

the

Lyme Times

NUMBER 24

Education, Support, Advocacy, Research

JANUARY-MARCH 1999

FDA clears new test for Lyme disease

The Food and Drug Administration has cleared a simple, new blood test for Lyme disease that can be used in a doctor's office. The test provides results in an hour at the point of care, compared to the standard laboratory tests which have to be performed in a lab, delaying test results. This means doctors will be able to make a probable diagnosis quicker and start treatment with antibiotics immediately.

The test, the PreVue B. burgdorferi Antibody Detection Assay, is intended to be used as the first step in testing people suspected of having Lyme disease. Positive results must be confirmed with a Western blot test done by a laboratory. Two-stage testing is recommended by the Centers for Disease Control.

The new test, made by Chembio

See **New test** on page 5

Inside...

Last chance to collect signatures on Lyme Alliance petition to send to Washington. See page 30.

Attorney General's office investigates patient complaints

by Brian Carroll

The following is a report of the February 24th meeting organized by Connecticut's Attorney General Richard Blumenthal in response to numerous complaints received by his office from Lyme disease patients who are being denied insurance coverage for Lyme-related expenses.

Connecticut is the insurance capitol of the world and host to academic institutions that have fostered many years of Lyme research. And, of course, Connecticut has also earned the dubious distinction of being the epicenter of Lyme disease. Bristol resident and patient

advocate Cynthia Onorato assisted Christopher Montes, a New Britain psychologist and Lyme patient, in getting the word out to the community that this meeting was one that should not be missed. Montes' battle with his health insurer, Anthem Blue Cross/Blue Shield of Connecticut, may well have been the proverbial straw that broke the camel's back as far as the Attorney General's office was concerned. Apparently, his was but one of many complaints filed by Lyme sufferers statewide.

The meeting was billed as a

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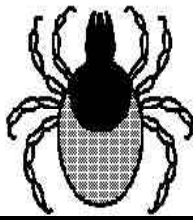
Chronic Lyme study already yielding important information

There was a big turnout for the February 25 update on the clinical trials of chronic Lyme disease. NIH Lyme Disease Program Officer Phillip Baker had invited members of the patient and professional community to a presentation by principal investigator Mark Klempner, MD, a researcher in infectious diseases at New England Medical Center in Boston. Among those present were Antony Lionetti, MD, clinician;

Karen Forschner, director of the Lyme Disease Foundation; Eliot Marshall, reporter for the journal Science; Jill Auerbach, Coordinator of the Hudson Valley Committee for Lyme Disease Patient Advocacy; Beverly Dyer, Washington, DC lawyer and Lyme disease patient; and Steve McLain, patient and chemist, in addition to NIH staff and members

See **Outreach** on page 16

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Lyme Times

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Erratum: The videotape available from the Lyme Disease Association of New Jersey costs \$9, not \$7 as reported in the last issue.

Dear Readers,

We are happy to bring you glad tidings of a new professional organization called the International Lyme and Associated Diseases Society (ILADS). ILADS' purpose is to educate physicians about Lyme disease and to offer effective support for doctors. See their first press release on page 19.

This is an organization which is sorely needed. Lyme disease is such a political football that one can hardly blame physicians for wishing to avoid the controversies. ILADS promises to provide professionalism, stability, and sanity to what has often been a frustrating roller-coaster course.

Patients will wholeheartedly welcome ILADS for the support it will offer their treating physicians. Too often patients have the devastating experience of their physician refusing to treat, or backing off from their care when they do not respond satisfactorily to the "standard" treatments.

Physicians will welcome ILADS for the educational opportunities, practice parameters, security, and legitimacy it will offer them. They will have professional support from experienced physicians who are trying to meet the many challenges of diagnosing and treating Lyme.

The creation of ILADS augurs better days ahead for the Lyme

disease community, which for too long has suffered under the stringent rules of double tier testing and truncated treatment courses. We commend the founding members of ILADS and wish them every success in the days ahead.

In other news, we hope you appreciate the coverage of the clinical trials of chronic Lyme disease. From my experience on the Advisory Committee I think that the study is in very capable hands with Mark Klempner as the principal investigator. The sheer volume of work and the organization required are daunting. He has it all under control. The preliminary findings are both interesting and encouraging.

Brian Carroll's account of the CT Attorney General's meeting was a generous impulse by a patient and patient advocate to share something of value and interest with the Lyme community. We appreciate his efforts.

And last but not least, don't miss Jean Hubbard's article on coinfections (p. 28). Thanks, Jean, for another excellent report.

One last thing - please sign and send in the petition on page 30.

Phyllis Mervine, Editor

The Lyme Disease Resource Center was founded in 1990 as a non-profit education and communications center for the public, for Lyme disease patients, for physicians, and other interested people. The goals of the LDRC are to educate the public about Lyme and other tick-borne diseases, including risk factors and prevention; to provide services for Lyme disease patients and their families and friends; to provide a forum for physicians and health care professionals for the exchange of ideas and information about symptoms, diagnosis, and treatment of Lyme disease; to be a communications center for individuals and groups who are working to help patients with Lyme disease; and to encourage Lyme disease research. The LDRC gratefully accepts tax-deductible contributions to assist its efforts.

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Guest Editorial**Federal bill addresses pressing problems of diagnosis and education****by Teresa Royer MacKnight**

In 1999 Lyme disease will be a frequent topic in the news, already there is a new bill in Congress and the FDA has approved the first Lyme disease vaccine.

It has been twenty-four years since Polly Murray a housewife in Lyme, Conn., alerted the State Health Department of the strange symptoms she'd been observing in her family and other area residents over a ten-year period. It is now known that Lyme disease is a widespread illness occurring across the country and around the world, and has become the fastest emerging infectious disease in the United States. Although some experts speak of Lyme disease as an uncommon illness that is easily detected and treated with short courses of antibiotics, there is a growing accumulation of compelling evidence which documents that this is not the case.

The present diagnostic guidelines developed by the CDC miss up to 40% of Lyme disease cases, depending on which study is quoted. And a recent survey done in New York, a state highly endemic for Lyme, revealed that less than 50% of patients diagnosed with Lyme disease recalled a tick bite or had the classic bull's eye rash. This means many people infected with Lyme disease are falling through the cracks and unknowingly missing the important opportunity for early curative treatment. For many there have been years of unwellness, and once the diagnosis has been made, lengthier and more difficult treatment has often been needed. Unfortunately for some, the disease has been incurable.

Federal attention is being drawn to this illness by Congressman Christopher Smith of New Jersey. New Jersey has experienced a rapid rise in the rate of new Lyme cases reported, and of note Governor Christine Todd Whitman and her husband have been afflicted with tick transmitted illnesses.

In May 1998 Representative Smith introduced to the House the Lyme Initiative Act (H-3795) and subsequently Senator Chris Dodd introduced the identical bill (S-2034) to the Senate. The bill has been endorsed by 65 Lyme disease information and support organizations and leaders around the country. In a speech the Congressmen credited this accomplishment in part to the tireless efforts of Patricia Smith, president of the Lyme Disease Association of New Jersey. Mrs. Smith is also the mother of two children who have suffered from severe Lyme disease for over ten years.

Rep. Chris Smith stated, "The Lyme Disease Initiative Act provides a program to fight Lyme disease on several fronts within the federal government." If passed the bill would bring \$100 million of funding to Lyme disease research and education. The primary focus is the development of a widely accepted and accurate detection test for diagnosing Lyme disease. Another component of the bill is the creation of a physician education program to help physicians stay informed of the most up to date knowledge regarding Lyme disease. The bill also requests re-examination of the controversial CDC criteria for reporting Lyme disease and the

Continued on next page

formation of a Federal Lyme Disease Task Force.

“Hopefully the 106th Congress will pass the Lyme Disease Initiative Act and mark a turning point in the fight against Lyme disease,” states

Patricia Smith.

If you are concerned about Lyme disease, contact your Senators and Representatives regarding this legislation.

negative in all blood tests and physical assessment. Concerned with his symptoms, my husband went to a doctor who, after examining him and listening to him a bit, told my husband that he would be out of business if all of his patients were as healthy as him. Then, when we decided he should take the LUAT anyway, we were really surprised to have it come back positive.

As for our three children, we went straight for the LUAT because we were sure that their symptoms (tiredness, emotional outbreaks, low attention, clumsy, etc.) were being caused by something other than having to live with a chronically ill mother, and we didn't trust the blood tests at all. The LUATs were only positive on one son, but we knew something was wrong, so we consulted another New York doctor who suggested we ask for blood tests for the children. All three ended up highly positive in the Western Blot. None of us were ever positive in the Elisa.

I feel what has happened to our family with our test results is a good cross-section of what is happening across the country. There is no “one way” to test for the disease for every person. We have learned that the antibody tests and the antigen tests in some cases complement one another. When the one doesn't show positive in a patient with Lyme, the other test may have a better chance of showing the disease.

Jean Brune
Decatur, Indiana

Amateur scientist needs help with education project

I live in Monrovia. I believe that I was infected during the 7 years I lived in a remote cabin in Big Santa Anita Canyon. I have collected over 100 ticks and have had the good fortune to find places to get them tested. After stirring up Los Angeles County Health, they came by and

Letters

We do not recommend any of the doctors or treatments which may be mentioned here by writers. You should discuss any treatment options with your physician. Signed letters of general interest may be printed.

Lyme educator blasts local paper for misinformation

Ms. Curtis wrote this letter in response to an article in a local paper.

As a Lyme disease advocate, patient, former support group leader, TV producer of Lyme videos which are available in many Fairfield County public and university libraries, I would like to take issue with Marsha Geller's article in the Westport News, October 14, 1998, on the Health District's fight against Lyme disease.

Fallen leaves, like all wet and damp environments, are prime locations for ticks to thrive. They do not serve “as tick deterrents if laid as a barrier on the perimeter of residential properties.” Quite the contrary.

According to Kirby C. Stafford III, PhD, Head of the Department of Forestry & Horticulture at the Connecticut Agricultural Experiment Station in New Haven, “as far as the leaves are concerned, you want to rake them up and remove them. You take a lot of the ticks with them (leaves).”

The reporter needs to contact Dr. Kirby Stafford and correct this misinformation which could do damage to many people.

A wood chip or decorative type of barrier could be used along lawn edges to reduce ticks coming onto the lawn.

There are enough people in

Fairfield County already infected with the spirochete that causes Lyme disease – which can become a chronic, lifetime illness – without more misinformation.

Dolly Curtis
Easton, Connecticut

Dolly Curtis's educational videos on Lyme disease are available by writing Dolly Curtis Interviews, 35 Flat Rock Rd., Easton, CT 06612, or call 203-372-4511.

Family health saved by Lyme Urine Antigen Test

Our family of five all have culture-positive Lyme disease, and the Lyme Urine Antigen Test (LUAT) was our salvation in beginning to finding out what terrible thing was happening to our family. Remember, we all have Lyme, but the LUAT was very negative on two of us, barely positive on one, and, thankfully, positive on the other two.

I was the first in our family to be tested, and had only an equivocal blood test and a neurologist that was shouting “conversion reaction”. The LUAT was ordered by a doctor in New York (we had to get totally out of our area to be taken seriously), and it was positive on two of the three days.

My husband, whose symptoms were vague (dizziness, headache, stiff neck, short temper), was totally

picked up about 3/4 of my ticks. They also asked me to help them by trapping rodents, live, at our cabin. Shortly thereafter, IGeneX Labs in Palo Alto offered to test twenty ticks at no cost to me. I have not heard back from either lab.

I have spent many hours in two local canyons collecting ticks and educating/raising the awareness of Lyme disease. I would like to prevent any unnecessary suffering caused by ignorant, if well meaning doctors. I would like to compile a list of people who believe that they were infected in Angeles National Forest. I remain negative on all tests so far, so any evidence of Lyme in my area would lend credibility to my claim. Fortunately, my doctor believes me.

The Crazy White Tick Hunter
Barbara Hunt
 240 N Shamrock Ave
 Monrovia, Ca, 91016 or
 CanynBarb@aol.com

The discovery of infected ticks in Los Angeles County parks has just been announced.

Tilt table testing revealed autonomic nervous system involvement

Lyme can cause chronic shortness of breath. Lyme can cause chronic shortness of breath. My Lyme has affected the autonomic nervous system, which in turn has given me a condition called neurocardiogenic syncope.

I've had Lyme for over 5 years. Eighteen months ago I began to have brief episodes of shortness of breath. The episodes disappeared for a while then came back with a vengeance. I was getting short of breath not just with very minor exertion, but also when just sitting down and talking. Sometimes shortness of breath was accompanied by lightheadedness. Lung tests were all ok. EKG and echocardiogram were ok. But my "tilt table" test was abnormal.

My Lyme knowledgeable cardi-
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ologist ordered this test because he's seen neurocardiogenic syncope in chronic fatigue and Lyme patients. All my symptoms were immediately (immediately) apparent on the tilt table test, indicating a "positive vasodepressor response". This meant that Lyme now involves my autonomic nervous system, which regulates involuntary things like heart rate, breathing, and blood pressure. You can only tell if the blood pressure is really fluctuating by doing the tilt table test. Taking blood pressure sitting/standing/lying down doesn't really reveal the condition. The treatment (in addition to continued antibiotics) is a very small dose of beta blocker (Toprol XL 25 mg) daily and a "volume expander" (Florinef .10 mg) twice daily. These medications have made all the difference — now I don't feel like I'm about to pass out from shortness of breath every day.

Carol Compton Glennon
 Brewster, New York

You can't donate blood if you have the Lyme vaccine

I find it interesting that the American Red Cross does not allow persons who have been vaccinated for Lyme disease to give blood for 12 months. That would mean that one could never donate blood if one received yearly Lyme disease vaccination boosters.

Art Doherty
 Lompoc, California

To inquire about donor eligibility guidelines, call the American Red Cross at 1-800-462-9400 and ask for the nurse of the day.

