LDA Meets With NIH Lyme Officials

Spring 2009, Dr. Betty Maloney, Minnesoto; Tim Lynagh, Legislative Director for Congressman Christopher Smith (NJ-4); and Pat Smith, President, Lyme Disease Association; in the office of Congressman Chris Smith (not pictured) after a meeting with NIH Lyme Disease Program officials on the problems with Lyme disease, a NIH Lyme research agenda, and how patients are being affected by the lack of knowledge of the disease.

The following officials from NIH were present at the meeting:

Carole Heilman, Ph.D., serves as Director of the Division of Microbiology and Infectious Diseases (DMID) at NIAID. DMID supports research to prevent and control diseases caused by virtually all human infectious agents with the exception of HIV, which is covered by the NIAID Division of AIDS.

Joseph J. Breen, Ph.D., Bacteriology Program Officer, Division of Microbiology and Infectious Diseases, NIAID

Adriana Marques, Ph.D., Head, Clinical Studies Unit, Laboratory of Clinical Infectious Diseases, NIAID, NIH

Click here for pdf of 5/18/09 minutes of the NIAID Council meeting where mention of the Lyme disease meeting 4/30/09 with the LDA was noted on page 3.

LDA and the US Army

The first portion of this article first appeared in Tiny Tick Tales published by the Lyme Disease Association of New Jersey (LDANJ), now Lyme Disease Association. The second article appeared in the Lyme Times. Updates follow each piece. This entire article appeared in the Time for Lyme Newsletter.

May 1999

THE LDANJ VISITS THE US ARMY CENTERS FOR HEALTH PROMOTION & PREVENTION, CHPPM by: Pat Smith, with input from Corey Lakin and USACHPPM

In May 1999, Association Vice President Corey Lakin and I visited the US Army Centers for Health Promotion and Prevention, USACHPPM, at Aberdeen Proving Grounds, Maryland. USACHPPM is the preventive medicine arm of the US Army. The visit was coordinated by NJ Congressman Christopher Smith's office as a briefing for us so that CHPPM could share the progress the Army is making in the area of tick-borne diseases, TBD. This year, CHPPM was required to submit an annual report to Congress, which is titled DoD Research and Surveillance Activities Regarding Lyme Disease and Other Tick-Borne Diseases, since Congressman Smith and Senator Dodd were able to get an attachment for TBD monies to the Strom Thurman National Defense Authorization Act for Fiscal year 1999. Congressman Smith was also successful several years ago in attaching Lyme disease monies to the defense appropriations.

Not really knowing the extent of Army involvement, we were surprised to find that the Army takes TBD very seriously. We were shown laminated tick cards designed especially for the Balkan theater where Lyme is transmitted through infected sheep ticks. We were given tick removal kits that are distributed to the Department of Defense (DoD) health clinics, so that ticks removed from soldiers can be submitted to USACHPPM for identification and testing. The DoD has a 3 prong Insect repellent system which they heavily promote: permethrin on uniform, DEET on exposed skin, and properly worn uniform = maximum protection. The DoD has developed a permethrin impregnation kit that soldiers can use to treat their

uniforms. The treatment offers protection for the life of the uniforms. We were also amazed to find the DoD has now made available uniforms that are actually impregnated with permethrin at time of manufacture, so that applications do not need to be done by the soldiers. They also use a state-of-the-art, long-acting DEET skin cream that is commercially only available through Amway.

The most exciting research was being done in the area of technology. In the lab, we saw how the Army has developed a prototype “in the field” PCR test kit, a virtual lab in a suitcase, to be able to perform testing for the presence of Borrelia burgdorferi right where the action is. It has been designed so that soldiers with limited training can operate it successfully. Individuals utilizing these kits could amass tick data including species, density, location (using a Graphic Information System, GIS), and results of PCR testing, which are then transmitted directly from the field to computers via a portable satellite uplink.

The development of a “heads up” display for tick populations is certainly some of the best use of technology in tick prevention that I have ever seen. If you are not familiar with this terminology, you are not alone. A soldier in the field wears a special helmet with a special “heads up display” visor. The soldier is also equipped with a Global Positioning System (GPS) receiver, which is able to pinpoint his/her exact location on earth, and also a small transceiver linked via satellite to the DoD’s GIS computer. The GIS computer tracks the soldier’s position and transmits critical information, including tick population densities, to the “heads up” display visor. This high tech system provides soldiers in the field with a real time assessment of the risks posed by ticks in the potential troop deployment area and offers guidance during maneuvers, so that if possible, personnel shifts can be made to avoid dense tick populations.

The mapping of tick populations has already started and the density overlays are reported to a military map. The map overlay image is transmitted via secure satellite links to whomever requests it. On the example shown to us, the graphic shows the “risk of infection with Lyme disease from ticks occupying this area” from 0% to 100%. Additionally, tick infection rates are being determined at all major military

installations and this data is being used to create overlays and analyze tick densities to protect those who are employed at these installations. This feat is accomplished by coupling GIS to field collected data.

The CHPPM officials were extremely cooperative. We had discussions on how these army developments can benefit the civilian population, and more importantly, how can this information be relayed to the civilian sector in a timely basis? We felt that this visit would be a first step in "opening up" communications. We, of course, can both benefit by us helping to promote monies in the Defense Authorization Act, as we have already done through Congressman Smith, and us ensuring that they receive monies through the Lyme Disease Initiative 1999 (current DoD appropriation in bill-$30M/5years). I have had preliminary discussions with Congressman Smith's office about the possibility of inserting language into the LD Initiative that would require DoD tick-borne illness projects to be made public within a specified time period after their development. It is too early to determine if this is a viable proposal.

Space limitations prevent me from printing the Report to Congress here, but I have selected several paragraphs that I feel reflect the tone of the report. The first three paragraphs of Section I of the report state: FINDINGS: Ticks are among the most important of all arthropod vectors of disease. There are over 850 recognized species worldwide. Ticks rank second only to mosquitoes in the number of life-threatening and debilitating diseases they transmit to humans. In the United States, ticks are responsible for more human disease than any other arthropod group. Tick-borne diseases represent potentially serious health threats to troops, their family members, DoD civilian employees, and other residents at military installations in many parts of the world.

In recent years, data indicate that tick-borne disease transmission has been increasing in the United States, both in terms of incidence of some diseases and the number of known pathogens transmitted by ticks. Tick-borne pathogens appear to be in the vanguard of a group of newly emerging diseases. Since 1957, at least 14 new disease agents have been discovered worldwide. Ticks transmit four of these, or almost 30%. They cause Lyme disease, human monocytic ehrlichiosis, human granulocytic ehrlichiosis, and human babesiosis. Deaths have been associated with some of these. To

further complicate matters, there is increasing evidence that individual ticks can carry and transmit two or more infectious agents simultaneously, thereby increasing the severity and complexity of symptoms, and compounding the difficulty of diagnosis and treatment.

