogens. Some disadvantages include a possible increased risk of cancer. Metronidazole has been widely used, however, and Dr. Atkinson-Barr's review of the studies suggests that this risk has been greatly over-blown. Long-term use of metronidazole has been associated with peripheral neuropathy that slowly reverses. On balance, Dr. Atkinson-Barr concluded that tinidazole was a better alternative since many such issues are reduced or eliminated.

While further controlled studies are needed, the 5-nitroimidazoles continue to have their place in the Lyme clinician's armory.

Dr. Atkinson-Barr died suddenly and unexpectedly in September, 2008. He was 56.

Drug-Supplement Interactions in Lyme Disease

by Leo Galland, MD

Interactions between prescription or over-the-counter drugs and nutritional supplements are common and often not well known. In creating the Drug-Nutrient Workshop (www.Nutrition-Workshop.com), a professional database of interactions between drugs and dietary supplements, nutrients, and food or food components, I found that over 400 drugs commonly used in the U.S. deplete specific nutrients and almost 500 drugs have their efficacy or side effects influenced by various foods. I also identified about a thousand adverse interactions between drugs and dietary supplements and several hundred beneficial interactions in which specific dietary supplements may enhance the efficacy or decrease the side effects of specific drugs.

People with Lyme and related diseases may receive prolonged therapy with antibiotics, sometimes combined with Prilosec or other proton-pump inhibitors (drugs that greatly reduce stomach acid) or Plaquenyl (an immune modulator) to alkalinize the intracellular vacuoles where the bacteria hide. Patients co-infected with babesia may be prescribed anti-parasitic drugs as well. Some potential interactions (negative and positive) between these drugs and dietary supplements are described below. Information on drug/food interactions is usually available from the pharmacist and included in the patient-package insert. This should be checked for each individual drug being taken, because the dosage form (sustained release vs. regular, for example) may influence the effect of food on drug absorption. Patients with chronic tick-borne infections may also be taking antidepressants and pain relievers, each of which may have its own interaction with nutritional supplements and nutritional status.

Drugs may interact with food or supplements through three primary mechanisms: drug absorption may be impeded by a food or supplement; the drug may impair absorption of nutrients; the drug, food or supplement may affect drug metabolism through the P450 pathway.

Food or supplements may interfere with drug absorption. This is especially important for tetracycline or quinolone antibiotics. (Although quinolones, like Cipro and Levaquin are not used for Lyme disease; they are used to treat bartonellosis, a common coinfection). Both groups of antibiotics form insoluble complexes with minerals, especially calcium, magnesium or iron. This process, called chelation, inhibits absorption of both the antibiotic and the mineral. Not only is tetracycline (though not minocycline or doxycycline) and all quinolones better absorbed away from food (especially mineral-rich foods like meat and dairy products), they must be taken several hours apart from any nutritional supplements containing minerals. Two hours of separation may not be enough. Several herbs, including fennel, dandelion, and Sanguisorba, have a high enough mineral content that their consumption has been shown to interfere with quinolone absorption.

Penicillins may have their oral absorption impaired by fi ber or food, although this is more likely for penicillin V and ampicillin than for amoxicillin. Food causes the drug to be retained in the stomach, where the presence of acid causes the drug to decompose. Psyllium has been shown to bind oral penicillin, decreasing its absorption.

Drugs may deplete nutrients from the body. The normal gastrointestinal bacterial flora synthesize B vitamins, biotin and vitamin K, which are absorbed and utilized by humans. Depletion of these bacteria by prolonged antibiotic therapy may produce vitamin deficits. Bleeding caused by vitamin K deficiency has occurred as a result of intravenous therapy with cephalosporin antibiotics[1], a group that includes Ceftin, Rocephin and Claforan. High-dose penicillin therapy causes increased excretion of potassium by the kidneys[2]. When combined with antibiotic-induced diarrhea or poor appetite, this eff ect may cause potassium deficiency, with fatigue and muscle weakness as primary symptoms. Proton-pump

inhibitors like Prilosec, used to enhance antibiotic absorption and cellular penetration, decrease formation of stomach acid, permitting overgrowth of bacteria and/or yeast in the stomach and upper gastrointestinal tract. This is also true for other agents that lower stomach acid, such as Zantac and Pepcid. Microbial overgrowth may be associated with gastrointestinal symptoms like diarrhea and bloating[3] and may cause malabsorption of nutrients. Prolonged use of stomach acid lowering agents has been associated with decreased absorption of vitamin B12, zinc, and carotene, and may create a need for supplementation[4].

