From the LymeLight Newsletter of the Lyme Disease Foundation

GAO Investigation Called - Probe Targets DHHS Agencies

The Lyme Disease Foundation's (LDF) annual rally at the Capitol May 3 to kick off the start of Lyme Disease Awareness Month culminated with an extraordinary announcement by honorary co-chair Senator Chris Dodd, (D-CT).

To an enthusiastic crowd of approximately 250 participants, Dodd announced he and several other legislators called for a General Accounting Office (GAO) investigation into Department of Human Health Services' (DHHS) Lyme disease (LD) programs.

The investigation is a result of a growing number of scientists', physicians' and patients' concerns of scientific bias and conflicts of interest in government LD programs. It will also determine if there has been retaliation by employees and grantees in DHHS agencies against others with differing scientific views about LD. (DHHS agencies include the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), and the Health Care Financing Administration (HFCA).)

Physician Harassment

The investigative arm of Congress will also investigate the multi-state harassment of physicians who recognize and aggressively treat chronic LD. Such an investigation will likely prove beneficial to Joseph Burrascano, Jr., MD, the latest Lyme doctor to be notified by the State of New York Department of Health's Office of Professional Medical Conduct (OPMC) that a formal disciplinary hearing on unspecified charges will be tried against him. Many researchers and doctors believe Burrascano is another victim of an ongoing "black listing" designed to eliminate doctors who treat LD with more than four weeks of antibiotic treatment. Should he be found guilty, he could be ordered to stop treating Lyme patients, pay substantial fines, and/or face the fate of Long Neck, NY, Lyme doctor Perry Orens, MD, and lose his license to practice medicine.

It is believed by many that it is those affiliated with DHHS agencies that are behind the investigations of Lyme physicians. Burrascano cites a specific event he believes was the impetus to the OPMC's investigation of his practice. "The reasons behind the charges against me are likely a result of my willingness to expose the true status of Lyme research," Dr. Burrascano said from his East Hampton office, an area hyperendemic for LD. "Shortly after publicly airing my grievances, I received notice I was being investigated for medical negligence."

Burrascano aired his comments during a 1993 Senate hearing called by Labor and Human Resources Senate Committee chairman Senator Edward Kennedy to determine the status of LD research. Unbeknownst to the Senator, his fellow, NIH, and CDC employees had orchestrated the hearing to show all was going well and great strides were being made in research. (See the essay, From Science to Circus: Enter Lyme Disease taken from From the Lab to the Hill, Essays Celebrating 20 Years of Congressional Science and Engineering Fellows. Anthony Fainburg, Ed. American Association for the Advancement of Science, Washington, DC 1994.) Former Yale rheumatologist Allen Steere, MD, CDC and NIH representatives, and a recovered patient were chosen to present.

The meeting was originally kept quite in hopes that people with opposing viewpoints would not interfere. Word of the hearing did get out, however, and patients, physicians, and researchers who believed Lyme was a serious and pervasive disease demanded representation. Burrascano was their medium, going up against Steere in physician testimony.

Despite his concern of facing almost certain retaliation, Burrascano testified that there were "many serious improprieties" by CDC and NIH employees regarding LD research. Among his concerns was that some of the grantees who were advocates of the "post-Lyme syndrome" theory, which attributes persistent symptoms to autoimmune problems rather than persistent infection, had conflicts of interest because they worked as medical consultants for insurance companies. Burrascano also accused a "core group of university-based researchers who exert strong, ethically-questionable influence" of, among other things, working with government agencies to bias the agenda of meetings on LD.

Retaliation

Just two months after the hearing, OPMC notified Burrascano he was being investigated for an "anonymous" complaint filed against him. In addition to adhering to the agency's request to send them his curriculum vitae (resume), Burrascano says he included a 7-inch thick binder of scientific documents detailing seronegativity in Lyme patients and instances of persistent infection despite extended antibiotic therapy. He has since turned over his medical records to the OPMC three times and has been formally interviewed twice.

"After Dr. Burrascano gave his testimony I was concerned he would face retaliation," said LDF chair Karen Vanderhoof-Forschner. "Those fears were heightened at a January, 1994 NIH meeting on chronic Lyme disease. Towards the end of the meeting, Dr. John LaMontagne, a director of the National Institute of Allergy and Infectious Disease [NIAID], said to me, 'Someone should sue Joe Burrascano for his [Senate hearing] testimony.' When I asked why, he replied: 'He committed slander and someone should get him for that.'