For other Lyme disease and blood donation information, see the Department of Defense website about blood donor rules at <http://www.ha.osd.mil/asbpo/medcond.html> or the American Association of Blood Banks Facts About Blood and Blood Banking at <http://www.aabb.org/docs/facts.html>

New test, from page 1

Diagnostic Systems of Medford, N.Y., uses antigenic proteins developed by recombinant DNA techniques rather than the whole cell *B. burgdorferi* preparations used in current laboratory tests. Antigenic proteins developed by recombinant DNA techniques allow for more accuracy.

FDA's clearance of the PreVue test was based on results of clinical studies conducted by the manufacturer at clinics and physician offices. PreVue accurately detected Lyme disease in 72 percent of one group of 120 blood samples, and 95 percent of another group of 42 blood samples. The test incorrectly identified Lyme disease in three percent of 100 blood samples in which it was not present. This "false-positive" rate is similar to that of laboratory tests for Lyme disease.

According to a press release from the manufacturer, The PreVue(TM) test can be used in physician offices and other point of care settings and provides results in 20 minutes, as opposed to standard laboratory tests, which can take several days to obtain results.

"It's a test that can be given anywhere where patients receive care, in doctors' offices and in hospitals," said Avi Pelossof, marketing director for Chembio. The company used technology developed by the Department of Medicine at the State University at Stony Brook to manufacture the test. Pelossof said the test would be inexpensive, but said the price has not yet been set.

Dr. Raymond Dattwyler, professor of medicine at SUNY, said, "The Wampole PreVue test is a significant improvement over existing tests for Lyme Disease, offering greater accuracy and ability to identify patients who have Lyme disease. Rapid diagnosis allows for faster treatment and better patient outcomes."

How dangerous is this particular tick bite?

Carol and Robert live in San Francisco and on weekends they like to drive up to Mendocino County to work on their country property. Recently they returned home and found a tick biting their little girl. They pulled it out and sent it to the Sonoma County lab. The test came back positive for Lyme disease. Their HMO doctor, however, refused to give the child antibiotics. What is the risk that the child will acquire Lyme disease?

Lyme disease comes from the bite of either an adult or nymphal stage tick. Adult ticks, perhaps because they are larger and more easily felt, seem to be to be less culpable. It is the nymphal stage which is implicated in most cases of human Lyme disease. These poppy-seed sized young ticks hatch out in the late spring. They live in the leaf litter under trees and come out when they sense a host is nearby. They feed to repletion in about 4 days. In an experiment on mice, 11% of the infected nymphal ticks transmitted the Lyme spirochetes after 48 hours of attachment. After 4 days, 80% of the mice became infected. Another study found that half of infected ticks transmitted spirochetes by two days, and almost all had transmitted spirochetes after four days.

European ticks seem to have shorter transmission times than American ticks, but one report has shown evidence of disease transmission by an American tick within just a few hours. Scientists in general agree that the longer the tick is attached, the greater the risk.

Carol and Robert's little girl was bitten by a nymph. They didn't know how long the tick had been on their little girl -- but probably about two

days. The tick's body had started to swell and the branches of the tick's gut were difficult to distinguish with a hand lens. Had it had time to transmit the infection?

In the case of adult ticks in California, UC Berkeley entomologist Robert Lane found that 33% carried the spirochetes in the salivary glands, which means that in theory

Half of infected ticks transmitted spirochetes by two days, and almost all had transmitted spirochetes after four days.

they would infect as soon as they bit. However, in experiments, the researchers were not able to culture the spirochetes out of any of these systemically infected ticks at all. It is not clear what this means at this point and more studies are needed.

But what happens if an infected tick does bite long enough to transmit the disease? It does not mean that you automatically develop the symptoms we associate with Lyme disease—some peoples' immune systems seem to be able to fight it off, at least temporarily. Screening studies show that 10% of populations in endemic areas may carry antibodies, indicating that they've been exposed, but they are not sick. But we do know that the spirochetes travel quickly in the bloodstream to all parts of the body. They have been recovered from guinea pig brains the day after intraperitoneal inoculation. And we just don't know if these exposed but not

sick people carry a latent infection which will cause problems later in life.

Within a week or two of being infected, many people develop a flu-like illness with fever, headache, and swollen glands which can progress to severe chronic problems if untreated. Only about 50% develop the Lyme disease rash, and we now know that the typical rash is not the most common kind. The vaccine trials, which enrolled 11,000 people, found that the most common rashes were diffuse erythematous lesions, i.e. uniformly red areas. Different shapes of rash were seen, and some were vesicular. Most people can be successfully treated at this stage, although one followup study found that previously treated Lyme disease patients were much more likely to have chronic musculoskeletal problems and verbal memory impairment than people without a history of Lyme disease. Early treatment led to a better outcome.

If you are bitten, proper removal is important also. You should remove the tick as delicately as possible, grabbing the mouthparts with a fine-pointed tweezers and pulling straight back. Avoid squeezing or mutilating the tick, which can force germs into the wound. Spirochetes are able to migrate through unbroken skin, and the ticks may carry more than one disease. Disinfect the bite site.

You can have the tick tested for Lyme disease as Carol and Robert did. Keep the tick moist—but not too wet— with a piece of damp paper towel in a small vial until you can send it in. If you are being bitten more than occasionally, it is time to get serious about using a tick spray and other preventive measures. Products containing permethrin are 100% effective, according to Dr. Robert Lane.

How do you calculate risk if you don't test the tick? In Mendocino County, from 1–14% of the nymphal ticks are infected, according to tests done in different areas. The infection rate of ticks in the area where you got

the tick will determine your risk. However there are only a few areas in the country where such specialized studies have been done, and new research can sometimes change the picture drastically. In Mendocino county, for instance, new studies have found small hot spots where up to 40% of the nymphal ticks carry the Lyme spirochetes. Obviously your risk is considerably higher if you live near such a spot.

Your risk of being infected from any one bite is relatively low, but if you find out that you have been bitten

by an infected tick, many authorities recommend prophylactic treatment, without waiting for a blood test.

Carol and Robert went outside their HMO to obtain treatment for their child. If they had waited three weeks to obtain an antibody test or waited for symptoms to occur, the spirochetes would almost certainly have seeded their child's central nervous system. It seemed too big a risk to take. Their doctor agreed. She prescribed four weeks of amoxicillin, hoping that would be enough prevent later complications.

liver enzymes, total body aches and pains and that “I just want to die” all-over feeling. Then the trek from doctor to specialist to doctor to specialist began — eight months of poking, prodding, testing—and no conclusions.

During this period I kept thinking it was Lyme disease but the doctors assured me that Lyme disease had nothing to do with my symptoms. At this point I took it upon myself to collect all the literature I could about Lyme disease. The doctors didn't know what was causing all these symptoms, however they were sure that it wasn't Lyme. I went along with them until one suggested a liver biopsy. At that point, I stopped and asked him if he felt I would die within a month if I did not go ahead with this biopsy. I am grateful that he had the decency to admit that he had absolutely NO idea what he was looking for.

I didn't walk at this point—I RAN. I canceled the scheduled biopsy. I was at a point where I felt like my demise was imminent. I contacted a doctor who treats hundreds of Lyme disease patients. She, herself, is one of us— she has/had Lyme disease. I sometimes wonder how different things would be in regards to research/funding/treatment of Lyme disease if some of the “experts” had it.

I was truly blessed to find such a person. The road was not easy. We would try one antibiotic, then another and another. I would always relapse when they were stopped — sometimes after a month, sometimes after six months — but symptoms always came back with a vengeance. Finally, about a year and a half ago, we (yes, I said “we.” You are your best advocate when it comes to this disease.) tried yet another antibiotic combination. I have been totally symptom-free for almost a year now. I am back to work, enjoying my grandchildren, exercising, traveling — I am LIVING AGAIN.

It is important that you find a

Patient stories

Is there any hope for people with Lyme?

by Mona Bradway

Lyme newsgroup lament: Please, someone, tell me that you HAD this damn disease and now that you are back to your old healthy self, please tell me that this just does not get worse when you think you're feeling better one day and worse the next. I thought once on doxycycline that everything would be ok, but I have read some absolutely awful stories. I've read about seizures, blindness, wheelchairs. Please someone say that life is back to normal

YES YES YES—it is possible. I contracted this horrible disease in 1993 and due to being undertreated, I relapsed in 1995 with cardiac/gastro/liver/CNS problems. After jumping from one specialist to another and being told by all that my problems had nothing to do with Lyme disease, fortunately, I had the will and fortitude to push on. I finally found a doctor who would listen to me and would do everything in her power to find the antibiotic/combination that would give me my life back.

I am a 55-year old grandmother who had the textbook rash in 1993 when I got bitten. I have a 2-acre yard that I used to take care of, mowing, trimming, planting, etc. until that little “speck” of a bugger bit me. My problem arose because I

All the specialists told me that my problems had nothing to do with Lyme disease.

was only given two weeks of doxycycline, after which time, I felt just fine. But unbeknownst to me at that time, this was not a long enough duration of antibiotics to eradicate the spirochetes.

Two years later I had a racing heartbeat, an enlarged spleen, CNS symptoms (I walked into walls at work very often), shortness of breath, dangerously high SPGT and SGOT

Lyme-literate doctor to work with you but you also must take responsibility for your own health and well-being. I have found that medication is not the only thing that gave me my life back. I have used acupuncture to balance and strengthen my immune system, enabling it to work more efficiently even when I am not on medication. I exercise, take the vitamins and supplements, and splurge on a massage now and then just to remind myself that I deserve and little pampering.

It had gotten to a point where my family and friends wouldn't even ask me how I was anymore. I think they were sick and tired of hearing all my gloom and doom, and believe me, I was "sick and tired of being sick and tired." No one can even imagine what you are going through unless they have had this horrendous disease. It can involve every system in your body. But you must know that in many, many cases there is a very bright light at the end of the tunnel. **YOU CAN BE NORMAL AGAIN!**

I have been reluctant to post my "success" story on this newsgroup for fear that it would do more harm than good. I am so happy that there are those out there who want to hear of the success stories. You must realize that most of the messages you read are from people who are at their wit's end and therefore it seems like NO ONE is doing well with this disease. They are looking for compassion, understanding and knowledge because they are so sick. I am sure you will read many more stories of people getting their lives back now that you have put out the word that these stories can help. Who knows, tomorrow I could be flat out again but for today I am just fine and I can only hope and pray for the same for everyone.

The author lives in Higganum, Connecticut.

Chronic disease resulted from doctor ignorance

by Phyllis Tyzenhouse, RN,DrPH

The author wrote this testimonial for the recent meeting organized by the Connecticut Attorney General (see page 1)

I am glad to have the opportunity to describe the problems I have had getting a diagnosis, treatment, and physician attention for my case of Lyme disease. Even though I am not a resident of Connecticut (I live in Virginia), share many of the unfortunate experiences, frustrations, and worsening disease that Lyme patients everywhere have had, and are still having due to bungled care.

I am in full support of the hearing that you have initiated with the Attorney General, and I would attend in person if I did not live so far away. If the physicians in my state had been informed about Lyme disease or were interested in learning about it, paid attention to my symptoms, listened to me, and either prescribed the proper medication or referred me to someone who could, in a timely manner, I would not now be suffering from chronic, entrenched Lyme disease that probably will be my curse for as long as I live. After six-and-a-half years, I have not yet found a Lyme-literate physician in my state, even though I live in a city that has a medical school with a large teaching hospital and a state health department. I have made numerous phone calls to both organizations without success and now have to travel to the East Coast to see a Lyme-knowledgeable doctor who is treating me.

The sad fact is that I found the engorged tick attached to my foot and saw the erythema migrans lesion forming and spreading at the site. Having some medical knowledge, I was aware of what this meant and went to see my family physician, carrying the tick in a bottle. The doctor brushed me off saying that he

didn't want to see the tick, nor, unbelievably, would he even look at the erythema migrans lesion on my foot. He said, "Oh, everyone gets bitten by ticks", and he claimed to have a tick bite with rash on his own leg. I left the office with no prescription for an antibiotic, determined not to return to see him again. Thus began my search for a doctor who would treat me.

Eight months later, another local doctor decided to give me one month's treatment with oral amoxicillin and asked me to return in a month. At that time, I said I felt no better (symptoms having developed in the eight-month interval), so he gave me one dose of intramuscular bicillin. When I felt no better after two weeks, he dismissed me saying that I must not have Lyme disease or I would now be better.

I did not have any success in getting treatment for specific symptoms: I consulted two recommended cardiologists about my heart arrhythmias and chest pain, and after extensive testing, said that my symptoms "were nothing to worry about." One of them prescribed a medication, but both cardiologists said that they had not heard that Lyme disease can affect the heart. I took some articles to one of the doctors to read. The orthopedist that I consulted for knee swelling and pain took X-rays and told me that I had osteoarthritis. He, too, did not know that Lyme disease caused joint problems. I saw an ophthalmologist about the floaters and blurring in my eyes. His response after examining my eyes was, "You do not have any of those Lyme things." All of this

Patient Support

convinces me that all physicians, specialists as well as family practitioners are in great need of education about Lyme disease, which has been designated one of the important emerging diseases.

A few months later during a visit to the Netherlands, a nurse-friend there referred me to a Lyme disease specialist, who examined me thoroughly, took tests, and declared that I had Lyme disease. I think it is absolutely mind boggling that I had to go to Europe to get a diagnosis that should have been made on my first visit to my family doctor a year previously. This specialist wrote a strongly worded letter to my newest family doctor (who did not believe I had Lyme disease) stating that it was well known in medical circles that Lyme disease is diagnosed on the basis of clinical symptoms and not on laboratory tests, although the latter can be used to confirm the diagnosis. He recommended a course of antibiotics that he felt I should have, including a long-term course of intravenous Rocephin.

Once back home, I called my insurance company to see if they would pay for the intravenous treatment. I spoke to a number of persons there who said that they could not pre-approve payment, but that I should go ahead and have the IV treatment, and then they would submit the claim to their team of nurses who would then decide if the treatment was medically appropriate. I protested, saying that I could very well be stuck with a huge bill, perhaps upwards of \$30,000. They agreed that this might well happen. I continued making telephone calls, including to the state attorney general's office, and there I was told that IV therapy for Lyme disease was "experimental" and could not be covered. I offered to submit articles documenting that IV therapy was standard, accepted treatment, but to no avail. I was told that this was the medical director's decision.