Drugs, supplements and food may affect drug metabolism. The cytochrome P450 (CYP) system is extensively involved in drug metabolism and may be strongly inhibited or stimulated by drugs, foods or dietary supplements. CYP enzymes are most active in the liver, intestines, lungs and kidneys. Humans have over 20 different CYP enzymes, all of which use oxygen to change the structure and function of the drugs they metabolize. CYP oxidation of drugs may produce metabolites that are less active or more active than the parent compound. The exact effect of inhibiting or stimulating any CYP enzyme will therefore depend upon the specific clinical circumstances and cannot necessarily be predicted from experiments done in a test tube.

Inhibition of intestinal CYP by grapefruit juice or other natural substances can increase absorption of drugs that are broken down by CYP, raising their concentration in blood. St. John's wort is one of the few products that stimulate intestinal CYP. Taking St. John's wort can decrease the plasma concentration of those same drugs and underlies many of the adverse drug interactions (particularly blood thinners and birth control drugs) reported for this herb.

Rifampin (an antibiotic sometimes used to treat Bartonella) and artemisin (a derivative of the herb Artemisia annua, a natural anti-malarial herb that may be used in the treatment of Babesiosis) may also stimulate some CYP enzymes, which decrease the blood levels of some drugs. If given long term, some physicians suggest three weeks on and one week off , so that the CYP enzymes are not over stimulated, leading to decreased blood levels of the drug. In contrast, macrolide antibiotics, azithromycin (Zithromax), clarithromycin (Biaxin) and telithromycin (Ketek) and antifungals like fluconazole (Diflucan), ketoconazole (Nizoral) and itraconazole (Sporanox) are inhibitors of specific CYP enzymes, which can increase the blood level of drugs. Prilosec is also a CYP inhibitor.

Some interactions demonstrated in clinical studies cannot be anticipated from laboratory experiments. The herb Echinacea, used for immune stimulation, has different effects on CYP enzymes in different parts of the body, so it may increase or decrease the levels of a co-administered drug, depending upon the extent to which it is metabolized by CYP. Unexpected results also occur with milk thistle, an herb used to support liver function that contains a group of bioflavonoids called silymarin. Although silymarin may inhibit liver CYP (which should increase drug levels), concomitant administration of milk thistle significantly decreased the blood levels of metronidazole (a drug used to treat the cyst form of Borrelia).[5] This interaction could not have been predicted from knowledge of the herb's effects on drug-metabolizing enzymes. Moreover, vitamin C (500 mg/day) and vitamin E (400 units/day) decreased the effectiveness of metronidazole in treating H. pylori infection of the stomach.[6] The mechanism of this interaction is unknown but suggests that antioxidants should not be used with metronidazole therapy.

Some Supplement and Drug Interactions	
Licorice	Anticoagulant/Antiplatelet Drugs: Licorice may potentiate activity and lead to complications of bleeding. MAO-inhibitors (MAO-I): Licorice may potentiate activity of MAO-I.
Gingko	Cytochrome P450: Preliminary evidence indicates that ginkgo can affect the cytochrome enzymes 1A2, 2D6, and 3A4, however controversial data exists regarding whether it induces or inhibits the individual enzymes.
Reishi	Anticoagulant / Antiplatelets: Reishi may increase the risk of bleeding. Antihypertensives: Reishi may further lower blood pressure.
St. John's Wort	Oral contraceptives: May decrease effectiveness by lowering levels to sub-therapeutic. Anti-coagulants: May lower the effectiveness by increasing metabolism.
Grapefruit Seed Extract	There are no data on grapefruit seed extract, although some physicians believe that it interferes with antibiotics. We do know that it takes lots of grapefruit juice to produce clinically significant drug interaction effects (a quart of double strength juice a day is used in many studies). The active ingredient is probably a substance called bergamotin, but we don't know if that is in the seed extract.