"Having a NIAID official in charge of a large portfolio of extramural grants make such a statement in front of

CDC and NIH employees and grantees suggests that the NIAID is in favor of some form of retaliation against [Burrascano]."

Conflicts of Interest

A disturbing aspect in Dr. Orens' case was the state of New York using Dr. Raymond Dattwyler, chief of Suny-StonyBrook School of Medicine's Lyme Disease Center, as an expert witnesses against him. Though Dattwyler says Orens lost his license for "inappropriately medicating a [chronic Lyme] patient who almost died as a result," one must wonder what impact Dattwyler's testimony that negative LD tests after early infection are highly accurate and short term therapy is highly curative had on the hearing committee's verdict.

There are reasons why Dattwyler, who is an adviser to the Centers for Disease Prevention and Control (CDC) and Food and Drug Administration (FDA), may not have been an impartial witness in Orens' case. In a 1994 case involving a patient of Dr. Orens' who sued Blue Cross/Blue Shield and Metlife for denial of payment for intravenous therapy, Dattwyler testified short term treatment is the best way to treat LD. The patient, then-Medford, NY resident Joanne McIntyre, won the case.

According to Dr. Orens, who also testified, Dattwyler refused to shake his hand after the verdict was announced, and said "something to the effect that he was not yet finished" with Dr. Orens. Dr. Orens, whose practice is in the same region as Suny StonyBrook, says many of Dattwyler's former patients switched to him after being told they do not have the disease. Dr. Dattwyler said he did not recall any such incident, and that he is not in competition with any other doctors for patients.

As president of Brooks Biotechnologies, Inc., Dattwyler has developed a LD test-kit, and therefore may have a vested interest in asserting the reliability of conventional ELISA-based LD tests. It is also possible that Dattwyler could feel threatened by Dr. Orens' use of non-ELISA based tests such as the urine antigen test (which Dr. Burrascano also uses), because his test, available since last year, could become obsolete should another testing methodology become more popular.

Dr. Dattwyler is also an insurance consultant and NIAID grantee that Ms. Forschner says was in the same room during the meeting in which Dr. LaMontagne made his remark about Burrascano. While Dattwyler denies any involvement in Burrascano's case and says he will not be an expert witness against him, it is anticipated that the case is Lyme-related and a university-based physician who consults for insurance companies may testify against Burrascano.

Would Dr. Dattwyler go out of his way to disrupt the lives of private citizens because of their scientific beliefs? Based on his past activities against the LDF, the answer may be yes. In a 1996 email document, NIH project officer Edward McSweegan expresses concern over LDF scientific and legislative comments. In his reply, Dattwyler says that he has contacted leaders of LD support groups to get them to oppose the LDF's comments. In a recent conversation, Dr. Dattwyler said he did not recall the email in question, but did say it is likely he contacted New Jersey support groups to oppose the LDF's effort.

Controlled Science

Researchers and clinicians say that as serious of an issue as Lyme physician harassment is, it is merely a byproduct of the ultimate problem in Lyme research. They say most mainstream science is controlled by a core group of researchers who, despite overwhelming scientific evidence to the contrary, maintain short term antibiotic therapy is highly curative, seronegative disease is rare, and persistent symptoms are most often due to autoimmunity problems or misdiagnosis. Researchers who believe otherwise, they say, are often excluded from DHHS committees that formulate LD protocols, or their views are ignored.

One of the main culprits blamed for this predicament is Dr. Steere, who identified what he believed to be a syndrome caused by a virus he termed "Lyme arthritis" among a group of children in and around Lyme, Connecticut in 1975. (In 1981, LDF founding board member Dr. Willy Burgdorfer discovered a corkscrew-shaped bacterium, Borrelia burgdorferi (Bb), was the causative agent of LD. At this time, NIH had assigned most Lyme research grants to its rheumatologic institute (NIAMS). Critics say Steere and other rheumatologic researchers try to keep it there.)

Steere steadfastly maintains the disease is primarily a rheumatologic condition that is overdiagnosed and overtreated despite being proven wrong on some theories that downplay the disease's ability to cause chronic multisystemic symptoms, and evidence that the central nervous system is one of the most seriously affected body systems by LD.