Lyme disease is now the most prevalent vector-borne disease in the United States, with approximately 100,000 cases reported to the Centers for Disease Control and Prevention (CDC) since it became a nationally reportable disease in 1991. It is estimates that the actual number of cases may be as high as one million or more….

I have always been an individual with a lot of questions, but this report has raised many more in my mind. Why are Lyme and other TBD's seriously considered threats to the troops who defend our country, yet not seriously considered threats to the civilian population? Why are military installations mapped and rated for tick densities and rates of infection, while public parks are not even posted with warning signs? Why would PCR's be reliable "in the field" and not at commercial labs? Why is the government impregnating uniforms with permethrin, when we all know that the civilian population is creating a climate of "Lyme hysteria" and that Lyme is "overdiagnosed and overtreated?" To quote the report: "In addition to directly transmitting disease, the adverse impact of psychological factors associated with tick attack, including fear, discomfort, and distraction, as well as indirect medical complications such as secondary infections, dermatitis or allergic reactions, should not be overlooked." The army has not labeled this "hysteria" but normal "complications" of tick attacks.

Why is the vaccine promoted to the civilian population yet the report states "…questions and concerns linger regarding the new vaccines safety…; effectiveness…; age restrictions…; frequency of boosters…; and the known limitation that it is ineffective against European strains of the Lyme disease agent. Confident decisions as to its value and use within the military cannot yet be made…." Why does this double standard exist? I do not have all the answers, but I think we need to work more closely with government and the military to get all the answers so that we can solve this enigma that has been called Lyme disease.

UPDATE 2001: Since this article was written, the LDA has had further communications with CHPPM. They sent a speaker to the LDA 2001 medical conference in Princeton entitled Lyme & Other Tick-borne Diseases: A 21st Century View. Dr Anthony Gutierrez discussed the Army's work with tick populations in a lecture titled Real Time Field Surveillance of Vector-born Disease pathogens (can be found on LDA videotape of the conference).

Although it is not technically military, LDA at the same conference featured a speaker from NASA, describing the joint NASA/ NIH 3-dimensional culturing project for Borrelia burgdorferi using microgravity chambers, which mimic conditions in space and in the human body. Researchers are culturing a number of organisms in this manner and getting a truer picture of how the diseases act in the body. Conventional culturing in the lab is two-dimensional (growing on a flat medium), whereas the bacteria exist in a three- dimensional environment in the body. Scientists can study how the real life setup (3-D) enhances bacteria's ability to communicate with one another causing much more damage than might be expected from looking at them in the two-dimensional state. Perhaps the enhanced communication holds the secret to their persistence in the body, but that is purely speculative on my part.

September 2002

At the behest of the Lyme Disease Association, Congressman Christopher Smith hosted a meeting in Washington, DC, with military leaders to discuss the issues surrounding Lyme disease.

In recent years, I have been contacted by a number of military families who were having difficulty obtaining treatment for Lyme disease. As complaints mounted, I became disturbed by their nature. The LDA had after all, visited Aberdeen Proving Grounds the home of US Army CHPPM several years ago and saw cutting edge technology being used to develop methods to prevent tick exposure and to permit immediate field-testing (PCR) of ticks so soldiers could be treated on the spot if necessary after an infected tick bite. Now I was hearing that military personnel were being "mustered out" of the service rather than being treated for the disease.

Someone needed to address this dichotomy in viewpoints.

The LDA took Doctors Burrascano, Fallon, and Liegner and flew in a military spouse, C.N., to address the meeting. I made an opening general presentation, Dr. Fallon discussed the neuropsychiatric aspects of the disease, Dr. Burrascano presented persisting infection, and Dr. Liegner talked about the similarities between LD and syphilis and made case presentations. CN discussed her difficulties as an Air Force spouse in obtaining treatment and in being taken seriously. I then presented the officials with a stack of complaints CN and I had collected from military families.

About a dozen officers from the army, navy and air force plus Congressman Smith and his staff attended the meeting. Unfortunately, the Congressman himself was called away for a vote during the presentations, and later confided to me that he was disturbed that he was not able to hear the entire discussion. The military were attentive, and although at the conclusion, questions and comments were slow in coming, eventually, these officials acknowledged that they too experienced some of the same types of problems that we have with the disease out here in civilian land. Some indicated they would contact us in the future after reviewing materials.

Doctors within the Army and Navy have subsequently contacted us and LDA has sent some materials. A few discussions have ensued, some with our doctors. The door has been open a crack and we do not intend to let it be slammed closed ever again. It is important that we work together with all officials who are willing to be open-minded and listen to the plight of Lyme victims.

UPDATE 2002: The LDA has also been communicating with a general (ret.) in Rhode Island, Brigadier General Amedeo C. Merolla who has experienced the ravages of Lyme disease in the military and civilian population. He wrote a letter to the LDA expressing his concern. The LDA sent it in a packet to Army officials after the DC meeting. It was also published in the Time for Lyme, New York program.

The Adjutant General of Rhode Island, Gen. Reginald A. Centracchio, also has written to the LDA expressing grave concerns about Lyme disease in

Rhode Island, “There are universal concerns regarding diagnosis and treatment problems of long-term Lyme disease, which affect our military and civilian populations.” This letter was also forwarded to the army officials with whom we met. Obviously, the problem has grown too large to continue to be ignored.

LDA Remarks Before Vaccines & Related Biological Products Advisory Committee

REMARKS OF PAT SMITH, PRESIDENT, LYME DISEASE ASSOCIATION, INC. BEFORE THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE, MAY 21, 2002. Why more adverse events were seen after the vaccine reached the market:

People receiving Lymerix after product launch lived in Lyme-endemic areas.

REMARKS OF PAT SMITH, PRESIDENT, LYME DISEASE ASSOCIATION, INC. BEFORE THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE, MAY 21, 2002

DISCLOSURE: No money from SKB.

The Lyme Disease Association, LDA, an all-volunteer organization with five nationwide affiliates, consists of patients and families of patients. The LDA has provded funding for research coast to coast, some published in peer review journals including *JAMA*. Along with our Greenwich affiliate, we were recently honored at a luncheon by Columbia University for partnering with them in the establishment of an endowed chronic Lyme disease research center at Columbia, and we also co-sponsored a fully accredited medical conference for physicians with

Columbia. Working with legislators, we developed a bill in Congress, HR 1254, which will provide $125 million for Lyme disease research, prevention, and physician education.