Drug Interactions

Some drugs are processed through the liver using the P450 pathway, and some supplements may induce or inhibit this pathway. Supplements that induce the P450 pathway may result in drugs using that pathway metabolizing faster, resulting in lower blood levels of the drugs than expected. Supplements that inhibit the P450 pathway slow down metabolism of drugs using that pathway, allowing drug levels in the blood to increase beyond that expected. Higher drug levels can increase the toxicity and side effects of the medication, while decreased drug levels may be sub-therapeutic.

Herb or Supplement or Food*	Inhibits P450 3A	Induces P450 3A
Milk Thistle	X	
St. John's Wort		X
Goldenseal	X	
Grapeseed extract	X	
Garlic		X
Cat's Claw	X	
Grapefruit	X	
Artemisia		X
Gingko	X?	X?
Medications**		
Macrolide antibiotics (Biaxin, Zithromax, Ketek)	X	
Erythromycin	X	
*Rifampin (Rifadin, Rimactane)		X
Antifungals (Diflucan, Sporanox, Nizoral)***	X	

*Memorial Sloan Kettering Cancer center at www.mskcc.org/mskcc/html/11570.cfm

**Flockhart's list at http://medicine.iupui.edu/fl ockhart/table.htm

***Also inhibit substrate 2C9

Quercetin, a bioflavonoid used as an anti-oxidant and for relief of allergic symptoms, competes with quinolone antibiotics for binding sites on bacteria. No interaction between quercetin and antibiotics has yet been demonstrated outside a test tube, but it would be prudent for people taking quinolone antibiotics to refrain from the use of quercetin and perhaps other bioflavonoids such as hesperidin.

Beneficial effects of dietary supplements for people taking antibiotics have been described. The most consistent benefits have been demonstrated for probiotics (beneficial bacteria) that can counter the gastrointestinal side effects of antibiotics. The best studied are *Saccharomyces boulardii* (a yeast, dubbed "yeast against yeast" in France)[7], *Lactobacillus rhamnosis* GG[8], *Lactobacillus plantarum* and *Lactobacillus sporogenes*[9]. Other bacteria are also beneficial, including *Lactobacillus acidophilus* and *Bifidobacterium*.

Proteases are enzymes that digest protein. When taken by mouth on an empty stomach, some of the preparation is absorbed intact and may be active in the body. Oral proteases have been shown to relieve pain and inflammation in patients with arthritis[10], may break down circulating complexes of antigen and antibody associated with Lyme disease, and may break down blood clots that form as a result of inflammation. Although research on proteases as adjuncts to antibiotic therapy is minimal, a study done in animals found that bromelain (a protease-containing extract of pineapple stem), increased penetration of tetracyclines into the tissues[11].

A recent study in JAMA found that drug interactions were one of the leading causes of death in hospitals.[12] Patients and physicians need to be aware of the interactions between foods, drugs, and supplements to avoid unintended effects that may occur when they are combined. The blood levels of some drugs may rise to toxic levels when the Cytochrome P450 pathway is inhibited. Alternatively, when the P450 pathway is enhanced, blood levels of drugs using these pathways may fall to subtherapeutic levels. Most importantly, because we are still discovering the nature of these interactions, some degree of restraint may be prudent when combining supplements with medications, even where no known interactions exist.

Nutritional deficiencies caused by drugs also may need to be addressed. Cholestyramine, utilized by some practitioners as part of a detoxification program, binds fats, including fat-soluble vitamins (A, E, K). This drug needs to be taken at least two hours before and after ingestion of food and supplements.

Dr. Leo Galland practices internal medicine in New York City. He is also president of Applied Nutrition, Inc, which develops software for the application of nutrition to health care at www.nutritionworkshop.com and is director of the foundation for Integrated Medicine, www.mdheal.org, an educational organization. He may be reached at 133 East 73 Street, New York, N.Y. 10021, 212-772-3077.