In 1994 court testimony against one of the first physicians prosecuted for overdiagnosis/overtreatment of LD, Steere testified that he "had written all chapters" on LD for virtually every authoritative medical publication, including Harrison's Principles of Internal Medicine, Mandell's Infectious Disease textbook, and Kelley's Textbook of Rheumatology. In addition to receiving major NIH/CDC research grants, Steere and his well-connected colleagues consult for various insurance companies. The LDF has never seen a disclosure indicating this in their writings or work.

Correspondence from Ansel Marks, MD, JD, Executive Secretary of the New York OPMC, that detail the agency's sources for determining appropriate care for LD states: "the CDC, American Lyme Disease Foundation (ALDF), Medical Letter, and a host of other sources provide guidance for the standard of care of Lyme disease. Rarely, if ever, have these published guidelines indicated that anything more than two to three weeks [of treatment] are required to cure Lyme disease." Besides the fact there is an abundance of medical literature detailing treatment failure for such duration, the sources cited by the OPMC are all written by the same small group of NIH/CDC grantees.

In addition to insurance consulting, some scientific advisers for the ALDF, including Steere, work as advisers to the CDC, giving these few academics the ability to promulgate "standard of care" guidelines and shape federal policy and activity. ALDF scientific adviser Robert T. Schoen, MD, a clinical professor of medicine at Yale University School of Medicine, has done consulting work for Blue Cross/Blue Shield, Connecticare, and Cigna. He and Steere write short-term protocols.

While the other cited OPMC source, The Medical Letter, markets itself as a nonprofit publication "dedicated to unbiased assessments of medical products," a recent letter from the publication to the LDF states it does not have a formal conflict of interest policy. Outside experts who author preliminary drafts are promised anonymity. In court testimony obtained by the LDF, Dr. Schoen admits to writing The Medical Letter's LD diagnostic and treatment protocol. It reads nearly identical to the ALDF's protocol, which cites The Medical Letter as a source document.

When asked about the one-sidedness of the OPMC sources, Dr. Marks said that he has amended his letter to state that the agency acknowledges that there are "equally qualified experts" with dissenting opinions about the appropriate management of LD. The revised letter, obtained at the request of the LDF, states that the OPMC "hearing committee weighs all the information from both sides and assesses the credibility of presentations given by both the prosecution and defense before reaching a verdict." It makes no mention however, of balancing its hearing committee by having it include an "equally qualified" expert member who believes in treatment beyond the short term (4-week) standard.

The recent experience of Sam Donta, MD, causes concern that DHHS employees and grantees are also making a concerted effort to not acknowledge chronic LD and the difficulty physicians encounter trying to treat it. Widely respected as a renowned expert in his field of infectious disease, Dr. Donta was a member of the guidelines subcommittee for the Infectious Disease Society of America (IDSA) while it was in the process of drafting a LD protocol.

The committee also included Dr. Dattwyler and Dr. Steere, who is a former CDC officer. As one who recognizes and treats chronic LD patients from around the country, Dr. Donta says treatment of early stage disease was the only part of the protocol the committee agreed on. Dr. Donta said he is not sure how the official protocol will address chronic Lyme, but said his efforts to make revisions to it were ignored by most members of the committee.

"The committee meetings were based on politics, not science," Dr. Donta said. "I think when the protocol is published it will be an embarrassment to the Society."

Dr. Donta said the committee tried but could not reach agreement on treatment beyond early stage disease, and disbanded without completing the protocol. According to Donta, the protocol was somehow taken from the hands of IDSA chairman Benjamin Luft, MD, who Donta believes wanted to add more to the protocol's late stage section, and was given to New York Medical College doctors Gary P. Wormser, MD, chief of infectious disease, and Robert Nadelman, MD.

While Dr. Donta described CDC Lyme Disease Program Director David Dennis as "one of the committee members who contributed to the protocol," Dr. Dennis said his role was limited to reviewing some contents related to the protocol, he was unaware if it was completed, and didn't know how it addresses late stage disease. While Dr. Dennis described Dr. Wormser as the IDSA chair, he said he did not know how Wormser became in charge of the protocol.

Dr. Donta said when he learned the guidelines were going to be published, he voiced his desire to make changes to its late stage section. Donta said Dr. Nadelman informed him unanimity was not required, and he could have his name removed from the protocol if he wished. Though no request was made, Donta's name was removed. Calls to Drs. Luft, Wormser, and Nadelman for comment went unreturned.