The Lyme Disease Association provided testimony to this committee in January 2001, seeking a moratorium on the vaccine, but felt no action was taken by the FDA, and to that end, in January 2002, the LDA had a private meeting with the FDA's Center for Biologics Evaluation and Research (CBER) and brought several experts to discuss the vaccine issue with FDA officials including Karen Midthun, Susan Ellenberg, Peter Beckerman, Norman Baylor, Miles Braun, and Robert Ball.

Donald H. Marks, MD, PhD, former lab director for Cannaught, fourteen years of clinical research and regulatory affairs experience in the pharmaceutical industry including Director of Clinical Research, in charge of the Lyme disease vaccine program at Aventis Pasteur, presented to the FDA. Dr. Marks was the leader of the competitive effort to manufacturer a virtually identical vaccine.

Currently, his focus is diagnosis of adverse events from medications, vaccines, biologicals, and medical devices. Lymerix associated cases he reviewed included athralgias and arthritis as well as complicated neurological problems and include adverse events that are long-lasting. A summary of Dr. Mark's power point presentation follows.

WHY MORE ADVERSE EVENTS WERE SEEN AFTER THE VACCINE REACHED THE MARKET:

- People receiving Lymerix after product launch lived in Lyme-endemic areas.
- Many people may have had prior exposure and clinical or subclinical infection. In these cases, Lymerix could be triggering or reactivating the damage caused by old and presumably cured Lyme disease.
- Pattern of symptoms experienced after Lymerix mimicked pattern of prior infections in many individuals. In these patients, Lymerix-related symptoms seemed to respond to antibiotics, as did the initial infection, bolstering the theory of disease reactivation.

ISSUES WHICH CONFUSED THE VACCINE PICTURE

- As proof of safety, the company inoculated arthritis-prone mice with Osp-A. But since the mice did not possess the HLA marker known to interact with Osp-A in humans, rendering the experiment meaningless.
- The company masked serious causally-related adverse events behind qualifiers, such as "…and which may have no causal relationship with the vaccine" and "…cannot be distinguished from the natural history of the underlying disease."
- The company says that "the possibility of a severe rheumatologic, neurologic, autoimmune adverse event is inherent in Lyme disease," attempting to shift the blame onto the patient and their illness, and does not inform physicians that the same adverse events can be separately caused by the vaccine, in addition to the symptoms of an underlying disease
- As a result of these actions, GPs in the US were kept in the dark about the life-threatening side effects of Lymerix, severe rheumatologic, neurologic, autoimmune adverse events.

SOME BASIC PROBLEMS.

- Non-specific hyper-activation of the immune system, often evidenced through swollen hands or arthritis, is an adverse event associated with Lymerix. This may be due to the presence of adjuvant.
- This hyper-activation creates "dirty" Western blots in which multiple Lyme disease bands appear, whether the individual has Lyme disease or not.
- The dirty banding makes it impossible for physicians to differentiate between Lymerix vaccination, new infection with Borrelia burgdorferi, or reactivation of infection.
- The net result is that cases of Lyme disease will go undiagnosed and untreated. Adverse reactions to Lymerix will be misdiagnosed as Lyme disease and people will be unnecessarily treated with antibiotics.
- The vaccine manufacture provides no warnings as to these possibilities.
- Physicians unaware of the spectrum of problems cannot appropriately treat these patients.

- The intention of FDA regulations is to provide a vaccine that is safe and effective. The intention of prescribing regulations is to provide sufficient information to prescribing physicians to enable safe and effective use of the vaccine. In both regards, SKB's actions appear to be contrary to FDA regulations and intentions, and contrary to accepted standards within the vaccine industry.

Dr. Marks provided some case assessments based on stringent parameters and his extensive experience in the field. "The adverse events I have examine from Lymerix are similar to those I am familiar with from another vaccine." In the cases Marks examined –in his opinion, the adverse events were not anecdotal but a medical certainty.

- 4 of 4 neurological adverse events were related to Lymerix with presentations including transverse myelitis, inflammatory polyneuropathy, radiculopathy and cervical throacic myelopathy with multiple neurologic, including CNS, symptoms, memory loss and difficulty concentrating with immune-related complex of joint pain and fatigue.
- 15 of 17 rheumatologic adverse events were related, including inflammatory seronegative spondyloarthropathy, polyarthropathy, arthralgias, and arthritis.
- 2 of 2 miscellaneous reports were unrelated. These included chest pain and myofacial pain.

Based on his research, Marks said, "SKB should have devised and conducted clinical trials, epidemiological studies, or after-the-fact investigations to study the causal relationship between severe rheumatologic, neurologic, autoimmune and other adverse events and the use of Lymerix….there is sufficient evidence that Lymerix is causally related to severe rheumatologic, neurologic, autoimmune, and other adverse events in some individuals. This evidence is such as to warrant a significantly heightened degree of warnings and possible limitations or removal from marketing of Lymerix."

Andrea Gaito, MD, a rheumatologist seeing 35 patients with vaccine problems described three categories (**bold)** of problems to FDA. The first case, no history of Lyme, presented with acute synovitis, tests showed negative rheumatoid factor, Western Blot suggestive of active Lyme

disease, with eight IgM and three IgG bands. Patient had minimal response to doxycycline, was prescribed and continues on anti-inflammatory medication. Conclusion: **autoimmune disease.**

The second case, **asymptomatic at time of innoculation, with a history of IV treated Lyme** meningitis. After Lymerix, patient experienced the onset of Obsessive Compulsive Disorder, headache, and fatigue. Upon testing, he had a positive ELISA and a Western Blot with every band positive. Retreatment with IV was not effective. Patient remains sick.
The third case, three shots of Lymerix, then bitten by a tick. S**he went on to develop symptoms of Lyme disease**, including night sweats and fatigue. Tests showed: a Western Blot with every band positive; positive for the HLA markers that have been associated with Lyme-related autoimmune disease. Two courses of antibiotics produced no response. This patient now has Lyme disease but does not respond to treatment.

Dr Gaito is concerned about the efficacy of this vaccine and boosters. Will vaccinated individuals with prior Lyme who ultimately present with symptoms respond to retreatment? Is the vaccine itself retriggering an autoimmune response? She felt it is possible that the difference between the pre- and post-marketing results of Lymerix relates to the fact that those using it post-marketing lived in endemic areas for Lyme disease.