My complaints are that physi-

cians should be better informed about this emerging, rapidly disseminating disease and taught that brushing off patients with such inanities as, "There is no Lyme disease in Virginia", "Your tick is not the kind that carries Lyme disease," "Your symptoms are due to lack of fitness," etc., clearly show lack of interest in treating the patient.

Not only did I have to go abroad to be diagnosed, but I had to contact the state entomologist to identify the species of tick that I had and send me written confirmation. I also had to contact a professor of acarology (an entomologist who specializes in ticks and mites), to provide data on the presence of that species in Virginia and the fact that they do carry the organism that causes Lyme disease. All of this investigation should not have been necessary for a patient to do, and I feel that expending the time and energy to do all this further delayed my obtaining adequate treatment. I learned a great deal about the factors relating to the spread of Lyme disease by ticks, but it would be more appropriate for the practicing physicians to be aware of this. Incidentally, my third family doctor read the entomologists' reports and was not impressed.

I sincerely hope that the upcoming hearing will result in better care for the Lyme patients in Connecticut, and that those of us in other states will benefit from your efforts as well. I hope that you will keep us informed and if I can be of any help to you, please let me know.

Pfizer Central Research offers an informative Lyme disease pamphlet with good illustrations. You can order 50 free pamphlets by calling 1-860-441-5544. Additional copies are 4 cents each.

Woman sues Dr. Peter Gott for failing to diagnose her Lyme

by Gale Courey Toensing

SALISBURY- A Salisbury woman has filed a medical malpractice lawsuit against Dr. Peter Gott, claiming she suffered severe and debilitating injuries because he failed to provide a prompt diagnosis of her Lyme disease.

Jennifer Zwicky, of (address) filed a civil action against Gott in Litchfield Superior Court earlier this week, claiming his failure to diagnose and treat her Lyme disease in a timely manner resulted in the progressive deterioration of her condition and caused her to suffer "great emotional trauma."

Gott declined to comment Thursday.

"I'm not commenting until we get into the courtroom," Gott said.

According to the complaint, a tick bit Zwicky on her right hip on June 29, 1997. The tick was removed that same day.

A week or so later, Zwicky consulted Gott about a swollen rash and pain in her hip, where the tick had bitten her.

Zwicky said she returned to Gott on July 11, 1997, and two more times during that month, reporting flu-like symptoms, including joint pain. Gott diagnosed Zwicky as suffering from a condition known as zoster, or shingles, and prescribed pain medication and two doses of a medication called Famvir.

Zwicky's lawsuit said her

symptoms worsened and she returned to Gott on Aug. 11, 1997, reporting a swollen jaw and an inability to chew.

Gott did not order a blood test between July and October, nor did her treat Zwicky for Lyme disease during that period, according to the complaint.

A blood test for Lyme disease was performed in November and resulted in a positive reading. At that point, Gott diagnosed Zwicky with Lyme disease and began antibiotic treatment. But Zwicky says the diagnosis came too late.

The delay "constituted a deviation from the applicable standards of care," which resulted in Zwicky suffering severe, painful and debilitating injuries, the complaint said.

Zwicky, who may be unable to pursue her usual activities, including employment, has incurred debts for

medical care and treatment, diagnostic studies, home care and medicines, "and will be obligated for further such sums in the future," the complaint said.

Zwicky could not be reached Thursday. She is represented by Kathryn Calihey of Ricassi & Davis in Hartford. A spokesman at the law firm said Thursday Zwicky is claiming damages of more than \$15,000. Claims must be more than \$15,000 to be filed in Superior Court, the spokesman said.

In Connecticut, plaintiffs do not ask for a specific amount of money in damages, instead, the court decides the amount of damages to be awarded, the spokesman said.

From the Waterbury, CT, Republican-American, Friday, March 5, 1999

she said. "Health care costs do go up -- the increase is around 1% and no more than 3%. But this is a slightly higher premium for much better coverage, coverage in which needed medicines, tests, and surgeries are no longer denied.... and lives of patients are not senselessly ruined or lost."

ERISA, the Employee Retirement Income Security Act of 1974, is the pension reform bill that contained a 'bought and paid for' loophole for the health care industry. Under ERISA HMOs and health insurance providers cannot be sued in state court. This means that a patient who is denied needed medical treatment cannot sue in state court for damages, in front of a jury.

Likewise this law takes away the right to sue the HMO for Breach of Contract, Medical Malpractice, or any Tort which in every other case is actionable in state court with a jury trial.

Under ERISA one can only sue in Federal Court for the medical treatment and cannot sue for compensatory or punitive damages. The trial is before a Federal Judge alone--there is no jury trial. If a patient has died because a needed test or surgery was denied, the dead person's family can only sue for the test or surgery.

Since the treatment is often no longer needed and since there is no chance to to recover money damages, very few people can afford to pay the lawyers tens of thousands of dollars to sue.

The insurance industry/ HMOs are virtually given immunity, or as one former Medical Claims Adjuster described it: "A License To Kill."

Pat Sprague is a coeditor of the "America On Lyme" internet newsletter. For a copy of the monthly internet copy of the Newsletter, please email PSpatches@aol.com For a postal mail copy send a self addressed stamped #10 envelope with 55 cents postage to: America On Lyme, Pat Sprague, 224 Vanderbilt Blvd., Oakdale, NY 11769-2000

Republicans stonewalling health care reform because of right to sue HMO issue

Republicans are stonewalling health care reform because Democrats want to guarantee patients the right to sue their HMOs.

According to a March 26 article in the Washington Times, Speaker of the House Dennis Hastert said that any overhaul of the laws governing the nation's health care system will be delayed as long as Democrats insist on legislation that would allow patients to sue health maintenance organizations.

This politicking outrages Lyme educator/advocate Pat Sprague.

"I hope that people write to every Republican politician and ask them to turn their backs on special interest

money from insurance companies. Ask them to allow us to sue our HMOs," she states.

She claims that Texas has already reformed this law and it has worked fine.

"Once there is a right to sue the HMOs, needed treatments are not denied and there is no need to sue,"

The New England Journal of Homeopathy has published an entire issue on Homeopathy and Lyme Disease (Vol 7, No 1). For information call 413-256-5949. The cost is \$22.

Blood Feud

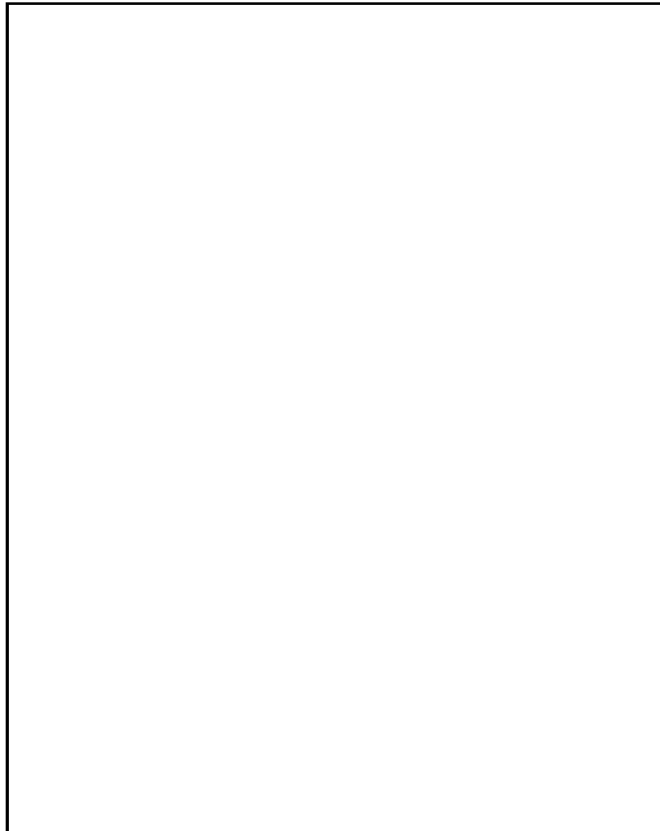
by Cynthia Mills

Look for it in the grass, not the bushes. Concentrate on the uphill side of the trail; it stays away from the downhill side as if it were taboo. Examine each blade of grass for spots—the spot might have legs. Breathe on it softly and the legs will flare out, reaching for you.

If it latches on, it might take a meal. Or maybe it will leave a visitor behind: an invisible, twisted germ called a spirochete — the kind that causes Lyme disease — or some other from its tribe of pathogenic hitchhikers. If conditions are right, it may inject a neurotoxin that paralyzes you, even to the point of suffocation.

As parasites go, a tick seems a simple, even stupid thing— less fleet than a mosquito, less insidious than a roundworm. From birth until death, some three years later, it leads a life of uncommon sloth: hiding in leaf litter as a larva and nymph, lumbering up grass blades as an adult, grabbing onto hosts when the need arises. But it rarely arises. Ticks spend 95 percent of their time lounging around, bloated and self-satisfied, digesting their last meal. (Thanks to pleats in their skin, some ticks can swell to contain nearly 100 times their weight in blood.) Entomologists long suspected that they entered diapause, a kind of arthropod hibernation, between feedings. Now it seems that

ticks are just lazy—so lazy they suck water from the air and only bother to



Electron micrograph of adult *Ixodes scapularis*, about 250 times actual size. Courtesy Pfizer Central Research.

breathe four times a day. As one investigator puts it, “Nothing’s on but the pilot light.”

And yet ticks make up in stealth and biochemical cunning what they lack in speed and industry. Using their bodies as miniature laboratories, they have evolved chemical compounds that can breach every one of a target animal’s defenses, from coagulation to inflammation. To top it off, ticks have reinvented their weapons again and again, species by species. Today, they transmit more disease in the United States than any

other insect or arachnid.

Ticks seem to have staked all their evolutionary resources on spit. Clustered together like grapes, the salivary glands form the second-biggest organ in a tick’s body, after its gut. Furthermore, the glands can swell 20 percent larger when their owner attaches to a host. Inside those elastic walls, a chemical

arsenal is made ready and strategically deployed: anticoagulants and platelet-aggregation inhibitors, prostaglandins and the latex-like cement that makes ticks so hard to remove. Some of the chemicals are huge proteins; some are only fragments; but each represents a substantial investment in energy, resources and genetic planning. Biologists discovered long ago that tick spit carries blood thinners, but in the past ten years they have found an array of other molecules as well — some of them entirely new to science. And each is designed to outmaneuver a host’s defenses in a different way.

Happily, there is a reassuring side to this creepy tale. By identify-

ing the chemicals that tick secrete, a few investigators are learning how to bolster the body’s defenses against them. Better yet, the same chemicals can be put to other uses. Blood sucking arthropods, biochemists are finding, have great ideas. In the course of hundreds of millions of generations, ticks have tested, modified and perfected potent compounds, applying the process of natural selection to zero in on the ones that work. As it happens, compounds that do what tick compounds do — anticoagulants, for instance — are worth billions of

dollars to the pharmaceutical industry. Inside every tick, it seems, there lurks a miniature Eli Lilly.

Biologists first began to appreciate bloodsuckers by smashing them. If a bug was flattened after it had eaten, investigators found the blood in its gut would remain liquid. Somehow, these creatures could keep blood from clotting. In 1914 two British Army officers in India, J.V. Cornwall and W.S. Patton began to suspect that the bugs inhibited coagulation with their saliva, thereby keeping their small suctioning mouthparts from getting gummed up. To test their hypothesis, the investigators mixed blood with crushed salivary glands from bloodsuckers; as they expected, the blood failed to clot.

At the time, that finding seemed an intriguing but useless fact. It was decades before anyone looked further, or bothered to extract the responsible agents. More than half a century later, however, a related fact caught the attention of Jose M.C. Ribeiro, a medical entomologist now at the Laboratory of Parasitic Diseases, part of the National Institute of Allergy and Infectious Diseases in Bethesda, Maryland. In 1977 Ribeiro had just finished his master's thesis on an enzyme called ATPase, which breaks down the molecule ATP. (ATP is a kind of molecular battery, storing energy in all cells.) He was looking for a new project when a friend, an insect physiologist, told him about a similar enzyme found in the saliva of bloodsucking parasites known as kissing bugs.

It seemed an odd place for such an enzyme. ATP was known to be useful only inside the cell. Why would an organism make the enzyme, only to spit it out? When Ribeiro gathered his own samples and tested them, he found that the kissing-bug enzyme was not as simple as reported: whereas ATPase broke off one phosphate group from the ATP molecule, the kissing-bug

enzyme broke off two. That put it into a controversial class of enzymes called apyrases. Now things were getting interesting. Many biochemists had argued that true apyrases did not even exist. When a test substance detached two phosphate groups, they maintained, it must contain two enzymes, not one, each of which took off only one phosphate group. Yet here, in a bloodsucker, Ribeiro had found a real apyrase, being secreted where it had no known purpose. Although Ribeiro had never intended to study bugs, he couldn't resist. He went back to the library and pulled every abstract he could track down on the putative apyrase. He read the argument that an apyrase could not be one enzyme. He learned that the level of apyrase activity was higher in potatoes than in any other source, and that Sigma Chemical Company in St. Louis, Missouri, purified, packaged and sold potato apyrase to hematologists, who used it to study platelets.

Platelets, Ribeiro knew, had come into the scientific limelight in recent decades. Although they had long been known to be minute components of blood, smaller even than red blood cells, they had been dismissed as cellular debris until the Second World War. A lot of people bled during that war, and physicians noted that people with fewer platelets than usual bled more. Their blood thickened and clotted normally, but they bled anyway.

When the physicians took a closer look with a microscope, they saw why. Whenever a blood vessel tore, platelets collected around the tear, stuck together and plugged it up. One substance that could keep the platelets from collecting was the potato apyrase — hence its value to hematologists. “When I found that out, I almost threw the papers on the ceiling,” Ribeiro remembers. “I realized why the bug has it.” Kissing bugs had found another way to keep blood flowing, not only through their own mouthparts, but from the host as well.

Ribeiro went on to expand his study, finding apyrase in the saliva of mosquitoes and fleas. But it was with ticks that he hit the jackpot.