According to Ms. Forschner, the protocol, which should be released in July or August, is expected to issue a "four weeks cures all" protocol. It remains unclear if the protocol will disclose which committee members have insurance consulting and/or expert witness arrangements or other conflicts of interest.

According to published reports, the protocol will recommend treatment durations as short as 14 days for early stage disease and up to 28 days of treatment for "severe arthritic" cases. "Should that be the case, many more patients will be prone to treatment failure," Ms. Forschner said. "As it is now, some patients diagnosed as early-stage disease experience treatment failures with weeks of treatment." She also said she believes the OPMC will cite the IDSA protocol in their case against Burrascano.

Even more alarming, the LDF has obtained NIAID documents that reveal, starting in 1996, the CDC had grantees from the American College of Physicians (ACP) and the IDSA coordinate their LD protocols so that they were identical. Ms. Forschner said she believes that after the ACP finished its short term protocol, Dr. Donta put the IDSA in a problematic situation of not having a similar LD protocol recommending short term therapy. By disregarding his concerns and appointing Dr. Wormser chair, it appears the IDSA was able to successfully formulate a short term protocol.

CDC Indifference

One way to end the controversy surrounding LD is to develop a more reliable test than the present two-tiered system using the ELISA and Western blot tests. The experience of University of Wisconsin Medical School professor Ronald Schell, PhD, and Gunderson Lutheran Medical research scientist Steve Callister, suggests the CDC is reluctant to find one. After having countless proposals for their borreliacidal antibody test pass CDC grant review but never receive funding, Schell and Callister believed their time had finally come. In late 1998, the CDC informed them they were sending blinded sera for analysis using their test. They would have 10 days to test the samples and send the results back to the CDC.

After being provided the unblinded test results, they were to fly to the CDC's Fort Collins, CO, branch for a two-day meeting. If the borreliacidal antibody test performed well, they were promised the results would be published in the CDC journal, Morbidity and Mortality Weekly Report (MMWR). Publication in MMWR is a vital "seal of approval" for validating the legitimacy of new testing procedures.

On February 25, 1999 Schell and Callister flew to Fort Collins for the meeting. The first session was to review the outcome of the test trials. In addition to the borreliacidal antibody test, two other novel testing procedures were being evaluated. One academic team's test failed to perform as well as the CDC's two-tier system. The other team, which included the OPMC's expert witness and FDA/CDC adviser Raymond Dattwyler, refused to participate in the evaluation. Rather than present the results of his PreVue test, Dr. Dattwyler noted his

patented test had already received FDA approval, and therefore he would not subject it to further scrutiny. (PreVue is a test kit that is mass-marketed to doctor offices for in-house testing that provides results in about an hour. Positive results remain subject to further antibody testing, thus keeping the two-tier testing system in place.)

Dr. Callister presented the results of the borreliacidal assay, which showed that the test outperformed the two-tier system using the sera picked by the CDC. The sensitivity (detecting any LD-antibody reaction) was equal and the specificity (detecting just LD antibodies) was superior to the CDC system.

In addition, the results suggested that the borreliascidal assay might differentiate active infection from past exposure. This would represent a major scientific breakthrough and mean it could be the elusive "gold-standard" test that will answer if patients who still suffer symptoms after treatment have experienced treatment failure, or if symptoms are due to something other than active infection. Callister also presented additional data demonstrating that previous vaccination against LD did not confound the accuracy of their test. The borreliacidal assay, therefore, could diagnose Lyme in vaccinated patients and determine if adverse reactions in vaccinated individuals could be vaccine-related or due to vaccine failure. Test results from the CDC trials for the borreliacidal antibody test were almost identical to Schell and Callister's previously published results, and validated their procedure as a more accurate alternative to the CDC-mandated two-tier system.

Schell said after the presentation, he and Callister were instructed to write a synopsis of their results for members of the CDC-sponsored panel while it met to formulate their recommendations. The recommendations were to be discussed the second day of the meeting.

Despite its promising results, Schell said that on the second day members of the evaluation committee refused to discuss the borreliacidal assay. Rather, they focused their discussion on their willingness to accept the current problems with the two-tier system until they could develop more accurate ELISAs and Western blots.

When Schell and Callister demanded to know why they were not interested in discussing the borreliacidal assay, especially since it was cheaper and more accurate than their current recommendation, Duane Gubler, CDC director at Fort Collins, admitted they were surprised the borreliacidal assay had performed as well as it did. However, Gubler said they were not prepared to endorse the procedure until he and his staff had time to more completely evaluate the test.