The LDA is concerned that despite presentations to the contrary by individuals at both the Vaccine Advisory Committee hearing in January 2001, the private meeting above, VAERS data, and other communications from the public, the FDA has not seemed to find any problems with this vaccine. LDA's concern stems from the fact that although the approved vaccine is not on the market currently, since it was a unilateral decision by the company to remove the product, this same or a similar product may be remarketed without the full implications of the safety and efficacy of the current vaccine having been fully assessed or integrated into the Lyme vaccine picture. The LDA asks this committee to advise the FDA that significant arguments have been raised about safety and efficacy of this vaccine and that objective studies should continue on safety and efficacy of this vaccine or any other future vaccine that may seek FDA approval. Thank you for your time.

LYMERIX Meeting; LDA Meets with FDA

SPECIAL REPORT: LDA MEETS WITH FDA ON LYMERIX On January 22, 2002 in Bethesda, MD., the LDA was able to get a private meeting with the FDA on the vaccine issue, despite reluctance by the FDA to grant the meeting. Congressman Chris Smith helped facilitate the setup of this meeting. Patricia Smith, President, Lyme Disease Association.

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Patricia Smith, President, Lyme Disease Association

LDA president Pat Smith invited Andrea Gaito, MD, President, International Lyme & Associated Disease Society, ILADS; Donald Marks, MD, former lab director for Cannaught; Steven Sheller, Esq., member, LDA's Professional Advisory Board; Albert Brooks, Esq.; and Pam Weintraub, former editor, Omni magazine, to present material to the FDA.

About a dozen major FDA officials involved with the vaccine were present. These included:

Karen Midthun, MD
Director, Office of Vaccine Research and Review
Center for Biologics Evaluation and Research

Susan Ellenberg, PhD

Director, Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research

Peter Beckerman, JD
Office of the Chief Counsel, FDA

Norman Baylor, PhD
Associate Director for Regulatory Policy
Office of Vaccine Research and Review
Center for Biologics Evaluation and Research

Miles Braun, MD
Director, Division of Epidemiology
Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research

Robert Ball, MD
Chief, Vaccine Safety Branch
Division of Epidemiology, Office of Biostatistics and Epidemiology
Center for Biologics Evaluation and Research

Mary Meyer
Director, Office of Communication, Training and Manufacturers Assistance
Center for Biologics Evaluation and Research

Cap Uldriks, JD
Acting Director, Division of Communication and Consumer Affairs
Office of Communication, Training and Manufacturers Assistance
Center for Biologics Evaluation and Research

Julie Zawisza
Chief, Consumer Affairs Branch
Division of Communication and Consumer Affairs
Office of Communication, Training and Manufacturers Assistance

A summary of the meeting follows, beginning with a digest of LDA presentations:

Patricia Smith, President, Lyme Disease Association

Most patients with adverse events are not reported to VAERS by physicians. I attend many events all over the Northeast, and the vaccine and associated problems are always brought up to me, unsolicited on my part. Last week I was at a large sportsmen's show. Just at this show alone, I heard about seven individuals who received the vaccine and experienced problems. One man had joint pains all over his body and his doctor did not think it related to the vaccine, nor did he report it. The man had cut down on hunting and fishing. He had stopped running.

When this individual went back to his physician and asked him to report the adverse response to VAERS, the doctor blew him off. The doctors are very much in the dark about this vaccine. We have doctors who do not understand that boosters are required. One man came up to me at the event and told me his doctor said no booster was required and he thought he was fully protected forever. Many physicians do not know the vaccine is contraindicated with a history of arthritis. Most people I spoke with who report side effects mentioned they occurred after the second shot. An employee at Rutgers approached me and said the University gave Lymerix. The professor knows four Lymerix recipients at Rutgers who are having significant trouble.

I hear the same thing from other groups. There are a lot of problems I do not think you are aware of. I hear from physicians that the vaccine causes Lyme disease to be retriggered. I'm out there a lot. I have no stake other than to keep people from getting Lyme disease.

Our organization has always had questions about the vaccine, and at the last FDA meeting in January 2001 we requested a moratorium.

Andrea Gaito, MD, President, International Lyme & Associated Disease Society, ILADS:

I have 35 patients with problems stemming from the vaccine. There are three categories of problem.

The first category includes arthritis-like presentations. These patients have symptoms that present, clinically, like rheumatoid arthritis. They seem to have an autoimmune reaction stemming from the presence of a genetic marker theorized to be a source of trouble, HLA-DR4. Some of these patients may have other relevant HLAs. Perhaps there are a cascade of other immunological reactions, including cytokines.

What I have found is that people with Lyme who become asymptomatic may, upon vaccination with Lymerix, experience a retriggering of symptoms. Those who never had symptoms of Lyme disease, meanwhile, will, upon vaccination, experience the symptoms of Lyme disease.

One example is a 55 year-old woman with no history of Lyme disease. She presented with acute synovitis and in her hands, wrists, ankles, and feet. The physician who administered the vaccine told her there was no relationship between these symptoms and the vaccine. He did not report them. It is possible that, like so many other physicians, he did not want to trouble with the paperwork. When the woman thereafter came to me, I ran tests. Her rheumatoid factor was negative but her Western Blot was suggestive of active Lyme disease, with eight IgM and three IgG bands. I prescribed for her a course of doxycycline, but she had minimal response. So I put her on anti-inflammatory medication. Now, two years later, she is *still* on anti-inflammatory medication.

The scenario for this woman is that of an autoimmune disease.

Even though she reacted to the vaccine in this adverse fashion, her physician made her feel guilty. Many patients have complaints but doctors are not receptive to them. The bottom line is that the doctor is afraid of being sued.

The second case I would like to present involves a 20-year-old white male with a history of Lyme meningitis. Previously, he had 4 weeks of intravenous Rocephin and before receiving Lymerix was asymptomatic. After receiving Lymerix, however, he had the onset of Obsessive Compulsive Disorder, headache, and fatigue. He had to leave college. Upon testing, he had a positive ELISA and a Western Blot with every band positive. We retreated him with another course of IV Rocephin, but he has remained sick.

The third case involves a 48-year-old woman and gardener. She received three shots of Lymerix and then, subsequently, was bitten by a tick. She had presumed she was one hundred percent protected, but she went on to develop symptoms of Lyme disease, including night sweats and fatigue. We performed a Western Blot test for this woman and found every band to be positive. She received two course of antibiotic therapy and had no response. She also tested positive for the HLA markers that have been associated with Lyme-related autoimmune disease. This patient now has Lyme disease but does not respond to treatment.

As I review my experience with Lymerix, I find the issues to be confusing. How can we get a handle on the efficacy of this vaccine? What about the efficacy of booster shots? Will vaccinated individuals with prior Lyme who ultimately present with symptoms respond to retreatment? Is the vaccine itself retriggering an autoimmune response?