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Milk Thistle and Vitamin C: Effect on Flagyl Treatment

Although P450 pathway inducers and inhibitors are known to reduce effectiveness of some medications or allow potentially dangerous blood levels of a drug to occur, other unidentified interactions can create problems. Leo Galland, MD, writing in the Townsend Letter June 2005, noted unexpected Flagyl interactions:

- Silymarin (milk thistle) has been shown to reduce blood levels of Flagyl by 30%, an effect that could lead to therapeutic failure.
- Vitamin C (250 mg twice daily) combined with Vitamin E (200 mg twice daily) reduces the effectiveness of metronidazole through an unknown mechanism.

Medication Side Effects and Interactions:

Online Information

As reported by Lazarou in JAMA, 1998, drug interactions are a leading cause of death in hospitals. It is advisable to know the side effects associated with the medications you are taking and whether there are any harmful interactions identified. For pharmacology, indications, contraindications, side effects, and precautions, try www.rxlist.com. For a drug interaction checker, try www.drugs.com/drug_interactions. Enter all your medications and learn if there are any known harmful interactions.

Other online sites include:

- Drug Digest: www.drugdigest.org/DD/Home
- Herb Med: www.herbmed.org
- Memorial Sloan Kettering Cancer Center: extensive information on supplements and herbs. www.mskcc.org/mskcc/html/11570.cfm
- Nutrition Focus: extensive information on supplements: http://nutritionfocus.com

Probiotics

by Polly Hattemer

Most Lyme treatment protocols include the use of antibiotics. Unfortunately these drugs kill beneficial bacteria and facilitate the overgrowth of antibiotic-resistant bacteria as well as yeast. This interferes with digestion, nutrition and the immune system. The normal population of bacteria is essential in the production of specific vitamins, lowering cholesterol, protecting against cancer, and recirculating hormones.

To help combat these complications of antibiotics, many people turn to probiotic supplements. Probiotics (which literally means "promotes life") are beneficial microorganisms that help maintain the normal intestinal flora. The most common type of probiotic is bacteria commonly found in yogurt and other fermented foods. These include *Lactobacillus acidophilus and Bifidobacteria*, including *B. breve* and *B. longum*. *Lactobacillus rhamnosus,* a bacterium found in some yogurts, has demonstrated particular benefits to the immune system. Certain yeast may also be used as probiotics. Another popular type of probiotic is soil-based organisms (SBO), which, as their name implies, are found in the soil.

All probiotics can be effective, yet all aren't appropriate for everyone. Probiotics should be used properly and judiciously; otherwise they may be ineffective or even harmful.

How to use

Keep the probiotics dry, and store them in the refrigerator or freezer. Do this even if the bottle says it is okay to be kept on the shelf, as the refrigerator will do a better job of maintaining live organisms. Most probiotics will retain their potency if you forget and leave them on the counter for a day or even a week. However, most probiotic products would be ruined if they were left in a very hot mail truck all day. So try to have your probiotics shipped to you on dry ice. This is particularly important in the summertime.

Since heat can kill the probiotics, they should not be mixed with hot food. Chlorination also kills microorganisms, so don't take them with chlorinated water. Stomach acid kills microorganisms, so don't take probiotics on an empty stomach unless you first drink some water, which will dilute the stomach acid. Food can also neutralize the stomach acid, so take probiotics with meals.

One way to get the immune modifying effects of probiotics is to brush your gums with them. Dr. Nagoya, a dentist from Japan, developed this idea. He found that it helps with periodontal disease. Theoretically, this protocol should help modify your entire immune system. For gum brushing, use a normal human food bacteria like L. acidophilus— don't use a soil-based probiotic. Use probiotics that don't have added lactose, inulin or artichoke, which may feed pathogenic bacteria. After brushing your teeth, apply the powdered probiotics on your toothbrush and gently brush your gum. In the beginning, brush five times a day (morning, after each meal, before bedtime). You should see some improvement in your gums in about three days; then reduce to twice daily (morning/night). Do not rinse after brushing with the probiotics.