Gubler said they would provide Schell and Callister with more serum samples for more extensive evaluation within the next couple of weeks. Schell and Callister were also assured any statements to be published in MMWR would be sent to them prior to publication for their approval. As the meeting was closing, Schell said CDC Director Duane Gubler, CDC Lyme Disease Program Director David Dennis, ALDF adviser and CDC grantee Alan Barbour, MD, and Dr. Steere stayed behind for what Dr. Schell described as a "private, informal gathering."

As Schell and Callister were being taken the airport, Marty Schriefer, a CDC research microbiologist who is a direct subordinate to Dr. Dennis, told them he would provide a letter, via Duane Guebler, confirming that the borreliacidal assay had performed well in the CDC-mandated evaluation. From February to December '99, Schell said he and Callister tried numerous times to contact Schriefer via telephone and email to find out when they would receive additional sera and the letter of validation, and when recommendations from the meeting would appear in MMWR. They received no reply.

Infuriated, Schell and Callister wrote to CDC Director Jeffrey P. Koplan to request his assistance. Again, they received no reply. Schell and Callister persisted, writing yet another letter this past January. By this time, they had also begun contacting a number of legislators for assistance. In early February, Schell finally received a response from Dr. Schriefer.

The CDC did an about-face. Schell said Schriefer told them that the CDC had only limited amounts of a small number of sera to provide them, and insisted that no one ever promised any results or recommendations would be published in MMWR. Schell, Callister, and a test with enormous potential to increase the performance of LD testing were back to square one.

"Given the short time I was allotted, the CDC didn't expect the test to perform as well as it did," Schell said, adding that in addition to being more accurate, the borreliacidal antibody test is cheaper and easier to perform than ELISA and Western blot. Saying the issue was between Dr. Schell and the CDC, Dr. Dennis refused to respond to Schell's allegations. (CDC Director Duane Guebler is presently out of his office on business travel.)

Schell also said part of the reason he believes the CDC is not embracing his test is because the agency has spent such an enormous amount of time and money promoting the two-tier system, it is reluctant to replace it.

Yet another plausible reason looms. A search of the World Intellectual Property Organization Patent Publication reveals that on 5/26/92, under patent publication #WO9324145, a subsidary of the SmithKline Beecham pharmaceutical company, in conjunction with the CDC, filed a patent on behalf of several CDC employees from the agency's Fort Collins branch who are named as inventors. (These Fort Collins personnel are directly involved in all CDC decisions regarding LD.)

This personal patent is for a specific strain of the LD spirochete and covers the development of an ELISA-based test, a potential vaccine, and more. (The updated patent mentions their "invention" could be used as a candidate to potentially add to the OspA vaccine then under consideration.) CDC employees named in the patent, therefore, may have a vested interest in keeping ELISA-based tests as the standard testing procedure. Schell, whose test is not ELISA-based, said at least one Fort Collins patent-holder, CDC research biologist Barbara J. Johnson, was at the meeting as a member of the evaluation committee.

Like the LDF, Dr. Schell acknowledges there are no definitive answers to the many mysteries surrounding LD. What Schell and the LDF also know is that mainstream science is failing to improve the standard of care patients receive. "Patients are definitely sick, and science needs to discover why," Schell said. "[Patients] are

desperate for answers and the medical establishment needs to do more than write off their complaints as hypochondria."

The stories of Drs. Burrascano, Donta, Schell, and Callister, are only a few of many other similar stories that the LDF knows have occurred over the past decade.

Are people affiliated with DHHS using state OPMC offices to eliminate front-line doctors such as Dr. Burrascano, who recognize and aggressively treat chronic LD, and publicly speak out against the way the government is addressing the issue of chronic Lyme?

Are people affiliated with the CDC refusing to recognize and evaluate other LD diagnostic tests because widespread use of these alternative procedures would hurt their egos, reputations, pocketbooks, and wallets?

Patients, doctors, researchers, and government officials feel the questions are serious enough to warrant answers.

Patients, doctors, and researchers also feel that if the GAO looks hard enough, it can find evidence that a core group of researchers with conflicts of interest have monopolized LD research. Their conduct has been to the detriment of the health of thousands of Lyme patients, greatly impeded progress in finding a reliable test and a cure for LD, and has left the door open for physician harassment to occur.

Now the proof moves to the GAO.