One final word: It is possible that the difference between the pre- and post-marketing results of Lymerix relates to the fact that those using it post-marketing lived in endemic areas for Lyme disease.

Donald H. Marks, MD, PhD, former lab director for Cannaugh:

First let me describe my background. I have fourteen years of clinical research and regulatory affairs experience in the pharmaceutical industry. My positions have included Associate Director of Clinical Research, Hoffman-LaRoche Pharmaceuticals, where I worked on Lyme disease; Vice President of Medical Afffairs, Immunomedics; and finally, Director of Clinical Research, Aventis Pasteur, where I was in charge of the Lyme disease vaccine program.

The focus of my medical practice today is on diagnosis of adverse events from medications, vaccines, biologicals, and medical devices. Among the issues I have worked on are the associations between Accutane and seizures, psychosis and suicide; Ephedra and hemorrhagic stroke; Fen-Phen and heart valve problems; Lotrenex and ischemic bowel disease; Posicor and Propulsid and arrhythmias, in the case of the former medicine, fatal arrhythmias; Quinolone antibiotics like Floxin and Trovan and tendon neuropathy, seizures, and hypoglycemia; Rezulin and liver toxicity and cardiomyopathy; SSRI antidepressants like Prozac, Zoloft and Paxil and suicide, psychosis, and seizures; and Lymerix and rheumatologic and neurologic complications.

Today I am here as a consultant of the Lyme Disease Association, which has asked me to review a series of adverse events associated with Lymerix: These include athralgias and arthritis as well as complicated neurological problems. They include adverse events that are long-lasting.

Dr. Marks proceeded to present a series of slides. We reproduce them here, with explanation and some editing, where needed, for clarity and brevity in the current context.

WHY MORE ADVERSE EVENTS WERE SEEN AFTER THE VACCINE REACHED THE MARKET:

- People receiving Lymerix after product launch were at

greater risk for adverse events because they lived in Lyme-endemic areas.

- Many of these people may have had prior exposure and clinical or subclinical infection. In these cases, Lymerix could be triggering or reactivating the damage caused by old and presumably cured Lyme disease.
- Pattern of symptoms experienced after Lymerix mimicked pattern of prior infections in many individuals. In these patients, Lymerix-related symptoms seemed to respond to antibiotics, as did the initial infection, bolstering the theory of disease reactivation.

HOW SMITHKLINE BEECHAM (GLAXO SMITHKLINE) USED CONFUSING LANGUAGE, KEEPING FDA AND PHYSICIANS IN THE DARK:

- The Company dismissed the significance of adverse events reported since marketing by stating the vaccine's profile had not changed "except as described below…" The description referred to, rendered with numbers but given no contextual explanation, in fact implied a huge change in safety. The company's confusing language made it sound as if the adverse events, many of them severe, had no particular significance at all.
- As proof of safety, the company inoculated arthritis-prone mice with Osp-A. But since the mice did not possess the HLA marker known to interact with Osp-A in humans, the experiment was, in fact, meaningless.
- The company has masked serious causally-related adverse events behind qualifiers, such as "…and which may have no causal relationship with the vaccine" and "…cannot be distinguished from the natural history of the underlying disease," all the while knowing these are confusing the issues.
- The company tries to shift the blame from the vaccine to the patient with statements such as "the possibility of a severe rheumatologic, neurologic, autoimmune adverse event is inherent in Lyme disease." The company does not inform physicians that the adverse events can result

from Lymerix, completely apart from the disease.

- As a result of these actions, GPs in the US were kept in the dark about the life-threatening side effects of Lymerix.

SOME BASIC PROBLEMS.

- Non-specific hyper-activation of the immune system, often evidenced through swollen hands or arthritis, is an adverse event associated with Lymerix. This may be due to the presence of adjuvant.
- This hyper-activation creates “dirty” Western blots in which multiple Lyme disease bands appear, whether the individual has Lyme disease or not.
- The dirty banding makes it impossible for physicians to differentiate between Lymerix vaccination, new infection with *Borrelia burgdorferi,* or reactivation of infection.
- The net result is that cases of Lyme disease will go undiagnosed and untreated.
- Adverse reactions to Lymerix will be misdiagnosed with Lyme disease and people will be unnecessarily treated with antibiotics.
- The vaccine manufacture provides no warnings as to these possibilities.
- Physicians unaware of the spectrum of problems cannot appropriately treat these patients.
- The intention of FDA regulations is to provide a vaccine that is safe and effective. The intention of prescribing regulations is to provide sufficient information to prescribing physicians to enable safe and effective use of the vaccine. In both regards, SKB’s actions appear to be contrary to FDA regulations and intentions, and contrary to accepted standards within the vaccine industry.

Dr. Marks provided some case assessments based on stringent parameters. His conclusions were based on pre- and post-marketing as well as supplemental data; internal company documents; published literature; international meetings;

special reports; patient medical files; and patient examinations. He used the standard methodological rule of "more likely than not" as well as objective, scientific criteria and objective procedures. The assessments themselves, according to Dr. Marks, were arrived at based on "clinical presentation, the medical records, telephone interviews and/or physical exams, temporal relatedness of the event to the vaccination, known adverse event profile of Lymerix, mechanism of action of Lymerix, opinions of the treating physician, articles from the medical literature on adverse events occurring as a result of vaccination with OspA-based vaccines for Lyme disease, my experience as a pharmaceutical industry medical safety officer, my experience having reviewed hundreds of clinical cases of potential medication adverse events, my experience as a vaccinologist and clinical researcher developing vaccines and antibiotic treatments against Lyme and other diseases, and my examination of alternative explanations." Added Marks: "The adverse events I have examine from Lymerix ARE SIMILAR TO THOSE I AM FAMILIAR WITH FROM ANOTHER OSPA VACCINE."

Marks examined 22 cases in all. In each of these cases, he said, the adverse event was not anecdotal but was, instead, a medical certaintly:

- 4 of 4 neurological adverse events were related to Lymerix with presentations including transverse myelitis, inflammatory polyneuropathy, radiculopathy and cervical throacic myelopathy with multiple neurologic including CNS symptoms, and memory loss and difficulty concentrating with immune-related complex of joint pain and fatigue.
- 15 of 17 rheumatologic adverse events were related, including inflammatory seronegative spondyloarthropathy, polyarthropathy, arthralgias, and arthritis.
- 2 of 2 miscellaneous reports were unrelated. These included chest pain and myofacial pain.

