Furor at Lyme Disease Conference

Patient-support groups got a dozen rejected papers reinstated at a Lyme disease meeting, angering researchers who had turned the work down as unscientific

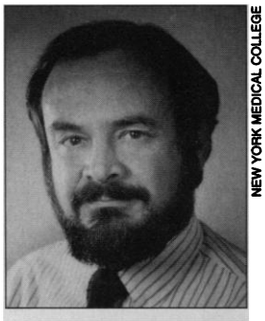
At most scientific meetings the program committee has the last word on what is presented at the conference—and what doesn't make the cut. That isn't the way it worked, though, at an international conference on Lyme disease held earlier this week in Arlington, Virginia. That conference included some presentations that had been rejected by the program committee as lacking in scientific merit. The rejected papers were reinstated by "popular demand," including pressure from Lyme disease patient-support groups—over the angry objections of some researchers on the program committee.

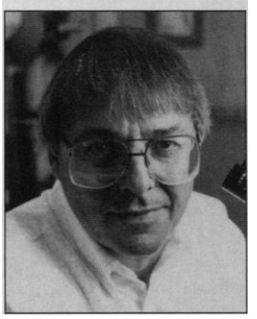
This skirmish may not seem significant in terms of the number of presentations involved—only a dozen of the 400 at the meeting—but it provides a window onto an intense controversy over the clinical diagnosis and treatment of Lyme disease. On one side are a group of clinicians and the patients they treat—patients who feel shut out by the medical establishment. On the other side are academic researchers who worry that many of these patients don't have Lyme disease and are receiving therapies that would be worthless even if they did. The controversy also raises the deeper question of whether academic scientists should offer a hearing to colleagues whose work runs counter not only to mainstream views but also to the scientific standards of their fields.

Crawling lawns. Much of the heat in this debate stems from the fears that Lyme disease arouses. In the Northeast, where lawns are crawling with disease-carrying ticks and tens of thousands of people have fallen ill since the early 1980s, anxiety about Lyme disease runs high. Lyme borreliosis, as the disease is formally known, is caused by the bacterium *Borrelia burgdorferi*—a spirochete similar to the syphilis organism. The disease is usually passed to humans by tiny juvenile ticks, which, unlike the adults, may feed unnoticed for the 24 to 48 hours it takes to transmit the disease. The illness usually begins with a rash, followed by arthritis-like symptoms. After a short course of antibiotics most patients recover, but in some the illness persists and the symptoms broaden to include chronic pain and fatigue, memory loss, muscle weakness, and palsy.

The diagnosis and treatment of this syndrome, often called "late Lyme disease," is the focal point of the controversy. Most Lyme researchers say the spirochete is wiped out in nearly all patients after 2 to 4 weeks of antibiotic therapy. Symptoms of late Lyme, they say, occur in some patients even after the spirochete is gone, and those symptoms don't respond to antibiotics.

Some of the clinicians who specialize in Lyme disease disagree with this view. They blame the late symptoms on persistent spirochete infections, arguing that their patients get better when they are treated with many months of antibiotic therapy. "There are people out there who really are sick, who go back on medicine and get better again," says Long Island internist Joseph Burrascano. Some clinicians also contend the diagnostic criteria established by academic researchers are so narrow that they miss many people who have late Lyme disease and would benefit from prolonged antibiotic therapy. "What do you do with all those people who may have Lyme or may not have Lyme?" asks internist Kenneth Liegner, of Armonk, New York. "Do you wait and not treat them for 5 to 10 years until we have better tests?"





NEW YORK MEDICAL COLLEGE

Ticked off. Durland Fish *(above)*, Russell Johnson.

Academic researchers bristle at this attitude because they think it results in people being given questionable treatment for a disease they don't even have. "Lyme disease has become an overdiagnosed illness," says one researcher who requested anonymity because he fears repercussions from patient groups. Even late Lyme can be diagnosed accurately, he says, if clinicians rely not only on symptoms but also on a battery of laboratory tests that give characteristic results in cases of Lyme. Because many clinicians are not rigorous in diagnosing Lyme, he says, "you see many...patients who do not have Lyme disease, but who think they do." And you see unreliable results from reports on the treatment of those patients, adds Lyme researcher Durland Fish of New York Medical College in Valhalla: "They are making claims, saying, 'I treated this patient for 5 or 6 months, and she got better.' That's an anecdotal case."