If any bugs should know how to keep a host bleeding, Ribeiro reasoned, ticks should. They have not survived some 300 million years simply by sticking their mouthparts into a host and hoping to hit an artery. Rather, they must slash through the skin, tear open a blood vessel — any vessel — and inject whatever is necessary to keep the food coming indefinitely. Then they can suck and drool, drool and suck at their leisure.

In fact, Ribeiro found, tick spit contains an apyrase as well as the anticoagulants others had found in it. But what else might it have? A host's body has three ways to stop hemorrhage: it can form a blood clot, it can plug a hole with platelets and it can constrict a blood vessel to pinch off the flow. If ticks already knew how to inhibit clots and platelets, had they found a way to prevent vessels from constricting as well? Ribeiro and others began to study how tick saliva affects the bands of muscle within blood vessel walls. Sure enough, tick spit carried enough vasodilators to make even the aorta relax.

Soon investigators were examining compounds taken from the saliva of ticks, mosquitoes, sand flies, kissing bugs, bat bugs, bedbugs, lice, fleas and more. Although there was some overlap, they found that many of the species had invented and used their own vasodilators, their own anticoagulants, their own platelet inhibitors. In 1995, when Ribeiro surveyed the scientific literature, he found that six bug genera made anticlotting agents, twelve made vasodilators and twenty-one made platelet inhibitors — and those were only the ones mentioned in the journals.

At the same time, investigators were finding a host of new compounds. There were molecules that blocked the pain of a bite; others that

blocked chemicals that cause inflammation, such as histamine and thromboxane; and the ticks' own versions of prostaglandins, which do everything from relaxing blood vessels to suppressing immune response. In fact, if you took the time to look for a molecule, it seemed that some bug probably carried it.

These were compounds that pharmacologists dearly wanted to learn to make, or make better. Anticlotting agents had turned open-heart surgery into a reality and made survival after a heart attack possible. The only drug that can reliably inhibit platelets is aspirin, and it has its drawbacks. As soon as

the bug molecules were found, isolated and purified, therefore, pharmacologists took them apart. Often the new compounds proved too large to be useful in and of themselves. But now that pharmacologists knew which salivary molecules did the work, they could design new compounds that had the same effect, and that the human body could tolerate. A peptide in tick spit was recently tested by investigators at Merck & Company as an anticoagulant, though it proved too powerful to be useful. A sand fly compound, the most potent vasodilator known, appears to help hair grow, and a vasodilator in black flies may help

heal wounds. And there are plenty of other compounds left to pick apart.

For a tick, Ribeiro insists, synthesizing new compounds is not such a huge evolutionary task. The salivary glands and the nervous system are, in a sense, cellular cousins. Both arise from the outer, or ectodermal, layer of the embryo, long before organs have differentiated into anything recognizable. It comes as no surprise, therefore, that some of the molecules in tick drool are modified neurotransmitters (molecules that convey messages between cells). If they benefit a tick in some way, the molecules continue to be secreted and are gradually improved

Desirable destinations for the discriminating tick

Every tick is a cabinet of wonders, replete with biochemical inventions and behavioral mysteries that investigators have yet to unlock. One of the most puzzling and potentially important questions is also the simplest: Why do ticks go where they go?

Entomologists all over the world have dusted ticks with fluorescent powder, then followed them day after day, month after month. They now know that ticks move only a few feet in a lifetime, and that in areas where they infest lizards and mice, ticks prefer the uphill side of a trail. But *why* ticks prefer the uphill side—and for that matter, how they know which side they are on—is still anyone's guess. It could be that lizards and mice are the ones that prefer the uphill side, and that ticks simply land on that side when they fall off. But that only leaves you wondering about lizards and mice.

Luckily, just knowing where ticks go is useful enough. If you want to kill ticks that carry Lyme disease, for instance, you need not spray an entire forest with pesticide. Instead,

you can line the uphill sides of forest trails with a device recently designed by the entomologist Gary Maupin of the Division of Vector-Borne Infectious Diseases at the Fort Collins, Colorado, branch of the Centers for Disease Control and Prevention, and tested by the entomologist Robert S. Lane of the University of California at Berkeley. Maupin and Lane make their tick traps out of PVC pipe. Inside the pipe they lay a block of paraffin embedded with grain to attract mice, and on both ends they glue pieces of carpet soaked with pesticide. When the mice squeeze through the openings, the poison repels or kills the ticks on their fur.

The bigger the trail, it seems, the less discriminating the tick. When Richard L. Stewart Jr. at Ohio State University in Columbus studied ticks in his area, he found that virtually all the adults headed for the sides of roads when searching for a host. Presumably they were drawn by the carbon dioxide, heat and vibrations that cars generate, much as the ticks' hosts do. Because ticks are seasonal,

Stewart reasons, spraying or mowing two to three feet along roadsides in June and July should help control their populations.

Nature also lends a hand in controlling disease-carrying ticks. In the Bitterroot Valley of Montana, for example, only ticks on the western slope carry *Rickettsia rickettsii*, the organism that causes Rocky Mountain spotted fever. Ticks on the eastern slope carry the benign *Rickettsia peacockii*. (As usual, no one knows exactly why.) In California, meanwhile, Lane found that adults of the tick species *Ixodes pacificus* are less likely to carry Lyme disease than are the nymphs. (In the northeastern United States, adult ticks are twice as likely to carry it as nymphs are.) Californians have lizards to thank for that, Lane found: the California tick nymphs prefer to feed on the western fence lizard (*Sceloporus occidentalis*), and that diet seems to rid them of the Lyme disease spirochete.

C.M.

through natural selection. As Ribeiro puts it, "The salivary gland is a place where you can shuffle the whole genome and see what comes out."

Luckily, the body has a formidable line of defense: the immune system. Immunologists and physicians long doubted that the body could fight off ticks. Antibodies and killer T cells might be a match for bacteria and viruses, but how would they fare against creatures billions of times their own size? And yet the immune system often does force ticks to drop off too early, before they can molt or lay eggs. On occasion, it can even kill a tick as it takes a meal.

When a tick punctures the skin, it breaks cells apart, tearing the membrane that binds them. If the immune system senses the damage, immune cells in the skin go to work, along with a series of activating proteins called the complement system. Those are only first-line defenders: although they may be able to harm a tick by themselves, they are mainly present to alert and recruit the rest of the immune system. If all goes well, white blood cells known as lymphocytes will soon be churning out antibodies for the chemicals in tick spit. Granulocytic white blood cells, meanwhile, will collect at the bite site, releasing histamine, peroxides and other molecules that cause inflammation. (A good dose of histamine can kill a tick outright.) Any white blood cells that get sucked in by the tick will explode like suicide bombers in its gut.

If a host has been infested before, things could go even worse for a tick. There may already be antibodies circulating through the host's blood. Those antibodies will help recruit white blood cells and may damage or clog a tick's mouthparts if it swallows them.

An aroused immune system is no pushover, clearly, but it does nod off from time to time. Even hosts unaccustomed to ticks will tolerate a few here and there; only a full-scale

infestation or two will trigger an immune response. And hosts accustomed to ticks — white-footed mice, for example — may never become immune to them. Over the course of millennia, ticks seem to have learned to hide from the mice as well as from their immune systems.

Hiding is what ticks do best. After all, a host's best defense is simply to scratch or pluck the raider off. Yet ticks can creep around on a host's skin or spend days feeding on its blood without ever being noticed — or at least not until it is nearly too

Host antibodies to tick saliva can sometimes cause the tick to drop off prematurely, but ticks can sneak by or inactivate most host defense mechanisms.

late. In 1996 in Spokane, Washington, a woman spent nine days in the hospital growing steadily weaker and more paralyzed. She could hardly breathe, and physicians were about to put her on a respirator when a careful resident made a critical discovery: a female tick was embedded in the woman's scalp. When the tick was pulled out, the woman improved within hours. In a sense, the discovery came as no surprise: that particular hospital has as many as six cases of tick paralysis a year (the neurotoxin that causes the paralysis has never been identified), and physicians had already searched the woman for ticks. Yet the tick almost got away.

If you have ever failed to feel an injection, you can imagine how easy it is to miss the bite of an arthropod. A tick's mouthparts, after all, are

quite a bit smaller than a hypodermic needle. Now think of a splinter. You may not notice it immediately, but you do before long, because as a foreign body it causes inflammation. But a tick knows how to stifle the inflammatory response before it starts. Among the chemical tricks hidden in its salivary glands is a molecule that breaks apart bradykinin, the chemical that causes pain at the bite site.

In fact, ticks can divert all of the immune system's reactions for a time. Tick-injected molecules can prevent the complement system from being activated and inhibit the natural killer cells. They can reduce inflammation, immune reactions, even sensations, giving a tick the time it needs to feed (an adult tick may hang on for a week or more). The effects of those actions can be detected in immune cells that lie as far away as the spleen.

But what a tick does to the second-line immune response is the most ingenious. Rather than blocking the white blood cells, it simply misdirects them, whispering in their ears like a miniature Iago: "Yes, you're in trouble; now just follow my simple advice." White blood cells known as macrophages and T lymphocytes are the field marshals of the immune system: they send out the chemical signals that tell the other white blood cells what to do. But when a tick latches on, it secretes molecules that selectively dampen those signals. White blood cells still rush to defend the body, but they largely pass the tick by, leaving it to suck and drool, drool and suck.

Sneaky as they are, most ticks get only a few drops of blood from people before they drop off or are discovered. Unfortunately, their subterfuges also help them spread disease. Stephen K. Wikel, an immunologist at Oklahoma State University in Stillwater, has spent twenty-four years intimately detailing how ticks and the pathogenic organisms they carry interact with

hosts. One of the first things Wikel noticed was that it took more disease organisms to induce disease if you injected them with a needle than if you let a tick do it for you.

How much, Wikel wondered, do the pathogens depend on the tick? Do they use the tick as more than just a traveling syringe? To find out, he exposed mice to uninfected ticks until the mice became immune to them. Then he exposed the immune mice to ticks carrying *Borrelia burgdorferi* — the spirochete that causes Lyme disease. Whereas all Wikel's control mice became infected, less than 20 percent of the immune mice did. Immunity to ticks conferred immunity to *Borrelia*.

“The vector is the pimp for the pathogen” — that is how the immunologist and veterinarian Nordin S. Zeidner puts it. Zeidner works at the Division of Vector-Borne Infectious Diseases at the Fort Collins, Colorado, branch of the Centers for Disease Control and Prevention. He repeated Wikel's work, but with a twist. Instead of immunizing the mice, he simply resupplied them with the signaling compounds that ticks suppress. When Zeidner exposed the hosts to infected ticks, 95 percent of them remained free of *Borrelia*.

Because they clear the way for pathogens biochemically, as well as giving them a free ride, ticks are among the most pernicious disease vectors in the world. Every year they cost the world's cattle industry alone billions of dollars. East Coast fever, louping ill, heartwater and numerous other diseases are passed on by ticks, and the same neurotoxin that nearly killed the Spokane woman can fell entire herds at once. More gruesome still, ticks sometimes literally bleed cattle to death. Adult females of the species, *Hyalomma asiaticum* for instance, can consume two teaspoons of blood apiece, and no cow's tail can dislodge them.

Although tick-borne diseases rarely kill people, they are still a

major health concern. Rocky Mountain spotted fever and relapsing fever, the first diseases found to be transmitted by ticks, tend to strike in unpredictable ways. Rocky Mountain spotted fever, for instance, was discovered in Colorado early in this century. Then in the late 1970s it suddenly appeared in the south and southeast, where it still afflicts about 800 people every year. New tick-borne diseases, meanwhile, are taking an even greater toll. In the United States, cases of Lyme disease — first discovered, along with the

Russian spring-summer encephalitis kills 40 percent of those who contract it.

tick species that carries it, in the 1970s — have risen from 491 in 1989 to more than 13,000 in 1994.

Lyme disease is now the most commonly reported vector-borne disease in the country. It can cause long-term arthritis, heart disease and neurological conditions similar to multiple sclerosis. There have been outbreaks in Western Europe and Eurasia, and suspected cases have been reported in Australia and South Africa. Unlike the Ebola virus, ticks do not need jets to travel between continents; they simply hop on migratory seabirds.

Like Lyme disease, most of the tick-borne diseases, if caught at an early stage, are easily treated. Not so the viruses. That makes the report last summer of a so-called “deer tick virus,” carried by ticks collected in Massachusetts and Connecticut, particularly alarming. The new disease fits into a family of tick-borne encephalitis viruses, one of which causes Russian spring-summer encephalitis. That disease kills 40 percent of those who contract it and leaves most survivors

with severe nervous system damage for months or years after infection.

If the tick is the landscape on which the pathogen evolves, as Ribeiro puts it, then we humans are an evolutionary landscape for the tick. Our skin has shaped its mouthparts, our blood inspired salivary masterpieces. Our complexity has led it to feats of biochemical genius. To thwart ticks, in turn, we will need to come up with some inspired inventions of our own. Wikel, Zeidner and others are now striving to do just that. “The Holy Grail is a vaccine,” Zeidner says, which would protect against ticks as well as all the diseases they carry. Australian investigators have already designed a vaccine against a specific local tick, *Boophilus microplus*. But Wikel and Zeidner have something more ambitious in mind. Wikel hopes to make a vaccine that blocks ticks as well as other vectors, such as mosquitoes. Zeidner wants to create an entirely new kind of vaccine—one that will beat the tick at its own game. First he plans to isolate the chemicals that ticks use to make the macrophages and T lymphocytes ignore them. Then he wants to combine those chemicals with others that tell the immune system, even more firmly, to defend against parasites. The resultant vaccine would teach the immune system to override the tick's instructions, and to attack it after all.

The idea has a certain poetic justice: the lags of the arthropod world tricked into telling the truth at last. For now, Zeidner's vaccine exists only in theory. But if it does materialize, people will have outmaneuvered their simple, spineless foes — if only for an evolutionary moment.

Cynthia Mills is a doctor of veterinary science and writer living in Salem, Oregon. She is a frequent contributor to The Sciences.

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Outreach efforts have been herculean

from page 1

of the Advisory Panel.

In his introductory remarks, Dr. Klempner explained the basic objectives of the study.