Based on his research, Marks told FDA officials, “SKB (Glaxo) has acted in an unreasonable manner by marketing Lymerix without adequate warnings about the risks of severe rheumatologic, neurologic, autoimmune and other adverse events, and by failing to caution and educate physicians about these dangers. In view of the evidence of a strong and likely causal relationship between Lymerix and severe rheumatologic, neurologic, autoimmune and other adverse events, SKB should market this vaccine, if at all, with prominent warnings and cautionary statement.”

“In my opinion, SKB should have devised and conducted clinical trials, epidemiological studies, or after-the-fact investigations to study the causal relationship between severe rheumatologic, neurologic, autoimmune and other adverse events and the use of Lymerix.”

Given that Dr. Marks lead the clinical trials for Lymerix’s competitor, the OspA vaccine produced and then abandoned by Aventis Pasteur, his conclusions mean a lot. “In my opinion,” he told FDA officials, “there is sufficient evidence that Lymerix is causally related to severe rheumatologic, neurologic, autoimmune, and other adverse events in some individuals. This evidence is such as to warrant a significantly heightened degree of warnings and possible limitations or removal from marketing of Lymerix.”

FDA answers LDA vaccine questions in writing weeks after meeting.

LDA PRESUBMITTED QUESTIONS TO EPA (Below)

The floor was then handed over to FDA to answer the following questions:

1. What does the FDA intend to do about the lyme vaccine?
2. Questions on the follow-up study of VAERS reports, especially, what is the primary endpoint and study design for the on-going telephone survey of a subset of

individuals who have reported adverse reactions to VAERS. Specifically, what is the inclusion/exclusion criteria? Subquestions include:

A. Assuming an inclusion criteria includes arthritis and/or arthralgia, which VAERS codes and/or keywords are used to identify such individuals? And, if the inclusion criteria consists of a specific injury and/or disease process, why has the study been so limited instead of addressing the various adverse reactions being reported to VAERS, including non-specific pain syndromes and development of Lyme disease-like symptoms, possibly constituting exacerbation of previously asymptomatic Lyme disease and neurological conditions such as Bells' Palsy, optic neuritis, and acute transverse myelitis?

B. Further, what is the FDA's case definition of "definite, probable and possible arthritis" for purposes of this study? The abstract of the "preliminary evaluation" reports completed interviews of 49 patients out of 85 attempted (out of 415 patients with VAERS reports of "arthralgia or possible arthritis following Lyme vaccine") reports 17 cases of "possible arthritis" and 14 cases of "physician-diagnosed definite arthritis"). Does this mean that the remaining 18 had "probable arthritis"and, if so, what if anything is being done to evaluate their cases?

C. How is the FDA dealing with individuals who test positive for Lyme disease after vaccination in terms of distinguishing between a new infection (i.e. vaccine failure) and the exacerbation of a previously asymptomatic or presumably "cured" infection (i.e. an adverse reaction)? It appears from the abstract that 7 of 14 cases of physician-diagnosed arthritis also had what is described as "concominant exposure or another medical condition, including Lyme disease". What, if

anything is the FDA doing to evaluate these individuals, especially in light of the fact that many people who have and who will receive LYMErix reside in Lyme-endemic areas and can presumably be easily dismissed as having "concominant exposure"?

D. Does the fact that 50% (7 of 14) of cases of physician-diagnosed definite arthritis post vaccination demonstrate the need for a warning and/or contraindication against the vaccination of individuals with "familial history of immune-mediated disease or inflammatory arthritis", "immune-mediated disease", and "prior history of physician-diagnosed Lyme disease"?

E. When does the FDA contemplate completion of the interviews of the 415 VAERS reports identified as "arthralgia or possible arthritis"? And what if anything is being done to identify such reports filed subsequent to October 2000?

F. Given the fact that FDA has now documented 7 case reports of physician-diagnosed definite arthritis which "could not be plausibly explained by concominant exposure, prior diseases, or familial histories" a number on par with those that triggered regulatory intervention in other pharmaceuticals such as "Fen-Phen", is the FDA prepared to call for an immediate moratorium and/or withdrawal of LYMErix and, if not, what is the threshold number of case reports needed to trigger such action? It should be noted that 14 cases of physician-diagnosed arthritis post vaccination were identified out of 31 patients whose medical records were reviewed (45.2%), and in 7 of those (22.6%) the arthritis could not plausibly be attributed to any other cause. If these rates hold for the remainder of the 415 VAERS reports identified, the FDA will have documented 187 cases of physician-diagnosed arthritis, nearly 93 of which will not have any other plausible

explanation.

G. In terms of determining the rate of adverse reactions, how can the FDA determine how many individuals have been vaccinated? The abstract of the preliminary follow-up study reports "approximately 1.4 million vaccine doses were distributed" between December 1998 and October 2000. Given the fact that this is a multiple-dose vaccination and that most vaccinees have received at least two or three (and sometimes actually more) doses of LYMErix, and the fact that the uptake of LYMErix has been unexpectedly low (as demonstrated by the difficulty in reaching even 25% of the enrollment goals for the Phase IV studies), can the FDA rule out the possibilities that the actual number of vaccinees is in the low six-figures, and possibly as low as 100,000?

3. How is the FDA dealing with individuals who participated in the clinical trials, but began experiencing adverse reactions (or recognized such reactions) only after the study site was closed? Since VAERS will not accept their reports, and it has been reported that GlaxoSmithKline has been dismissive of such reports, how can the FDA ensure that these reactions are included in the total number of adverse event reports?
4. More specifically, how does the FDA deal with study participants who were in the placebo group during the trial (with no adverse reactions) but who received the vaccine after the study was unblinded and went on to experience adverse reactions to the actual vaccine?
5. If an individual gets the vaccine and they show Lyme disease symptoms, how does the FDA distinguish between 1.someone who had asymptomatic Lyme disease, 2. a new case of Lyme (vaccine failure), 3. an immune response
6. Why has the FDA not contacted and interviewed physicians who oversaw the study sites for the clinical trials,

particularly in light of the fact that some such doctors, …, have publicly endorsed LYMErix stating that they saw no adverse reactions when the FDA is aware of reports of adverse reactions by several of …'s study participants?