One way of introducing good bacteria directly into the large intestine is to give a baby enema of low dose *Bifidus*. *Bifidus* is the most predominant bacteria in the colon, and therefore the safest bacteria to use. Use warm non-chlorinated water for the baby enema. Another option is a suppository of a low dose *Bifidus* capsule, perhaps two billion microorganisms. Make sure the capsule is the type that dissolves easily in water (gelatin, not cellulose). Some people prick the capsule with a needle to enhance dissolution. Don't use a high dose probiotic product for the baby enema or suppository. It is not necessary, and you don't want a strong reaction. If you are quite ill, seek the advice of a physician before trying this route.

How much is needed?

The probiotics on the market usually contain 2-30 billion bacteria per pill. This is very little compared to the trillion bacteria in the intestines. So probiotics have no chance of replacing the existing flora by the might of sheer numbers; nevertheless, taking probiotics can alter the environment of the intestines enough so that eventually different flora will take over.

Most studies of normal resident probiotics (like *L. acidophilus* and *Bifidus*) are done with 30-200 billion bacteria per day. Studies with soil-based bacteria use much less (only 2 billion bacteria per day). We know that these doses are effective in most people, and anecdotal experience suggests that less usually isn't going to help. Look at the amount on the product before you decide to purchase it. Be careful with the higher counts — always start with less and work up to be certain you tolerate them.

Yeast

Yeast/fungus is commonly found in the intestines of people who live in industrialized nations. Although quite common, yeast in the intestines is not necessarily good for health. In fact, an overgrowth of yeast is quite harmful, and can lead to gynecological

problems, intestinal upset, thrush, sinus infections and systemic allergies.[4] The lactic acid produced by *L. acidophilus* serves to keep yeast species such as *Candida albicans* from overgrowing.

There is, however, one circumstance in which yeast can be utilized to improve the intestinal environment. A yeast called *Saccharomyces boullardii* is the best probiotic available for controlling antibiotic-induced diarrhea. It can even control *Clostridium difficile*, a virulent infection that can occur after the administration of oral antibiotics. However, one must be careful even with this yeast, since an overgrowth of *Saccharomyces boulardii* can occur in highly immuno-compromised individuals, such as AIDS patients.[5]

Precautions

Probiotics may increase the growth of amoebic/protozoan parasites.[1] Therefore, eliminate these parasites before trying probiotics. If you have had long-term intestinal problems, ask your physician to test you for parasites. Up to 10% of Americans harbor these single cell organisms, so don't think you have to travel to an exotic locale to become infected. [Dr. Dan Kinderlehrer highly recommends Parasitology Center in Tempe, AZ (480-767-2522) as perhaps the best parasite detection lab in the U.S. Technicians in most hospital labs are not well trained in parasite detection, and Parasitology Center is much more likely to pick up these critters.] If you have parasites, they can adversely impact immune function and cause systemic problems, such as arthritis. There are herbs, homeopathic remedies and specific antibiotics that will help you eradicate them.

Check the other ingredients in your probiotics. FOS (Fructooligosaccharides), inulin, and artichoke (which contains FOS) are often found in probiotic products. These additives could be helpful for some, yet possibly harmful for others. These additional ingredients are added to promote the growth of the beneficial *Bifidus* bacteria. However, certain yeast and harmful bacteria can also use these ingredients as food.[2,3] If you happen to have an overgrowth of these latter organisms, then the FOS and inulin might make you worse. Be particularly wary of these additives if you have bloating after meals, which may be a symptom of a bacterial overgrowth in the small intestine, although it is also a symptom of *Candida* overgrowth. If intestinal symptoms worsen after taking a probiotic with FOS or inulin, then try a probiotic without these additives. Plant sterols/sterolins are added to some soil-based probiotic products. These purportedly lower cholesterol and may benefit men with prostatic hypertrophy, but they can also interfere with absorption of fat-soluble vitamins—A, D, E and K. The main plant sterol, beta-sitosterol, has also been shown to harm the reproductive systems of rabbits and fish.[7] Plant sterol /sterolins may not be appropriate for everyone.