- Does intensive antibiotic treatment benefit patients with chronic Lyme disease?
- Can evidence of persistent infection with *Borrelia burgdorferi* be found in patients with chronic Lyme disease?
- Is there evidence of coinfection?
- Do specific clinical or laboratory parameters improve in patients who receive antibiotic treatment compared to patients who receive placebo?
- Do specific parameters predict a response to therapy should it be observed, which would enable construction of a predictive model?

Recruitment efforts

Recruitment methods have been nothing short of heroic. Dr. Klempner's team has been collecting data on patient inquiries in order to discover which outreach method works the best. The most effective method so far has been screening clinics where free testing is offered. Clinics are held on Saturdays in towns around New England. Each clinic is preceded by two weeks of intensive advertising in local media. The disadvantage of the clinics is that many people come to take advantage of the free testing but do not meet entry criteria for the study (88 had no symptoms. 35 patients had already exceeded the maximum for IV antibiotic treatment, while 40 could not document an erythema migrans rash. [See Table 1] However the percentage of patients enrolled per screened population (10% of 700) is not unusual for this type of study, and the researchers see that the way to increase numbers enrolled will be to increase the numbers screened.

Presentations in community settings have generated more interest than presentations to doctors. Mass mailings

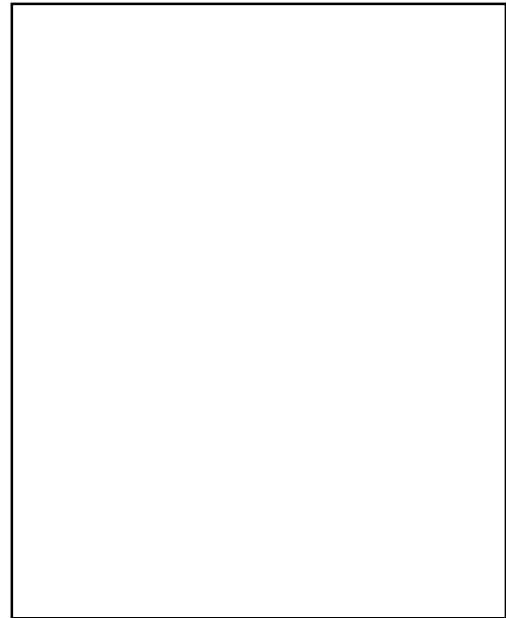
to all rheumatology and infectious disease doctors in a three-state area brought no response. Klempner commented that patients are coming in spite of their doctors, not because of their doctors.

"I gave 26 grand rounds and did not get a single patient calling to say, 'My doctor told me to call,'" he lamented.

Letters and posters have been sent to libraries, houses of worship, and village managers, but whether they were used is not known. In contrast, talks by the researchers at schools, senior centers, hospitals have been well-attended. The screening clinic strategy is successful and the researchers are scheduling more as well as planning to add at least one new center. It is hoped that adding new screening centers will make the study more convenient and accessible to patients. Pulling charts in selected doctors' offices and calling potential patients has been productive but is labor-intensive and slow.

There was a suggestion to approach HMO managers, which have traditionally not been a source for patients for clinical studies, on the assumption that early identification of patients could save them money. The Lyme Disease Foundation may assist the effort by doing a targeted mailing to their database.

Although enrollment is somewhat behind schedule, both



Research director Mark Klempner seeks patients for study

scientists and patient advocates agree that it is important not to liberalize the entry criteria, which would have the effect of admitting people who may not have Lyme disease, and who therefore would probably not respond to the treatment.

The screening and enrollment process

Screening and enrollment are a two-step process. First is an evaluation visit to ensure eligibility and collect samples. Second is the actual enrollment visit when the first treatment is given. Patients are sorted into the seropositive and seronegative study groups, and any who had a) positive PCR for *Borrelia* DNA in plasma or cerebrospinal fluid; or b) evidence of synovitis are referred to either the NIAID Intramural Clinical Study on Chronic Lyme Disease or elsewhere for appropriate treatment.

During the first visit at the center, patients are asked to fill out a detailed history which asks such questions as: "Did any symptoms improve in the past with treatment? Are you taking any nonstandard therapies, such as herbs?" They receive a physical exam that will detect any quantifiable neurologic abnormality (reflexes, strength

testing). Samples of blood, cerebrospinal fluid, and urine are collected for laboratory assays. This visit lasts about 1.5 hours.

Approximately two to four weeks later, patients return to the center for more testing. At this time they complete the SF-36 questionnaires which require the patient to indicate

whether they are worse, the same, or better on both physical and mental measures. Although it is a subjective test, the responses are quantifiable and the scales have been calibrated through huge population studies. A composite score is calculated. Controls are built into the questionnaire so that if a patient fails to answer a few questions, his score is

still accurate. Plus or minus 6.5 points from baseline indicates improvement or deterioration. Categories are marked separately so that positive and negative changes in different areas may be detailed. Patients also complete additional tests of neuropsychological function.

This intake visit lasts over four hours and includes starting an IV line. All patients receive a number which randomizes them to either the treatment or placebo group. Neither patient nor investigator knows who is in which group (double blind). The first IV infusion is made under the supervision of the physician at the study center. Subsequent infusions may be made in the patient's home. Klempner stated that by the time they have completed this process, the patients are very invested in the study. They must return at 30, 90, and 180 days for repeat evaluations.

The study assumes that 40% of the patients in the placebo group will report significant improvement. This is called the natural healing rate. The number of participants required for the study is calculated using this figure. The researchers want to be able to observe a difference of 25% more patients in the active treatment group reporting improvement (i.e. 65% of patients saying they are better during or after antibiotic treatment) with a 90% confidence. If they also assume a 15% dropout rate (only one person has dropped out so far), they will need 194 patients for the seropositive group, 66 for the seronegative. It is anticipated that if the Data and Safety Monitoring Board (DSMB) which reviews progress quarterly, notes any striking trends (eg. all treated patients improve, untreated patients worsen), then the study will be terminated and treatment offered to control patients.

Dr. Klempner addressed the issue of possible drug resistance in patients who had previously been treated with ceftriaxone. The only published work on resistance he was aware of was that of Russ Johnson (UWisc) who

Figure 1

Inclusion criteria for seropositive cohort*:

1. IgG seropositivity at the time of enrollment into the study for an immune response to *B. burgdorferi* antigens according to the currently accepted CDC (Dearborn) criteria defined in Dressler et al. (Western Blotting in the serodiagnosis of Lyme disease. J Infect Dis. 1993;167: 392-400.).
2. 18 years of age or older.
3. Able to give informed consent.
4. Physician documented history of prior antibiotic treatment with a currently recommended antibiotic regimen that was appropriate for the patient's clinical features of Lyme disease at the time of presentation (table on page 8 of the technical proposal).
5. A past history of one or more of the following clinical features typical of Lyme disease acquired in the United States:
 - a) A past history of erythema migrans defined as an erythematous skin lesion that expands over a period of days to weeks to form an annular lesion.
 - b) Multiple erythema migrans lesions indicative of disseminated disease.
 - c) Early neurologic disease that includes lymphocytic meningitis, cranial neuritis (e.g. facial palsy), or radiculoneuropathy not attributable to other causes.
 - d) Acute cardiac illness consisting of signs and symptoms associated with various degrees of A-V block not attributable to other causes.
 - e) Lyme arthritis defined as recurrent, brief attacks of objective joint swelling in one or a few joints, especially the knees, sometimes followed by chronic monoarthritis not attributable to other causes.
6. One or more of the following symptoms that have persisted for at least 6 months and are not attributable to another cause or condition:
 - a) Widespread musculoskeletal pain and fatigue that interferes with usual function and which began coincident with or within 6 months following initial infection with *B. burgdorferi*.
 - b) Symptoms of memory impairment that interfere with usual function and which began coincident with or within 6 months following initial infection with *B. burgdorferi*.
 - c) Symptoms of radicular pain, paresthesias and/or dysesthesias that interfere with usual function and which began coincident with or within 6 months following initial infection with *B. burgdorferi*.

* Criteria for the seronegative cohort are identical except item 1 is replaced by physician documented erythema migrans.

Figure 2

Exclusion criteria:

1. A history of hypersensitivity to ceftriaxone or doxycycline.
2. Currently, or within the last 7 days, taking beta lactam, tetracycline or macrolide antibiotics.
3. Previously received a total of ≥ 60 days of parenteral ceftriaxone or cefotaxime therapy for:
 - a) Widespread musculoskeletal pain and fatigue that interferes with usual function and which began coincident with or soon after initial infection with *B. burgdorferi*.
 - b) Symptoms of memory impairment that interfere with usual function and which began coincident with or soon after initial infection with *B. burgdorferi*.
 - c) Symptoms of radicular pain that interfere with usual function and which began coincident with or soon after initial infection with *B. burgdorferi*.
4. Having received ≥ 14 days of parenteral ceftriaxone or cefotaxime therapy within the last 60 days.
5. Patients with active inflammatory synovitis.
6. Patients whose symptoms of CLD (a, b, c above) have been present for ≥ 12 years.
7. Patients who have comorbid disease(s) that could account for symptoms of chronic Lyme disease (a, b, and c above). Examples include severe clinical depression, rheumatic illness such as rheumatoid arthritis or SLE, other potential causes of radiculopathic pain such as intervertebral disc disease, etc.
8. Patients who have a serious comorbid disease (e.g. hematologic malignancy, cirrhosis, metastatic cancer, etc.) or an active infection (e.g., HIV, tuberculosis, etc.).
9. Patients who are receiving chronic medication therapy that could interfere with the evaluation of symptoms in a, b, c above (e.g., narcotic analgesics, prednisone ≥ 10 mg/day).
10. Patients who cannot tolerate or do not have adequate venous access for an indwelling venous access catheter or are at increased risk of acquiring an intravenous catheter related infection.
11. Patients who are pregnant, lactating, or unable to use birth control measures during the treatment period of the study.
12. Patients who have previously enrolled in this study.
13. Patients who have positive PCR for *Borrelia* DNA in plasma or cerebrospinal fluid at the time of initial evaluation for this study.

did not find that *Borrelia burgdorferi* developed resistance. Ceftriaxone has been proven to be one of the most efficacious agents. Over 80% of the study participants report having already had an experience of improving with antibiotic treatment.

Soon after the trial started, the researchers discovered that numerous potential participants were being disqualified because they had been experiencing chronic symptoms for more than four years, so after

consultation with the DSMB, this restriction was liberalized to 12 years.

Preliminary findings

Dr. Klemmner emphasized that this is far more than a treatment study. It is the first time people with chronic Lyme disease have been profiled using tests which are recognized as being accurate and sensitive measures of self-reported quality of life. Patients are also being

profiled in terms of symptoms, spinal fluid abnormalities, coinfections, and antibody status. Other data points are being systematically looked at and correlated.

Currently over 9000 specimens have been collected and over 45,000 specimens will have been collected by the end of the study. These specimens are stored in an enormous bank which will be available for future studies, for example should more sensitive diagnostic tests be developed.

By January 1999, 658 people had been screened. More were expected after a lag during the winter holiday season (they also experienced a summer holiday lag). The vast majority had more than one symptom; most had at least three. Grouping the complaints together, 383 patients complained of musculoskeletal symptoms, 341 of memory impairment, 318 of symptoms of polyneuropathy.

The ratio of seropositive to seronegative individuals is about 2:1. Based on their findings, Klemmner stated that he does not consider the ELISA a good screening test for people with chronic disease. Using the MarDx strip in Dr. Allen Steere's laboratory, only 19 of a group of 45 were ELISA positive. Twenty-eight patients were western blot positive, including 7 who were ELISA equivocal and 2 who were ELISA negative. The researchers have demonstrated very good reproducibility of the Western blot results within their laboratory.

Preliminary results of the Lyme Urine Antigen Test (LUAT – IGeneX) show figures that are typical of a Lyme-infected cohort but which are not conclusive. Of the first 39 patients, 21 have positive Lyme urine antigen (>32 ng/ml) No patient has yet proven positive for coinfections with tick-borne encephalitis virus (Powassen virus group) or Babesia by IgG seroreactivity.

Blood cultures are being done in conformity with the protocol recently

published by S. Phillips, et al, so far with negative results. However Drs. Klempner and Phillips are trying to make arrangements to process blinded specimens in parallel, which should provide verification of the method.

Patients screened so far have not shown any consistent spinal fluid abnormalities except for one. For several years Dr. Klempner has been looking for matrix metalloproteinase (MMP) and gelatinase in the cerebrospinal fluid (CSF) of people with neuroborreliosis. He recently published a paper reporting that a 130 kilodalton CSF matrix metalloproteinase without the 92-kilodalton MMP-9 is found in 79% of untreated patients with neuroborreliosis (confirmed by CSF antibody index > 1.2 or positive PCR). This pattern was found in only 6% of control patients and thus may be a useful marker for neuroborreliosis (J. Infect. Dis. 1998, Feb;177(2):401-8). Now he has found that 64% of the study patients also have 130 kilodalton CSF matrix metalloproteinase without MMP-9, i.e. the same pattern. Klempner hopes that these proteins might be useful as markers to predict response or lack of response to treatment. He also discussed efforts to better characterize chronic Lyme patients by developing new objective tests based on serum and CSF cytokines.

There is much interest in neurologic symptoms; 80% of enrollees complain of neurologic symptoms. The intramural study is looking at reactivity to peptides. They will attempt to determine whether patients with chronic Lyme disease have autoantibodies to human brain proteins. Serum from patients with post treatment chronic Lyme disease recognizes a 60kDa protein from human brain extract (10/20 patients reacted).

Dr. Klempner sees the SF-36 and other tests of self-reported quality of life as validating patient complaints which have previously been catego-

rized as "vague and/or subjective." He is struck by how physically disabled the patients are.

"These patient-reported, health-related quality-of-life measures are extraordinarily sensitive," he said. "The patients we have seen so far are severely physically disabled, two to three standard deviations below the norm. The mental composite scores are also significantly below the norm, but more cluster near the norm and some are actually above."