Given those views, it is not surprising that when the program committee for the Fifth International Conference on Lyme borreliosis met in Washington, D.C. in February to consider 400 or so submitted abstracts, some from nonacademic clinicians were rejected. Program committee chairman Jorge Benach, of the State University of New York at Stony Brook, says seven of the dozen or so rejected abstracts were from clinicians who were reporting either new conditions associated with Lyme disease or results from prolonged antibiotic treatment. "We were looking for information that would help us determine whether somebody had been rigorous about their definitions of Lyme disease," says a program committee member who requested anonymity. "The patients [in the rejected abstracts] were not demonstrated to our satisfaction to have Lyme."

A different view. Lyme patient-support groups took a different view. The committee was "pulling out the abstracts they didn't like," says Lyme patient Jessica Rose of the Lyme Disease Association of New York, a patient-support group. Rose says she heard of the rejections in April at a meeting of clinicians and patients in Stamford, Connecticut. "This clinician said to me, 'I need your help, I need you to write some letters...[the conference] is going to be slanted, there is a hidden agenda.'" Rose alerted other groups, and they wrote to their congressmen and to meeting organizers Lawrence Shulman, director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, and microbiologist Russell Johnson of the University of Minnesota. Johnson and Shulman consulted with program committee chairman Benach, and the three decided to accept all the abstracts that had been previously rejected. "When we saw the concern of...the patients and support groups, we felt that maybe we had made a mistake" in rejecting the abstracts, says Benach. As a precaution against lending undue credibility, however, the organizers added a disclaimer to the meeting's program, saying that the listing of abstracts "does not constitute endorsement by any of the sponsors or committees" of the conference.

But that disclaimer did not satisfy Fish, of New York Medical College, who says the presentations will be "legitimized" by being part of the meeting. "I'm on the program

California Rides Its Own Bi-Cycle

The Lyme disease capital of the United States is the Northeast. But that doesn't mean the rest of the country is free of the illness. Several hundred cases, for example, show up in Northern California each year, and in that region the disease has presented a biological puzzle: What is the animal reservoir that sustains the disease? For people to get Lyme disease there must be an infected animal population in the area; in the Northeast the reservoir is the white-footed mouse. That creature provides a meal for the deer tick, *Ixodes dammini*, and the feeding process keeps the disease thriving by infecting each generation of mice with the Lyme-causing spirochete. The ticks also bite and infect people. In California, a different tick, the western black-legged tick, *Ixodes pacificus*, gives the disease to several hundred people each year, but until now, no one knew where the ticks themselves were picking up the spirochete.

Now Richard Brown and Robert Lane of the University of California, Berkeley, have filled in a big piece of the puzzle. On page 1439 of this issue of *Science*, they report that the dusky-footed woodrat, a common California rodent, is a Lyme disease reservoir. Their findings reveal a pattern of Lyme disease transmission different from the one in the Northeast—a two-cycle pattern that requires not just one but two ticks. Brown and Lane, along with colleagues at the University of California, Davis, have also found the Lyme spirochete in a woodrat from the Los Angeles area, the first sign of the organism's existence in Southern California. These findings could sound the alert for public health officials by suggesting that Lyme disease may exist at low levels in more parts of California than was thought—and at the same time point to strategies for controlling the disease.

One reason Lyme disease is much less common in California than in the East is that only 1% to 5% of *I. pacificus* ticks are infected—far fewer than the 25% to 50% typical of *I. dammini* in the Northeast, and a fraction too small to maintain an animal reservoir. That left biologists puzzling over two questions. First, "the issue of where [the ticks] acquire the infection has always been wide open," according to medical entomologist Joseph Piesman of the Centers for Disease Control's Center for Infectious Diseases in Fort Collins, Colorado. Then there was the question of how the reservoir was being maintained. Brown and Lane resolved both issues by finding that not only woodrats but also 15% of ticks of a separate species (*I. neotomae*) were infected—enough to maintain endemic disease. Since *I. neotomae* doesn't bite humans, both ticks are required for humans to become infected: *I. neotomae* to keep the woodrats infected and *I. pacificus* to pick up the disease from the rats and pass it to humans.