7. What steps if any has the FDA taken to analyze the data gathered during the clinical trials of the Connaught (now Aventis Pastuer) OspA-based Lyme disease vaccine ImmuLyme for adverse reactions?
8. Why has the FDA failed to invite scientists and physicians not affiliated with, or employed by GlaxoSmithKline, such as Ronald Schell, Ph.D. who has published an article documenting serious adverse reactions to OspA in hamsters, and Carlos Rose, M.D. and Paul Fawcett, Ph.D., who have published an article documenting arthritogenic reactions to LYMErix in adults and the exacerbation of pre-existing asymptomatic Lyme disease in participants in the pediatric trials of LYMErix, to present their findings and opinions to the Advisory Committee or any other body considering the safety and efficacy of LYMErix?
9. Why was LYMErix permitted to include an adjuvant, especially given that the manufacturer used a lipidated version of the OspA protein? Further, since the inclusion of the adjuvant in LYMErix necessitated the inclusion of the adjuvant in the placebo, what if anything was done to adjust for the likelihood that complaints of adverse reactions to the adjuvant among the placebo group were not permitted to improperly "cancel out" adverse reactions to OspA among the vaccinees, and therefore reduce the likelihood of finding a "statistically significant difference" in adverse event rates between the two groups?
10. What if any steps has the FDA taken to implement the recommendations of members of its Advisory Committee from the January 31, 2001 meeting regarding enhanced warnings and limits on the indicated use of LYMErix

(including geographic limits) as well as increased education of both the general public and the medical community of the continued unanswered safety risks associated with LYMErix?

11. Is the FDA, and/or its Vaccine Advisory Committee aware that the Tufts Laboratory run by Dr. Steere, the principal investigator for the Phase III clinical trials of LYMErix, filed for a patent on March 21, 2000 with the World International Property Organization, which received an International Publication Date of September 27, 2001 (patent # WO 01/70252 A1), and that the official patent holders, including Doctors Meyer, Huber and Gross are the scientists who worked along with Dr. Steere on his research documenting the auto-immune responses exhibited by people with certain genetic markers to OspA?
12. Is the FDA aware that "this invention was supported by National Institutes of Health Grant AR45386 and the government of the United States has certain rights thereto?"
13. Is the fact that this group of scientists, working under a grant from the government of the United States of America, has demonstrated in this patent that "An additional problem with OspA as a protective immunogen [i.e.: vaccine] is cross-reactivity at the T cell level observed between OspA and LFA-1." Id. At 4, and "Given the potential cross-reactivity between OspA and LFA-1, the use of OspA as a protective immunogen in vaccines may be associated with the induction of an auto-immune reaction in certain populations, including individuals expressing the HLA-DRB1-0401 allele. Thus it would be highly desirable to generate modified OspA polypeptides with diminished or no binding to the DRB1-0401 allele.
14. How does the FDA reconcile the fact that research conducted and completed by the principal investigator for LYMErix prior to FDA's approval of the vaccine, and largely ignored by the FDA or dismissed at "theoretical"

in its review and oversight of LYMErix, nevertheless led the scientists involved to pursue and patent a genetically modified version of OspA aimed specifically at avoiding the risk of auto-immunity from the OspA utilized in LYMErix demonstrated in that research?

15. Does the FDA believe that the medical community and the public at large should be advised of the fact that scientists and researchers of this caliber consider the risk of auto- immunity from LYMErix so great that they applied for, received, and worked pursuant to, a NIH grant to produce a modified version of OspA to minimize or eliminate the risk? If not, why?
16. In light of this documentation, why has the FDA not demanded that GlaxoSmithKline produce in full any and all research which they claim disproves the risk of auto-immunity from LYMErix rather than simply accepting the manufacturer's summary claims without supporting data?
17. In the abstract of the researchers' application for the NIH Grant #1R01AR045386-0, they state that "LFA-1/DR4 double transgenic mice on an MHC class II -/- background will be created and tested for the development of chronic Lyme arthritis after exposure to Bb. This is based on the observation that mouse LFA-1 does not express the OspA cross- reactive epitope." Indeed, the researchers observed an auto-immune arthritic reaction when these mice were exposed to natural OspA, but not when they were exposed to the patented, modified version of OspA. In this regard, what will the FDA do to determine what if any steps GlaxoSmithKline took to "create and test LFA-1/DR4 double transgenic mice" for its research, as the NIH grantees did, and whether or not the manufacturer did produce such mice and conduct studies which supported the risk of auto-immunity and suppressed those results? Further, what are the implications of GlaxoSmithKline's presentation at the January 31, 2001 Advisory Committee Meeting of a study

on mice which it claimed disproved any auto-immune arthritic risk, without revealing the fact, until questioned, that the mice used in their study lacked the cross-reactive epitope, and therefore rendering the study, as one member of the committee stated, "irrelevant"?

FDA said they would answer most questions in writing since time was running short, but asked LDA to choose a particular question. LDA's Pat Smith chose question number 5: If an individual gets the vaccine and they show Lyme disease symptoms, how does the FDA distinguish between 1.someone who had asymptomatic Lyme disease, 2. a new case of Lyme (vaccine failure), 3. an immune response?

The issue, emphasized the LDA team, was answering this question in light of all the *dirty* Western blots labs have been generating from Lymerix recipients. If Lymerix Western blots are dirty, asked LDA, how could FDA and its pharmaceutical sponsor differentiate between actual Lyme disease and an adverse event? The question was not, just, were the blots disguising the safety of the vaccine but, also, did the filthy blots make it impossible to arrive at any true conclusion as to the efficacy of the vaccine, estimated by the sponsor at almost 80 percent?"

Attempting an answer was FDA's Karen Midthun, MD, Director, Office of Vaccine Research and Review Center for Biologics Evaluation and Research. Midthun said vaccine investigators attempted to confirm Lyme disease itself through culture or polymerase chain reaction (PCR) of joint fluid, spinal fluid or the erythema migrans rash itself. "In cases identified as definite Lyme disease," she said, "seventy to eighty percent of the individuals were identified by culture and fifty to seventy percent via seroconversion by Western blot."

The LDA team responded that this answer was further proof the FDA could not, in fact, answer the question. Indeed, no one debated cases of "definite" Lyme disease proven through

culture, but rather, those cases of “possible” Lyme disease —especially in light of the fact that the manufacturer’s studies embraced the faulty CDC standard for Western blot by excluding consideration of two definite Lyme disease markers —bands showing presence of *Borrelia burgdorferi’s* two outer surface proteins, OspA and OspB.

Commented attorney Steven Sheller, “When I hear that disregarding OspA and OspB is not a problem, when I hear people say there are no dirty blots, or that they are not a factor, I have to wonder how this research was done. You can’t just take the manufacturer’s word for it. You have to look at the original Western blots to come to your own conclusion. You might just be surprised.”

LDA’s team advised FDA to look at data in its rawest form in just two or three of the study sites.

Dr. Marks added that FDA would have to rethink its notion of “statistical significance” for Lymerix. “You’ll never find statistical significance for the worst adverse events,” he told FDA, “because they are so rare. You have to look at individual patients. You should have individual cases analyzed in depth by an impartial group of observers.” Just because an adverse event is rare, he said, does not mean it is not associated with a vaccine. In these instances, you must weight the risk of the disease with the risk, even if extremely low, that an individual could be damaged by the vaccine.