Dr. Klempner emphasized that to prove efficacy of treatment, patients do not have to become normal, they merely have to move toward normal (i.e. improve) on the scale. He is confident that the SF-36 component scale and the other tests they have chosen will allow them to evaluate changes objectively and to compare the treatment with the placebo group with a high degree of sensitivity and accuracy.

"They are starting out very impaired and we should be able to detect small changes," Klempner said. "It will require very small changes to note improvement."

Added to the results of the direct testing methods and the specimen bank, the study will contribute a great deal of information to our knowledge about chronic Lyme

disease. The researchers will be reporting some of their preliminary findings based on 45 patients at the upcoming international conference in Munich in June.

"We all agree that this is not the only treatment," said Klempner, "but it should give us some indication of whether we should go forward."

Patients who are unsure if they will meet the entry criteria should not hesitate to call. It was only after realizing that most patients had had symptoms for more than 4 years that the researchers saw that restriction as unrealistic and changed it. They are keeping detailed records on all the people who pass through the screening center, and even that information will be useful.

For more information on the study, contact Gary Johnson at New England Medical Center in Boston (toll free 888-596-3287; email gary.johnson@es.nemc.org) or Delona Norton at New York Medical College in Westchester County, NY (phone 914-594-4311; email norton@nymc.edu).

The Lyme Times is looking for stories about patients' experiences with the extra- and intramural studies. Contact the Editor.

Physicians, scientists form professional Lyme Society

A group of physicians and scientists recently gathered in Boston to form a professional medical and research organization called the International Lyme and Associated Diseases Society. The purpose of the professional Society is to educate physicians about Lyme Disease and to offer effective support for doctors engaged in the treatment of patients suffering from these illnesses. Once the Society's practice parameters are documented and the many medical

papers supporting them are catalogued, they will be made posted on the Society's web page. Within a few months membership opportunities will be extended to other Lyme literate physicians. A professional support network and a directory of physicians will be made available. In-depth workshops will be developed for educating any interested physicians. As a group of licensed professionals the Society will be able to respond in an organized manner when their insight is needed.

Regional News

Modest projects add to knowledge about Lyme in Ontario, Canada

The Lyme Disease Association of Ontario, Canada, [LDAO] is battling for recognition of Lyme disease in their part of the world. The results of a survey undertaken by the LDAO are reported in their newsletter, Lyme Alert (vol. 8, no. 3). Twelve patients responded on a questionnaire distributed by LDAO that it had taken from .3 to 18 years (average 8.1 years) to be diagnosed with Lyme disease after seeing from 1 to 25 different physicians (average 11) with up to 200 doctors' visits (average 92). Doctors have been heard to remark, "We don't have Lyme disease in Ontario," and, "We don't have any ticks in Ontario."

According to Lyme Alert editor John Scott, the survey clearly shows that most physicians in Ontario are not knowledgeable about Lyme disease and as a result, diagnosis is much delayed.

The patients were initially misdiagnosed with an array of diseases including stress, nerves, depression, a virus, allergic reactions, fibromyalgia, chronic fatigue syndrome, menopause, PMS, lupus, kidney disease, multiple sclerosis, arthritis, mercury and lead poisoning. All but one patient had a positive or equivocal Lyme disease serology test using ELISA and/or

western blot.

Faced with such denial and ignorance, LDAO members have undertaken several projects to change the situation. They initiated a collection of ticks and have accumulated a total of 224 blacklegged ticks in Ontario, with no history of travel. During the summer, two families went public with their Lyme disease stories, which were published in local Ontario newspapers. Several people have undertaken fundraising ventures to support Lyme disease research. Scott urges people to write to provincial and federal Ministers of Health to demand a training program about Lyme disease for Ontario doctors.

For more information about the Lyme Disease Association of Ontario or Lyme Alert, write or call John or Kit Scott, 365 St. David St. S, Fergus, Ontario N1M 2L7, tel. 519-843-3646.

Map of Canada showing locations of ticks and/or animals positive for *Borrelia burgdorferi*

Summary of findings

1. Long Point, Ont. 1987: *I. scapularis*, white-footed mice. (Barker et al, 1992)
2. Prince Edward Is. 1992: *I. scapularis*. (Artsob et al)
3. British Columbia 1993-95: *I. pacificus*, *I. angustus*, mice. (Banerjee et al)
4. Northwestern Ontario 1994-97: Scott et al, Banerjee et al)
5. Southern Ontario 1995-98: *I. scapularis* (Banerjee et al)
6. Alberta 1995: *H. leporispalustris* (Banerjee et al)
7. Quebec 1996-98: *I. scapularis* (Lyme Alert)
8. New Brunswick 1997-98: *I. scapularis* (Lyme Alert)
9. Manitoba 1997: *I. scapularis* (Lyme Alert)

Insurance companies take serious hits at AG meeting

from page 1

“Hearing on Insurance Coverage of Lyme Disease.” Attorney General Blumenthal presided from 8:30 am until the very end, nearly eleven hours later, well into the evening. He seemed particularly interested in the stories of those in which Lyme treatment or insurance coverage for Lyme treatment had been affected by academic institutions such as Yale and University of Connecticut (UConn). He was joined for the day by State Insurance Commissioner, George M. Rider, Jr., Asst. Attornies General Jennifer Jaff and Thomas Ryan and State Representative Claudia Powers (R-Greenwich).

A few other lawmakers came by and sat in for a short while to observe the goings-on. An estimated 200 people attended the meeting - close to a full house - and public participation was extensive. At least twenty-three personal stories (some quite lengthy) were read into the record. Approximately fifteen others who had planned to provide testimony left

before doing so. Over 100 written testimonials were entered into the official record.

During 1998, Connecticut had a total of 3,465 reported cases of Lyme disease which met CDC’s surveillance criteria, the highest annual total ever reported in the state. The 1998 incidence of Lyme disease in Connecticut also reached a new record high of 105:100,000. However, the first speaker, Matthew Carter, MD, Epidemiologist, Connecticut Dept. of Health, stated that the best estimate that has been established in a recent study was that for every case of Lyme disease reported, 9 others go unreported.

Hallie Krider, PhD, Microbiologist, University of Connecticut, discussed his new Lyme disease test method as well as the Lymex vaccine, emphasizing the vaccine’s deficiencies. State Senator Melodie Peters (D-Waterford) stated that she was considering getting the vaccine

and asked Dr. Krider if he would take it himself and without hesitation he loudly responded, “No.” This, of course went over very well with the crowd. It’s worth noting that Senator Peters said that she had Lyme disease twice in the past and so her comment that she was considering the vaccine was of concern, though Dr. Krider probably changed her mind without even mentioning the possible

“Shouldn’t these decisions be between the doctor and the patient?”

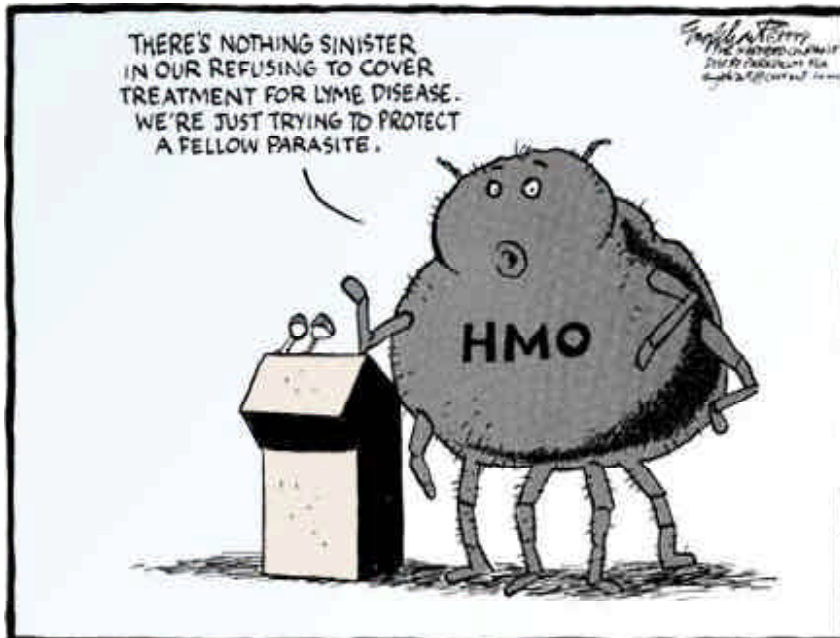
**Richard Blumenthal,
Connecticut Attorney General**

contraindication. [Ed. Note: Some scientists are concerned that the vaccine may cause arthritis and/or reactivate latent cases of Lyme.]

Montes told his personal story and Carolyn Cramoy told her daughter’s story, both brilliantly relayed as they neatly wove in the political and insurance issues. Karen Forscher discussed the work of the Lyme Disease Foundation, the awards and recognition they have received, and she touched on a longstanding disagreement with Yale’s Durland Fish.

Edward Eisenberg, MD, Director for Medical Affairs and Infectious Disease Management, Oxford Health Plans, Inc. and John Federico, MD, Senior Medical Director, Physicians Health Services, were pressed by Attorney General Blumenthal for clarification of their treatment guidelines. Blumenthal’s recurring comment was, “Shouldn’t these [treatment] decisions be between the doctor and the patient?” At one point, boos emerged from the audience aimed at Eisenberg and were met with a stern instruction by the Attorney General to refrain.

Steven Phillips, MD, a Ridgefield



Bob Englehart cartoon. Reprinted by permission.

physician who has developed a new culture test for Lyme disease, brought the house down with his slide show. In rapidfire succession he showed one peer-reviewed journal article after another, demonstrating persisting infection. At the top of each of these half dozen or so slides was the header "And Again.., And Again.., And Again..," the final one saying "And Yes, Again...." His presentation was clear, concise, convincing and 200 miles an hour. A well-deserved standing ovation followed his presentation.

Dr. Amiram Katz, a Yale neurologist, was a wonderful breath of fresh air. He made it abundantly clear that not all Yale minds think alike. He explained his diagnostic

methods, which were quite reasonable, and he shared his frustrations regarding health insurance companies and their lack of cooperation. He stated that insurance companies are only interested in one thing, their bottom line. He hammered home the point by suggesting that with conditions like neurologic Lyme disease, "the insurance companies stall and stall and eventually the patient develops dementia and then the insurance company no longer has to talk with them." His tongue-in-cheek commentary was met with applause and laughter as the audience overwhelmingly agreed.

Robert T. Schoen, MD, Rheumatologist, and Director of the Yale Lyme Disease Clinic, began by stating, "Now I see what it's like to have the home field advantage," obviously referring to the white-hot response to Dr. Phillips' presentation and his (Schoen's) apparent anticipation of how the crowd was going to receive his own remarks. The rest of his talk was the standard party-line, though considerably watered down, most likely for safety's sake. Attorney General Blumenthal did get Schoen to say that the CDC case definition is for surveillance purposes and not intended to be used for clinical diagnosis.

The other presenter on this panel was Henry Feder, MD, UConn Health Center. From early in his presentation came the strange quote of the day: "Most of the mysteries of Lyme disease have been resolved." The high point of Feder's talk was when State Representative Powers, who was

present for almost the entire proceeding, mentioned to him the earlier discussed shortcomings of the Lymerix vaccine pointed out by his colleague from UConn (Dr. Krider). Dr. Feder wasn't there for Krider's remarks and he was in apparent disbelief that someone from UConn had said something bad about the vaccine. As he shuffled through his papers seeming to look for the day's schedule to see who it was from UConn, he asked, "Someone from UConn said that?" It was a Kodak moment, indeed. After that exchange he slogged his way through three case histories of people who were either "misdiagnosed" as having Lyme disease (when in his opinion they did not) and/or people who once had Lyme but were overtreated to the point that their health was put in jeopardy. He also stated that he does not endorse the use of IV antibiotics to treat Lyme disease. There was no applause for this panel.

The Public Commentary testimonials were compelling, heartfelt, tragic and even angry in some cases. The recurring theme was that certain "experts" in the field of Lyme disease (one in particular who participated in the day's proceedings but then left in a hurry) were responsible for hurting people and downplaying the seriousness of the illness. Also there were a number of stories of insurance companies doing their best not to pay for much needed antibiotic therapy.

There can no longer be any doubt in Attorney General Blumenthal's mind that something needs to be done. It defies any reasonable logic that so many people could come out to tell virtually the same story over and over. Judging from the questions he asked and the expression I saw on his face much of the time, I suspect something will be done. In one exchange with the two insurance companies' representatives, Attorney General Blumenthal made it perfectly clear that the entire reason we were all there was because of the extraordinarily large number of complaints his office has received

Bites By County

The entire state is endemic to Lyme disease, but there are pockets with higher risk than others, as shown in the following town-by-town and county-by-county listings.

The first column is the number of reported cases, the second, the relative risk of getting Lyme disease — the number of cases per 100,000 population. In Salisbury, for example, there were 54 cases, but since that represents 1,320 cases per 100,000 residents, in Salisbury, that translates to more than 1 case per 100 residents.

While high, the following numbers are estimated to be just 15 percent of the actual number of cases, said Starr H. Ertel, an epidemiologist and the Lyme disease surveillance coordinator for the state Department of Public Health.

COUNTY	CASES	RATE
Fairfield	796	96.18
Hartford	192	22.54
Litchfield	335	192.43
Middlesex	313	218.58
New Haven	382	47.5
New London	605	237.29
Tolland	294	228.44
Windham	377	367.72
Unknown	118	
Total	3412	103.8

From the Hartford Courant

from people with Lyme disease who it appears have been treated unfairly. This Attorney General doesn't strike me as the type of person who is big on lip service. I suspect something will be done.

Lyme bill introduced by CT Attorney General

In the wake of the February 24 Lyme hearings, Connecticut Attorney General Richard Blumenthal proposed a bill that would require insurance companies to pay for the treatment of Lyme disease. The bill, Senate Bill #1318, is currently in committee. Connecticut residents are encouraged to contact their legislators to support this bill.

Mother relates battle for insurance

Carolyn Cramoy of Westport, whose daughter has battled the disease – and her insurance companies – since 1992, said current laws provide a license for insurance companies “to steal from people at the time of their greatest need.”