Soil-based organisms have been hugely beneficial to many people (See *Patient Heal Th yself* by Jordan Rubin, Freedom press ©2003). Unfortunately, we don't know what the contents of these products are. Soil-based probiotics contain a wide mix of organisms, many of which are not identified, and can be dangerous for individuals who are immunosuppressed, such as people with AIDS or chemotherapy patients. There are case reports of systemic infection in individuals after intake of SBO. *L. rhamnosus* could also be harmful to the highly immunocompromised population.[6]

You might tolerate one type of probiotic better than another. For example, some people must avoid *Bifidus* but find *L. acidophilus* to their liking. Other people love what *Bifidus* does for them, but they can't tolerate *L. acidophilus*. In some individuals, *L. acidophilus* produces so much lactic acid that the intestinal environment becomes too acidic. Everyone is different. Always start with a little and gradually increase the dose to the recommended level. Observe your personal experience and see what feels the best.

Children under the age of two have a different intestinal flora composition from that of adults (*Bifidobacteria* are particularly important in children), therefore, make sure to purchase a probiotic made especially for youngsters.

Polly Hattemer provides information and a discussion forum for yeast, GI and probiotics issues on her website: www.healthyawareness.net.

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How to Respond to Insurance Denials Based on IDSA Guidelines

by Lorraine Johnson, JD, MBA

Now that the Connecticut Attorney General has released his findings of the antitrust investigation into the IDSA guidelines, what should you do about insurance denials? If you are denied insurance coverage for Lyme disease based on the IDSA guidelines, you should:

- **Send your insurer a letter** objecting to the denial. Point out that the Connecticut Attorney General found the IDSA guidelines were seriously flawed and that the IDSA "allow[ed] individuals with financial interests—in drug companies, Lyme disease diagnostic tests, patents *and consulting arrangements with insurance companies*—to exclude divergent medical evidence and opinion," specifically, evidence and opinions supporting the diagnosis and treatment of chronic Lyme disease. You may download the sample letter from the CALDA website, http://www.lymedisease.org/resources/insurance.html.

- **Attach a copy of the Attorney General's press release to the letter.** This is also available on the CALDA website.

- **Send your State Attorney General a copy of your letter to your insurance company**. You can locate your state Attorney General's address at http://www.naag.org/ag/full_ag_table.php

What do you do if your insurer does not respond to this request? Take it from Joanna Smith, a patient advocate who runs Healthcare Liaison Inc. in Berkeley. "I always say to people, 'Appeal, appeal, appeal,'" she said. "And then, 'Appeal again.'" Follow all of your internal and external rights of appeal and call your state Attorney General to complain about your insurer. Although this will not always work, Attorneys General are becoming more active and more concerned about health care denials. Your job is to let them know your health care insurer is denying you medical care based on flawed guidelines that are under attack.

Lorraine Johnson is Chief Executive Officer of the California Lyme Disease Association (CALDA).

Tell Your Healthcare Provider About ILADS

YOU CAN HELP increase membership in the International Lyme and Associated Diseases Society (ILADS) by making healthcare professionals aware of this important medical society. Physician members treat tens of thousands of patients with chronic Lyme disease.

Tell your doctors about the ILADS website – www.ILADS.org – and print out the diagnostic and treatment guidelines to share with them. Make sure your doctors know about the fully accredited annual ILADS (and LDA) medical and scientific conferences, as well as the CALDA grants to help defray their expenses for attending.

ILADS supports the sharing of clinical experience among doctors who treat tick-borne diseases. An online group open to all ILADS members facilitates discussion and distribution of information. ILADS has published peer-reviewed treatment for chronic Lyme disease and is designing a training course.

If your healthcare provider is interested in receiving information about ILADS or applying for membership, they may contact the executive director, Barbara Buchman, at lymedocs@aol.com or call 301-263-1080.