That information suggests that Lyme disease could exist in other places where the woodrat and the two tick species are found. And this triad inhabits some populous areas. Veterinary parasitologist Walter Boyce of the University of California, Davis, along with Brown and Lane and other colleagues, reported in the May issue of *Medical Entomology* that they had found the spirochete in a woodrat from mountains near Los Angeles. Boyce says Lyme has since been found in *I. pacificus* ticks there as well. "What it means is you have a [Lyme cycle maintained in wildlife] in one of the prime recreation areas for the greater Los Angeles metropolitan area," says Boyce.

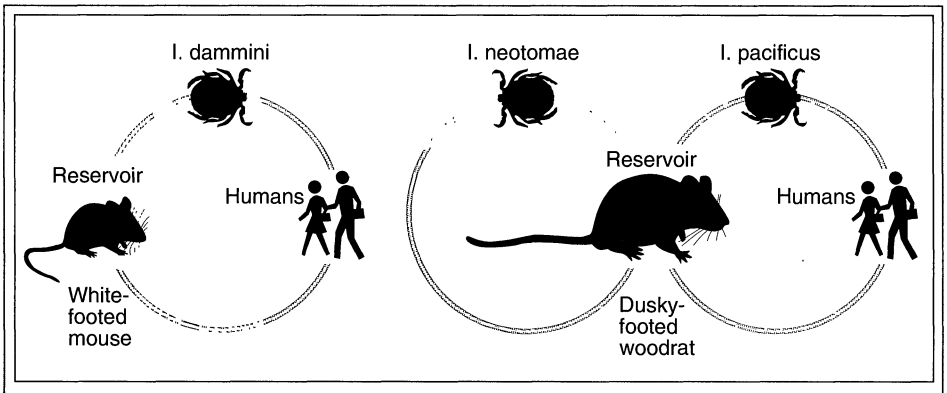


ILLUSTRATION: D. DEFRANCESCO

Of mice and men. In the Northeast *(left)*, Lyme disease is maintained by an animal reservoir (the white-footed mouse) and a single tick. In California *(right)*, one reservoir is the dusky-footed woodrat—and two ticks are required to sustain the endemic disease.

Finding the disease in woodrats will help researchers design disease-control strategies. For example, the woodrats—also known as packrats because they collect things to hoard in their nests—would be ideal targets for a scheme in which insecticide-soaked cotton balls would be put out for the rats to take home to their tick-infested nests. "Whether any of that is going to work will be left to future studies," says Brown. "What we've provided," he adds, "is a good first step toward understanding what is going on in nature." When the whole picture is filled in, he adds, it may be complicated by additional animal reservoirs. Nonetheless, Brown and Lane's work has given researchers a running start on understanding and controlling Lyme disease in the West.

–M.B.

committee and I'm damn annoyed, because I wasn't even consulted," he says. "These lay pressure groups are interfering with research. ....There is science and there is nonscience, and nonscience doesn't belong at a scientific meeting." The five other members of the program committee all told *Science* they were not consulted about the decision. One member who requested anonymity says the support groups have the ear of congressmen from districts where Lyme is a big problem. "It was done over a fear...that the power within the Congress is great enough that it would prove to be a problem for the arthritis institute."

Organizers Benach, Johnson, and Shulman all deny that they were caving in to political pressure or fear of funding retributions. "There was no congressional pressure at all," Johnson told *Science*. Accepting the abstracts "was the human and nice thing to do," Shulman adds. "That is all that is meant by this."

To some authors of the controversial abstracts the grudging acceptance is too little too late, from a close-minded research community. "If [a finding] is not part of a controlled study, they ignore it," says Long Island internist Burrascano. San Francisco rheumatologist Paul Lavoie, a proponent of prolonged antibiotic therapy who had no abstracts rejected, acknowledges that "there is some validity" to the concerns about some of the clinical reports, but says they nevertheless "need to be on the table," where they can be discussed openly as part of a scientific meeting.

In the end, Benach says, that is what the organizing committee concluded. "Whoever goes to a conference of this nature...will certainly have to defend [his work]," he says. "Legitimacy comes from your defense, from whether you can show that this is what you say it is."

–Marcia Barinaga