“Lyme disease is a political illness,” said Cramoy, a nutritionist whose 21-year-old daughter, Samantha, is a senior at Bryn Mawr College in Pennsylvania. “This is a truly nefarious, symbiotic relationship. It's a true no-lose situation for the insurance companies.”

Cramoy told the hearing that Oxford Health Plans said it would not cover the treatment because “the documentation on file simply does not demonstrate that the treatment is medically necessary.”

Attorney General Blumenthal said after hours of testimony that he's convinced the HMOs are stonewalling service to a needy group. Dr. Edward Eisenberg, medical director for disease management of Oxford Health Plans, said Oxford has expanded coverage for IV treatments from three weeks to six.

He noted that some cases that have been turned down for coverage

have eventually resulted in unrelated diagnoses of multiple sclerosis or rheumatoid arthritis.

“Oxford's policies are based on established medical protocols, are consistent with the opinions of nationally recognized experts and are embodied in our medical policy for therapy of Lyme disease,” he said.

From the Connecticut Post, 2/25/99

Lyme Disease Foundation founder criticizes insurance company policies

by Karen Vanderhoof-Forschner, CPCU, CLU, MBA

This is an abbreviated version of the testimony given on February 24, 1999 at the CT Attorney General's Hearing.

The history of Lyme disease spans over 100 years and several continents. What we now call “Lyme disease” was first described in 1883 by German physician Dr. Buchwald. Joint involvement was first described in 1921 and the debate about the causative agent, manifestations, and treatment have continued for over a century.

In 1970 the first U.S. acquired case was published by Wisconsin physician Dr. Scrimenti. The first cluster of cases was reported in 1976 by doctors at the Groton submarine base. In 1982, LDF founding Board Member and National Institutes of Health researcher Dr. Willy Burgdorfer discovered the causative agent of Lyme disease, which was named *Borrelia burgdorferi* in his honor.

In 1985 I contracted Lyme disease while pregnant and transmitted the infection to my unborn child, Jamie. My life was forever changed. In July of 1985 Jamie was born and the first article of maternal-fetal transmission of Lyme disease (with fetal death) was published. On his first day of life, Jamie started

showing signs of the infection. He became multi-handicapped, and eventually died in 1991 during a relapse. Jamie and I had positive tests. When Jamie received antibiotics his condition dramatically improved, but he was never “cured.” On autopsy pathologists found Lyme bacteria in his eyes. Similar cases have since been published.

In 1987 I attended a Lyme disease conference. I was surprised to discover a polarized scientific community. The lack of camaraderie, clash of egos, and competition for limited research funds was disturbing. However, I did find a core group of compassionate, cooperative researchers who wanted to start a nonprofit organization dedicated to this disease. They were seeking a scientific forum to present a range of differing research results, conduct vigorous debate, maintain friendships, and support colleagues research. These believed Lyme disease was serious and pervasive - and had the research to back-up their assertions.

So, in 1988, I, my husband Tom, scientists, clinicians, business

leaders, government workers, and patients established the Lyme Disease Foundation (LDF), the first nonprofit organization dedicated to finding solutions to Lyme disease. Our focus is on education, research, and advocacy. The LDF's website receives over 200,000 hits a month. We conduct medically accredited conferences, publish a peer-reviewed journal, produce educational videos (including two award-winning TV programs), and offer training for support groups. I have volunteered full-time for eleven years. Many researchers support LDF activities. In 1997 the LDF received an award

taking 7-12 months needed an average of 5 doctors to get diagnosed and cost \$68,000. Insureds taking over 12 months to get diagnosed needed an average of 7 doctors and had an average cost of \$92,000.

Insureds experience both lost income and medical expenses. Of the costs, 40% is spent before the diagnosis, 10% is lost income after the diagnosis, and 50% is medical bills after the diagnosis. Non-cash losses are common. 71% of patients experience mental anguish, 41% have permanent physical damage, 19% lose time at work, 17% lose time from school, about 3% experi-

care for insureds. Their medical consultants are often well-funded physicians. Patients with serious illnesses hang by a thread, knowing one serious medical episode can - and often does - bankrupt them. The LDF has witnessed cases where medical treatment is approved by the insurer, continues for weeks, and then the insurer abruptly changes its mind and retrospectively declines reimbursement - forcing private lawsuits and patient bankruptcy.

In 1992, there was a major gatekeeping effort by insurers. Companies were hiring "experts" that increasingly declined coverage. A presentation to the American Academy of Insurance Medicine provided an excellent opportunity to reach all insurance medical directors. This is the year the LDF was swamped with complaints by patients about being denied medical coverage. Shifting costs from one disease code to the next doesn't decrease total costs - it just decreases the ones coded to Lyme disease. Patients still suffer and "doctor shop", looking for someone to restore them to good health.

There are medical and published articles that prove that short-term treatment (e.g. 4 weeks) does not cure everyone and that additional treatments are sometimes necessary. It also clear that not everyone tests positive. In the Food and Drug Administration testimony in June of 1994, physicians from Stony Brook School of Medicine testified that only 73% of patients with an EM rash develop a positive test. The other 27% remain seronegative. It is a mystery why this is never cited by the gatekeepers.

I would consider the following in evaluating the intent of an insurer:

1. What percent of the time does the insurer or consultant decline coverage - either because the patient doesn't have Lyme disease, doesn't need testing, or doesn't need treatment? Is the decision rigidly applied to everyone?

Costs increase with delayed diagnosis

Time to diagnosis	Number of doctors seen	Cost
<7 months	3	\$35,000
7-12 months	5	\$68,000
>12 months	7	\$92,000

from the National Institutes of Health for Outstanding Educational Effort.

Between 1980 and 1999 there were over 123,000 cases of Lyme disease reported by 49 states. In 1990 the LDF, Society of Actuaries, and Stern School of Business conducted the most extensive survey of chronic patients - resulting in over 1,000 patient questionnaires. This study showed Lyme disease costs society over 1 billion dollars per year. And, it took patients an average of 5 physicians to be diagnosed. Those patients lucky enough to have the tell-tale rash - also took an average of 5 doctors to get diagnosed. The hallmark indication of the disease did not result in a more rapid diagnosis. Twenty percent of newly diagnosed cases are serious enough to need intravenous antibiotics. Early diagnosis and treatment decreases insurer costs. Insureds diagnosed in less than 7 months needed an average of 3 doctors to get diagnosed and cost about \$35,000. Insureds

ence divorce, and 1% actually die. And, of the pregnant women there were 55 live births, 19 miscarriages, and 7 neonatal deaths. In the US in 1992 the national average per 1,000 live births is 7.4% fetal deaths and 5.4% neonatal deaths. Clearly, something is wrong.

We have been a society that has not spent enough effort on prevention of diseases - but rather of playing catch-up after illness occurs. Insurers should be spending their time and money toward prevention and early diagnosis - not denying them treatment. In 1995 I met with the Insurance Department and the "Blues" to find a middle ground to insurance denials. The meeting turned into a simple one-sided (Blue's consultant) presentation. The meeting ended and nothing changed. There was no intention of resolving the problems.

Insurers are powerful financial institutions with a fiduciary responsibility to cover necessary medical

2. Did the patient have any manifestations or positive tests that have been described in the medical literature? If the FDA approves the PCR DNA test to be used in the 20,000 person vaccine trials, why would it be “experimental” when done in a federally approved PCR lab? Do they require specific tests be done at specific labs - and exclude other testing methods?

3. What percent of time do they or their consultants approve extended treatment past 10 weeks?

4. How much does the consultant make from insurance consultations per year and how many times does he/she reject the diagnosis or decline treatment?

5. Has the insurer ever conducted a study of how they could save money through denials of coverage?

6. Does the insurer fund the consultants, their institutions, or their private foundations?

7. Do they disclose the names of their experts and the reasons for declining coverage?

8. Do they have a system of providing coverage for one class of insureds while having a policy to deny others?

9. Do they send medical experts to meetings that present other viewpoints? Or, do they rely solely on their hired consultants?

10. Does the insurer deny coverage because the patient does not have or is cured of Lyme disease - and then deny life insurance because the patient has Lyme disease (which is now considered an increased risk of death or disability).

Not all insurers are the “bad guys”. Some are quietly providing coverage and case management for their policy holders. Improvements in case management could provide for speedier diagnosis and treatment, and test for confounding factors such as coinfections.

It is appropriate to request that doctors support the medical necessity with citations from medical litera-

ture. I cite the excellent work by MD HealthPlan which printed and distributed brochures on Lyme disease and the following year on tick-spread disorders to ALL of their insureds. This is an example of doing the right thing.

The debate is really between two schools - The Gatekeepers and the Realists. The Gatekeepers dogmatically adhere to the belief that only certain academics/researchers know the truth about this disease. Members of this elite group feel an “obligation” to stop those with opposing views in order to “protect the public”. Gatekeepers believe Lyme disease is easy to diagnose and treat. They have a “my-test-is- perfect” mind-set and claim “overdiagnosis” when patients with positive tests test negative in their lab. They avoid conferences that challenge their views and can honestly say in court that they are unaware of information stating otherwise.

The Realists know and accept that there is no test that can prove infection and then prove a patient bacteria-free. Because of this science doesn't have all the answers, therefore diagnostic and treatment decisions are a complex, private matter between the doctor and patient. Realists know that persisting infection despite short-term treatment is a reality, but is not always the explanation of persisting manifestations. This is the viewpoint of the LDF. This is why the LDF has never adopted a diagnosis or treatment protocol. Intellectual differences are to be expected as our understanding evolves. However, some have made it their mission to ruthlessly go after individuals who think “outside the box”. For some, keeping the gate closed is their personal war. Patients are the casualties.

Gatekeepers not only block individual access to necessary medical care, they also block a doctor's right to treat. What better way to cut-out problem doctors who

incur expenses, than to cancel them from the insurers plan - or better yet, haul them before the medical licensing board. Even more disturbing, is that some physicians resort to personal or professional behind-the-scene smear campaigns - mocking patients (even at medical conferences), accusing colleagues of overdiagnosing or overtreatment for personal profit, or spreading rumors about patients' confidential medical records. It is this type of action that proves the debate is not about science - but about power.

What is the solution? 1. Until there is a perfect test, insurers should take a balanced approach - with patients being allowed to seek their own second opinion. The insurer should then honor the recommendation, especially if there is support for the recommendation in medical literature.

2. Medical licensing boards should let physicians know they will no longer be subjected to attacks - that Connecticut will be a place where physicians can treat patients without fear of retaliation.

3. Insurers should disclose who their “expert consultants” are, how much they are paid, and how they have ruled on all other Lyme cases. This would be helpful for all diseases, not just Lyme disease.

4. Since education about prevention and early diagnosis is critical, insurers should work with the LDF in overall educational efforts.

5. A clear message should be sent by the Insurance Commissioner and Attorney General that patients' rights and access to care are being protected. Abuses by insurer/HMO's need to be vigorously investigated - this includes for individuals that are having their coverage denied, physicians being cancelled from programs, and physicians being turned into the health department for “overdiagnosis” or “overtreatment”.

Thank you for the opportunity to speak here today.

Insurance companies deny persistent infection in spite of scientific evidence

by Steven Phillips, MD

This is the text of Dr. Phillips' testimony at the Attorney General's meeting

Lyme disease is an illness which is perfectly positioned to engender controversy. The bacteria that causes the illness, *B. burgdorferi*, has been, to date, exceedingly difficult to grow from patients. As a result, there has been no definite method for diagnosing Lyme and no definite method for defining its cure. If *B. burgdorferi* could not be grown from a patient before antibiotic therapy, then there is no reference point with which to compare to indicate whether that individual is cured of the infection after therapy.

Questions regarding diagnosis, treatment efficacy, and definition of cure, although still lingering problems, were virtual black holes for many years after discovering Lyme disease. As such, several assumptions made by early researchers have proven to be invalid. In recent years there has been a tremendous amount of solid peer reviewed medical data debunking the prior dogma that this is an easily diagnosed and cured illness. Yet, the insurance industry and some tertiary care centers have refused to accept the necessary changes in paradigm.

There has been considerable criticism as to the accuracy of currently available blood testing for Lyme disease.¹ Seronegative Lyme borreliosis (Lyme disease with a negative blood test) has been widely reported.^{2,3,4} Although it has generally been accepted that there are multiple problems with current Lyme testing, with the recent development of a high yield culture technique for spirochetes, there is now dramatic comparative evidence that the currently available antibody assays

are woefully inadequate.⁵ As such, negative Lyme serology cannot be relied upon to rule out infection with *B. burgdorferi*. Further, a negative spinal tap in patients with Lyme disease does not mean that central nervous system (CNS) infection has not occurred. There are many studies to support CNS infection with *B. burgdorferi* despite negative spinal fluid by routine antibody, cell count, and chemistries.^{3,6} Although the Centers for Disease Control has echoed the sentiment that Lyme disease is first and foremost a clinical diagnosis, with antibody testing playing merely a supportive role, many insurance companies feel it appropriate to rule out a case of Lyme disease based on a negative antibody test and define cure by same.

The lack of complete cure with antibiotic therapy does not mean that the underlying etiology is not active infection with *B. burgdorferi*. There are volumes of human data demonstrating persistent infection with *B. burgdorferi* despite multiple and extended courses of aggressive antibiotic therapy. This has been demonstrated time and again by both PCR (a method for amplifying the DNA of *B. burgdorferi* and therefore proving its presence)^{7,8,9} and by culture,^{10,11,12,13} even in patients with negative standard blood tests for Lyme.

Even in early disease at the bullseye rash stage, which most think is easily curable, there is strong data demonstrating positive cultures despite standard antibiotic therapy.^{14,15} As if all of this wasn't enough, new studies have demon-

strated by culture that even intravenous antibiotic therapy for 3 months did not eradicate *B. burgdorferi* in 91% of the late stage Lyme patients studied.⁵

To further complicate matters, there are a great many strains of *B. burgdorferi*, varying in their ability to cause disease patterns. Studies have demonstrated that even in animals who do not manifest overt disease after infection with *B.*

Since many of the tertiary centers are rather occupied in the denial of its existence, those very institutions which are in a position to find a cure, are not looking.

burgdorferi, the bacteria could be isolated from them by culture.¹⁶ Human studies have further documented high rates of asymptomatic infection with "non-pathogenic" strains (those that do not cause disease).¹⁷ This needs to be taken into account when analyzing the assumed "false positive" rates of Lyme tests. However, although so-called "non-pathogenic" strains do not appear to cause overt disease in the short term, it is unknown, but certainly possible, that long term infection with these organisms may be responsible for a spectrum of late stage neurologic disease.