The Registry – Be part of the solution!

by Joseph Burrascano, Jr., MD

One of the major challenges for physicians whose patients struggle with Lyme disease is the lack of professional agreement on how best to diagnose and treat tick-borne diseases. The ongoing debate surrounding the medicine and science of Lyme disease leaves the practitioner with ambiguous if not inconclusive guidelines and conflicting standards. Unlike other areas of medicine, clinical practice guidelines have yet to be universally adopted.

Thanks to funding from **Turn the Corner Foundation**, however, I have established the **Lyme and Associated Diseases Registry**™. The goal of the Registry™ is to gather data from as many physicians and patients as possible, based on their experience with the diagnosis and treatment of Lyme disease. Resulting statistics may then be compiled, analyzed and summarized to help practitioners develop more consistent and effective treatment plans for their patients.

The Registry program invites patients and their physicians to answer questions about their symptoms, medication levels, test results and treatment side effects, for example. The templates are *designed to make data collection as simple as possible*. No one need enter data into a computer. Using a regular No. 2 pencil, participants mark their answers on forms designed to be scanned. Making the program accessible to practitioners is especially important to growing the database. To date, we have received over 500 forms. Hopefully, we will add an Adolescent Registry to the program by the end of 2009.

For more information or to participate, please email Colleen Nicholson at Jcn4jc@aol.com or phone 516.286.7196 M-F 9am to 3pm EST.

Wonderful! Awesome! Incredible! Amazing!

CALDA's new website

***www.lymedisease.org** offers a wealth of information and resources!*

- **Lyme 101** – Basic information about Lyme and other tick-borne diseases
- **Lyme Times** – Regular and Special Issues, Archives
- **Activism** – Contact Legislators, Make a Display, Posters, Handouts
- **Resources** – Doctor Referrals, Children, Insurance Disputes, Professional Education Grants
- **Research** – Contribute or apply for grant
- **News, Views, Alerts, Events** and **Videos**

Sign up for the free online newsletter – no obligation – to keep up with the latest important happenings in the Lyme world.

Participate in community-based research by completing our Survey!

Become part of the national Lyme disease community by joining CALDA!

CALDA is based in California but operates on a national basis, cooperating with all LDA affiliates and chapters to support patients in all states, by:

- Collecting and disseminating data on behalf of the Lyme community through the LYME TIMES;
- Sharing best practices with other state and national organizations;
- Acting as a central resource for patients, physicians and support groups;
- Providing technical support for local education and advocacy efforts.
- Supporting research.

Join CALDA online at www.lymetimes.org

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Clip or copy and mail, or join on our website www.lymedisease.org

YES! Please begin a 1-year membership in the California Lyme Disease Association:

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- ***$35 - Basic***
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I enclose an additional $_____ as a tax-deductible contribution to the CALDA Fund for education and research.

We have wristbands...

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I'd like ___ Lime-green T-shirts with the CALDA logo and the caption: *Ticks suck...and give you Lyme disease!* Adult Sizes S___ M___ L ___ XL___XXL__Youth Sizes M__ L __ XL__ I enclose $15 for each.

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Please consider donating to honor family and friends at important occasions such as anniversaries, birthdays, holidays, graduations, memorials and thank yous, etc. Make your check payable to CALDA and mail with this form to CALDA, 2 Jasmine Lane, San Rafael, CA 94903.

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Lyme Links

California Lyme Disease Association

www.lymedisease.org

Basic information about tickborne diseases, CALDA grants, community education materials, resources, Spanish, online state support and information groups, news.

Lyme Disease Association

www.lymediseaseassociation.org

National patient advocacy organization. Research grants, news, politics, activities, events, schools, rash gallery, doctor referrals, brochures, books, videos.

IGeneX, Inc.

www.igenex.com

Reference laboratory specializing in tick-borne diseases: what's available, when to use which test, and how to interpret results.

International Lyme and Associated Disease Society

www.ilads.org

Position papers and practice guidelines, diagnostic methods and treatments in the management of tick-borne diseases.

Lyme Disease Network

www.lymenet.org

Flash discussion groups, support group listing, online library, legal resources and more.

Online State Support Group

Http://health.groups.yahoo.com/group/statenamelyme

Find your online state information and support group by going to this site. Military and Spanish also available.

Medical Diagnostic Laboratories

www.mdlab.com

Reference laboratory for Polymerase Chain Reaction (PCR)-based testing for tick-borne diseases.

Lyme Info

www.lymeinfo.net

Medical literature summaries, legislative hearings transcripts, news articles, pending legislation.

Patient's Medication Assistance and Insurance Dispute Resources

California Patient's Guide

www.calpatientguide.org

Amazing resource, explains your healthcare rights in insurance disputes. Sample letters, etc. Info useful in other states as well.

Drug Digest

www.drugdigest.org

A noncommercial, evidence-based, consumer health and drug information site. Drug library, drug interactions, compare drugs, and more.

Needy Meds

www.needymeds.com/indices/brandname.shtml

Extensive information on patient's assistance programs online forum for advocates.

Medline Plus

http://www.nlm.nih.gov/medlineplus/

Health topics, drugs and supplements, medical encyclopedia, dictionary.

Patient's Medication Assistance Programs

www.edhayes.com/indigent.html

Contacts for major assistance programs, such as Roche, Pfizer, Abbot, Glaxco.

Health Care Advocates

www.healthcareadvocates.com/lyme.html

Help with medical questions, billing issues, insurance disputes, physician referral service, fee negotiation

RxList, the Internet Drug Index

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Health Admin. Responsibility Project

www.harp.org

Resource for people seeking to establish the liability of HMOs. List of free legal aid services nationwide.

IGeneX Reference Laboratory is a highly specialized Lyme testing facility with several industry-leading procedures that have advanced the detection and treatment of Lyme and associated tick-borne diseases. Recognized as the pioneer of state-of-the-art tests like the western blots, Lyme Urine Antigen Detection Test (LDA) and Lyme Multiplex PCR tests, IGeneX is the preferred Lyme testing facility of many physicians and patient groups around the world.

Lyme Western Blots detect antibodies to *Borrelia burgdorferi,* the bacteria causing Lyme disease. IGeneX western blots are prepared from a specially formulated mixture of different strains of *Borrelia* cultures to ensure that antibodies to all the different strains of Lyme-causing bacteria are detected.

IGeneX's Multiplex PCR tests examine DNA and look for multiple markers of Lyme disease. The PCR is a major advancement for patients. Urine and blood typically have substances that block the detection of Lyme-causing bacteria. The IGeneX procedure removes these "inhibitors" so Lyme-causing bacteria can be accurately identified in serum, whole blood and urine samples.

IGeneX's Lyme Dot Assay (LDA) is a urine antigen test for the detection of pieces of Lyme bacteria. It is patent-pending and demonstrates how IGeneX is achieving its goal of providing the most sensitive and specific tests available to fight Lyme.

The tick harboring Lyme-causing bacteria also transmits coinfections such as *Babesiosis* and *Ehrlichiosis*. In order to effectively treat Lyme disease, coinfections must also be identified and treated. IGeneX has developed exclusive tests to help identify strains of *Babesia*, *Ehrlichia* and *Bartonella*. IGeneX's patented FISH Assay is one of the most sensitive tests available for *Babesia*, detecting *Babesia* RNA in a few drops of blood.

IGeneX staff, some of the most respected medical and scientific experts in their field, have published multiple peer-reviewed articles in medical journals and textbooks. IGeneX's innovative advancements have been the focus of dozens of news articles in national newspapers, magazines and television stories. IGeneX provides financial support for many Lyme programs and patient groups as well as physician-based Lyme organizations such as the International Lyme and Associated Diseases Society (ILADS). IGeneX is on the forefront of the political, medical and social fight to bring more awareness and education to this serious cause.

For more information about IGeneX, visit www.igenex.com or call 800-832-3200.

CALDA members can order the Lyme Times in bulk. These are ideal for outreach efforts with patients, physicians, schools, and legislators. Why not order a quantity for your physician's office, support group, or school as part of your community outreach effort? CALDA members may acquire bulk issues (minimum 10 issues) for a suggested donation of $3.00 each. Individual copies are available to non-members for a suggested donation of $10.

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