Lastly, studies very clearly demonstrate that even in healthy animals "cured" with standard 4-week antibiotic treatments for Lyme disease that the infection has not been eradicated.¹⁸ These studies plainly illustrate that the bacteria evade complete destruction with antibiotics, even in "cured" cases, and can lie dormant for extended periods of time. This explains the

observation of patients who are well for years after "cured" Lyme, only to relapse while going through a significant stress, such as divorce, or death of a loved one.

In light of overwhelming scientific evidence that the *B. burgdorferi* persists in patients despite extensive treatment, insurance companies and some tertiary centers still magically proclaim patients cured and in no further need of therapy. The real need is to find a definite cure for this illness. However, since many of the tertiary centers are rather occupied in the denial of its existence, those very institutions which are in a position to find a cure, are not looking. However in the absence of a definite cure, the very least should be mandates requiring insurance companies to cover extended treatment for this often devastating illness. It has already been shown that longer treatment durations, although certainly not necessarily curative, may be more effective than shorter durations.^{19,20} Insurance companies, and their paid consultants, have no ethical, moral, or scientific basis to deny coverage for these seriously ill patients. Considering the foregoing data, anyone who declares a patient cured simply because 4 weeks of standard antibiotic therapy has been given, or denies the diagnosis of a Lyme patient simply based on a negative blood test, is sadly misinformed.

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Dr. Phillips is the author of a recently published study of a new culture method. He practices medicine in Ridgefield, Connecticut.

Host and vector coinfections complicate diagnosis of Lyme

by Jean Hubbard

Many ticks and many infections await those who venture into the woodland areas of New York State's Shelter Island and Long Island, according to Edward Bosler, PhD, of the Stony Brook School of Medicine. At the 1998 Lyme Disease Foundation Conference, Dr. Bosler, who has been studying tickborne infections that cause disease in humans for more than a decade, talked about his group's most recent field studies in this area, describing their methods and some preliminary observations [1].

The three known tickborne infections that share the same reservoir hosts—small mammals like the white-footed mouse and chipmunk—and the same vector tick to humans—*Ixodes scapularis*—have long been known to be endemic in this region; *Borrelia burgdorferi* and *Babesia microti* were first found in the small mammals and *Ixodes* ticks there in the early 1980s, and later the infectious agent for human granulocytic ehrlichiosis (HGE). Recently even more tickborne diseases have been found on Long Island, including, in Dr. Bosler's words, "Rocky Mountain spotted fever, brought to you by a different tick, the dog tick, and last year *Ehrlichia chafeensis*, brought to you by *Amblyomma*."

Last year Dr. Bosler and his colleagues at Stony Brook, responding to new information about the serious human disease potential of co-infections [see "The New Lyme" in Lyme Times #22] and armed with their newly developed PCR techniques, turned their attention once again to *Ixodes scapularis* ticks and small mammals, assessing the frequency of infections and co-infections of *Borrelia burgdorferi*, *Babesia microti* and HGE.

They collected questing adult *Ixodes* ticks from vegetation in wooded areas in several areas of Long Island at sites that "pretty much coincide with patient populations" — Shelter Island, Wildwood State Park on the North Shore, and sites along the Bay. They also trapped wild rodents to collect subadult ticks feeding on them. The adult ticks, the wild rodents and the younger ticks were all tested by PCR for all three of the *Ixodes*-vectored infections. Rates for PCR-detected infection with *B. burgdorferi*, the agent of Lyme disease, were "pretty consistently" 50% in adult ticks at all sites studied. Rates of PCR-detected infections with *Babesia microti* and HGE varied from site to site.

Rates of infections in questing adult ticks:

At Wildwood State Park on the North Shore of Long Island, 50% of the adult questing ticks, which were collected mostly from wooded locations, were infected with *B. burgdorferi*; 13% were infected with *Babesia microti*, and 20% carried HGE. Co-infection rates at this site were significant: 13% of ticks were infected with both HGE and *B. burgdorferi*, 8% with both *Babesia microti* and *B. burgdorferi*, and 3% had co-infections with *Babesia microti* and HGE. At Montauk, the farthest point east along the south shore of Long Island, again 50% of

ticks were infected with *B. burgdorferi*; almost 20% were infected with *Babesia microti*, and 20% with HGE. None of the ticks had PCR-detectable co-infection with *B. burgdorferi* and *Babesia microti*; 12% were co-infected with *B. burgdorferi* and HGE.

Farther east at Cedars Point State Park — again 50% of ticks were infected with *B. burgdorferi*, but only 7% with *Babesia microti*. No HGE infections were found in ticks at this site, and none were co-infected. Dr. Bosler states that *Babesia microti* is not "readily detected" in adult ticks, and rates are usually higher in nymphs.

Mammal trapping was done during July and August, when larval *Ixodes scapularis* ticks are most abundant. The mammals — 30 mice and six chipmunks — were also tested for the three tickborne infections, by PCR analysis of samples of their blood, urine and punch-biopsy tissue from their ears. Larval ticks were collected from the mice and chipmunks and allowed to molt to nymphs, when they too were tested for all three infections by PCR.

After ticks were collected from the mice and chipmunks, they were marked and then released where they had been trapped. Several were re-trapped later during the season, allowing the investigators to study tick burdens and tick infection rates over time.

This is, as Dr. Bosler said, "very labor-intensive, considering that one mammal may yield 300 ticks, all of which have to be analyzed by PCR for three different infections," all, of course, in separate PCR assays.

Tick infection rates at parks on Long Island

Park	Bb	Bm	HGE	Bb/HGE	Bb/Bm	Bm/HGE
Wildwood	50%	13%	20%	13%	8%	3%
Montauk	50	20	20	12	0	ND
Cedars Point	50	7	0	0	0	0

Lyme Alliance, Inc., Petition

"Advocates for TRUTH in Lyme Disease"

We, the undersigned, believe that Lyme disease can and does exist as a chronic illness with persisting infection, and that the disease is greatly underdiagnosed and undertreated. To this end we insist that:

1. Physicians on the front lines of Lyme disease patient care not be harassed, persecuted or made to fear for their medical practices because they do not adhere to the conservative "short term" care for Lyme disease.
2. Insurance companies not be permitted to deny payment for treatment of Lyme disease as no conclusive diagnostic tests exist and the prevailing conservative "short term" care is not backed by definitive scientific research.
3. Access to treatment methods which are both the patient's and treating physician's choice not be denied or blocked based on guidelines that are controversial and not thoroughly researched.
4. Research into Lyme disease and other tick-borne illnesses be adequately funded in order to develop better diagnostic and treatment methods.

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Given this, he went on, it was convenient that the 1997 summer season was one when ticks were relatively less abundant. Over the years he has been studying ticks in the area he has observed cycles of tick abundance, with tick populations peaking every seven to 10 years.

Twelve mice and chipmunks were captured more than once, and Dr. Bosler described what happened over time in one of them. On the first capture, several ticks from one mouse were co-infected with *Borrelia* and HGE. When the same mouse was recaptured one week later, the infection rates and co-infection rates in the ticks feeding on it had doubled or more. Dr. Bosler wonders if mice are continually amplifying the infections they carry, so that they become increasingly able to infect more and more ticks. This happened during the height of the larval tick season, and he believes it could result in more infected nymphs next season, a possibility his group is testing in followup studies this year.

Infection rates in mice and sub-adult ticks:

By culture, nine of 30 mice, about 30%, grew *B. burgdorferi*, but Dr. Bosler believes this gives a low estimate of actual infection rates since there were problems with the cultures. By PCR, 53% had active *Babesia microti* infections, and about 16-17% had HGE infections. Culture or PCR evidence of simultaneous active co-infections were found in many mice — *Borrelia/Babesia* in 30%, *Borrelia/HGE* in 7%, and *Babesia/HGE* in 13%. All three pathogens were found in 7% of the mice.

Looking at the nymphal ticks collected as larvae from the mice: 45% of the nymphs were infected with *Borrelia* (again by PCR), 30% with HGE, and 10% with *Babesia*. Co-infection rates in these ticks were *Borrelia/HGE* 17%, *Babesia/HGE* 8% and *Borrelia/Babesia* 7%. All

three infections were found in about 7% of the nymphal ticks.

Dr. Bosler believes these tick and mammal infection rates are high enough to suggest substantial risk of co-infections in people bitten by ticks. He noted that there is evidence that in humans co-infections with more than one tickborne disease not only complicate the diagnosis and treatment of illness, but increase its severity. He is now working to develop animal models that will be infected with one or more pathogens so that the effects of infection with multiple tickborne pathogens can be studied in the laboratory.

Other studies find multiple infections in ticks and mammals

Investigators in other regions are also examining ticks for multiple pathogens. Varde et al examined 100 questing adult *Ixodes scapularis* ticks collected (by drag cloth or from personal clothing) at 10 sites in Hunterdon County, New Jersey — the county with the third-highest CDC-confirmed case rate for *B. burgdorferi* in the United States as well as many suspected but not proven human cases of HGE. They used PCR to test the ticks for infection with *B. burgdorferi*, HGE and *Babesia microti*. At least one of the three pathogens was present in 55% of the ticks. Most were positive for *B. burgdorferi* — 43% of the 100 ticks, and fewer for HGE (17%) and *Babesia microti* (5%). Co-infections were found in 10% of the ticks — *Borrelia/HGE* in 6%, *Borrelia/Babesia* in 2% and *Babesia/HGE* in 2% [2].

Telford et al examined adult ticks on Massachusetts' Nantucket Island for infection with the three pathogens and found 36% of the ticks positive for *Borrelia burgdorferi*, 11% positive for HGE, and 9% positive for *Babesia microti*. Four percent of the ticks were co-infected with *Borrelia* and HGE, but none with *Borrelia* and *Babesia* [3].

In a separate study, Telford did find *Babesia microti* infections in the

short-tailed shrews of coastal Massachusetts, however. The shrews were infected with *Borrelia burgdorferi* as well as *Babesia microti*, and at respectable rates: 11 of 14 were infected with *B. burgdorferi*, and 11 of 17 shrews had visible babesial parasites on blood smears. Three of the shrews transmitted *Babesia microti* to the ticks feeding on them, but there were so few immature ticks on the shrews that the investigators believe they would “contribute only minimally to populations of infected nymphs” [4]. Schwartz et al studied ticks at a single site in Westchester County, New York, testing them only for *B. burgdorferi* and HGE; 52% were infected with *B. burgdorferi*, and 53% were infected with HGE. *Borrelia/HGE* co-infection was present in 26% of these ticks [5].

Hofmeister et al cultured *B. burgdorferi* spirochetes from ear biopsies of 46% of 81 mice captured from four different sites in Minnesota and Wisconsin. Mice from Morrison and Pine Counties in Minnesota and Burnett County in Wisconsin had infections with *Babesia microti* detected by PCR, with rates ranging from 5% to 30%, and always in mice that were also culture-positive for *B. burgdorferi*. *Borrelia/Babesia* co-infection rates in these mice varied from 20% to 54%. Of 20 mice captured in Wisconsin's Monroe County, 75% were infected with *B. burgdorferi*, but none with *Babesia microti*. Although four mice were PCR positive using a primer set intended to detect Ehrlichia, on analysis the infection turned out to be a new Bartonella species instead of HGE; i.e. the researchers had discovered a new infection. There is no evidence that this infection causes disease in people [6].

People have reportedly been infected with HGE in these counties, and Hofmeister et al argue that their lack of success in detecting HGE infections in mice does not necessarily throw those diagnoses into question. They point out that

experimental HGE infections in mice become undetectable by PCR by about a month after infection, although infection can again be demonstrated if they are splenectomized; the sub-detectable infections can even be transmitted to uninfected mice via blood transfusion [6]. There seem to be no data about how soon naturally acquired HGE infections in mice become undetectable by PCR.

In these various studies, ticks demonstrated *B. burgdorferi* infections at rates ranging from 36% to 52%. Mammals appeared to have slightly higher rates of *B. burgdorferi* infection, although this was more variable; 75% of mice at one Wisconsin site carried *B. burgdorferi* infections, and 79% of a small number of shrews in coastal Massachusetts. Ticks were infected with *Babesia microti* at rates ranging from 5% to 20%, and with HGE at rates of from 0 to 30%, with one high infection rate of 53% in Westchester County. Co-infections with two or more pathogens were seen in from 7% to 17% of ticks, although several sites had no co-infected ticks at all, and in Westchester County 26% of ticks were co-infected with *Borrelia*/HGE.

Varde et al, based on the tick infections found in New Jersey, advise that when residents or visitors to endemic areas have flu-like symptoms and a history of a tick bite, physicians should consider all three of these tickborne infections [2]. After reviewing other findings of co-infections in both ticks and humans, they also offer the intriguing idea that "human co-infection by multiple tickborne agents may account for the variable nature of the clinical manifestations of Lyme disease."

Dr. Bosler observes that even the co-infection rates that his group have found thus far are sufficiently impressive that "it is not hard to envision that one tick bite can bring a multitude of infections" [1].

Calendar

Lyme Disease Seminar

May 23, 1999
Peconic, New York

A Lyme Disease seminar will take place on Long Island at the Southold Recreational Center on Peconic Lane. Registration will begin at 5pm, seminar to begin promptly at 6pm. Speakers: Joseph Burrascano, MD, Olaf Butchma, DO, Russell Cancellieri, MD, Chuck Timpone, DVM, Jerry Simons, PA, Stephen J. Nostrom, RN. Questions and answers will follow the presentations, ending at 9pm. Contact Stephen J. Nostrom if planning to attend - 516-298-9606 or email Borrelia@aol.com.

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VIII International Conference on Lyme Borreliosis and other Emerging Tick-Borne Diseases

June 20-24, 1999
München Park Hilton
Munich, Germany

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