FDA asked LDA if the team had anything to add. Here, Pat Smith responded: “We have found that, due to word of mouth on the dangers of this vaccine, physicians will no longer give it out in their offices. Even HMOs and clinics no longer want to be involved. Instead, Glaxo is marketing the vaccine on college campuses, where nurses who distribute it may be unaware of the issues involved. We are very concerned that our young students will be the next victims of this vaccine.”

Smith concluded with this query: “We want to know if you are going to do anything with the information we have presented today.”

“We’ll need to discuss this among ourselves,” said FDA’s Susan Ellenberg, PhD, Director, Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research. “We take your presentation very seriously. Any action will be announced to everyone in the public at the same time.”

On February 25, 2002, a month after meeting with FDA, LDA received written answers to its questions from FDA and, also, learned that Glaxo SmithKline had quietly pulled Lymerix from the market, citing “poor sales.”

CLICK HERE FOR THE RESPONSE

LDA Remarks Before Vaccines & Related Biological Products Advisory Committee

I am here today because we do favor a safe and effective vaccine, but we are unsure whether an OSP A based vaccine can meet those criteria. Since the inception of OSP A vaccine trials, we heard from individuals experiencing difficulties after immunization. The information was startling, not only because of the problems described, but also because of doctors’ apparent incomprehension of the problem.

REMARKS OF PAT SMITH, PRESIDENT, LYME DISEASE ASSOCIATION, INC. BEFORE THE VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE, JANUARY 31, 2001, BETHESDA, MD

The Lyme Disease Association’s mission is Lyme disease education, prevention, and research funding, so one might automatically assume we’re favorable to a safe and effective vaccine for Lyme disease. That’s certainly a valid assumption.

The Association's board consists of patients and families of patients—all of whose lives have been personally touched by this disease, and all who are dedicated to preventing others from experiencing the physical, mental, and emotional devastation Lyme disease can produce. To that end, we fund research projects, sponsor medical conferences and continue to work with Members of Congress developing federal legislation providing $125 million for Lyme disease research, physician education, and prevention.

I am here today because we do favor a safe and effective vaccine, but we are unsure whether an OSP A based vaccine can meet those criteria. Since the inception of OSP A vaccine trials, we heard from individuals experiencing difficulties after immunization. The information was startling, not only because of the problems described, but also because of doctors' apparent incomprehension of the problem. At a vaccine meeting sponsored by the LDF where pharmaceuticals reps were discussing how well the trials were going, I questioned, without satisfaction, the issue of these trial-patient complaints.

After vaccine approval, LDA received inquiries about the vaccine, many from individuals who had received all or some of the vaccination series. Most proceeded to talk about symptoms they developed subsequent to receiving the vaccine. When asked if they had reported this to the administering doctor, and if the doctor had reported the adverse event, the usual response was that the doctor did not take the complaint seriously or did not think the symptoms were related.

Sadly, none were aware of the HLADR4 situation, and several were in the midst of the immunization series and did not know whether to continue taking the shots. Some called to ask if they should get the shots if they had had Lyme in the past, a question which appears to have no clear answer—particularly in light of the unreliable antibody response tests used to determine who has or had Lyme disease. A few insisted they had gotten "full blown Lyme" from the shots, and after further discussion, indicated they had had Lyme disease in the past.

I want to share an email I received Monday. “I live in Wisconsin. I received your name from person X who told me you may be able to give me some direction. I received two vaccines in the spring of 2000. Couple days within the first shot my neck and higher back stiffened up severely. In a month I went back for the second shot and asked the nurse and doc to check for side effects before I took the second. They informed me there were none. I took the second dose and the problem with my neck and back worsened within a couple of days. My family doctor gave me anti-inflammatories but they did nothing. I’ve tried a chiropractor but the only relief was for a couple of hours. Never tried one before but am getting desperate. Then I went to a orthopedic and am now on anti inflammatories again but not helping. He told me that I have a disc that is somewhat smaller than the others in my neck and maybe the vaccine somehow aggravated it. Prior to the vaccine I have had 0 neck or back problems. I am looking for treatment somehow someway.” I called him. He is 39 years old. He asked me to help him. He wants treatment for what he has.

Today you are hearing about how this vaccine has physically impacted human lives. It appears that little can be done to stop whatever process triggers some of these reactions, or if something can be done, it remains as yet undiscovered. I listen to the despair and bewilderment of those adversely impacted: How can this happen from a medicine to keep me from getting sick? Who can help me get better? I can only comfort them as I do not have any answers, and I do not know who does.

This committee has the authority to formulate recommendations that may prevent others from potentially suffering the same fate. You can revisit the original data and research which appears to show a link between OSP A and adverse reactions and view it in light of the adverse events you have now heard about. You can recommend further studies. You can find out why many doctors who treat chronic Lyme disease are not giving the vaccine.

The Advisory Committee on Immunization Practices recommends under future considerations in their report on the Lyme disease vaccine, June 4, 1999 MMWR, “establish post licensure

epidemiological studies of safety, efficacy, prevention effectiveness, cost effectiveness, and patterns of use." We concur with that recommendation and would like to see a moratorium on vaccine administration until those studies are completed and the results critically analyzed.

Thank you for your time.

FDA Public Health Advisory

Assays for Antibodies to Borrelia burgdorferi; Limitations, Use, and Interpretation for Supporting a Clinical Diagnosis of Lyme Disease

July 7, 1997

Purpose
FDA is advising you about the potential for misdiagnosis of Lyme disease. The results of commonly marketed assays for detecting antibody to Borrelia burgdorferi (anti-Bb), the organism that causes Lyme disease, may be easily misinterpreted. To reduce this risk of misdiagnosis we are providing guidance on the use and interpretation of these tests. It is important that clinicians understand the limitations of these tests. A positive result does not necessarily indicate current infection with B. burgdorferi, and patients with active Lyme disease may have a negative test result.1-5

For link to FDA website and full article click here

Lyme Disease and the US Army

THE LDANJ VISITS THE US ARMY CENTERS FOR HEALTH PROMOTION & PREVENTION, CHPPM by: Pat Smith, with input from Corey Lakin and USACHPPM

In May 1999, Association Vice President Corey Lakin and I visited the US Army Centers for Health Promotion and Prevention, USACHPPM, at Aberdeen Proving Grounds, Maryland. USACHPPM is the preventive medicine arm of the US Army. The visit was coordinated by NJ Congressman Christopher Smith's office as a briefing for us so that CHPPM could share the progress the Army is making in the area of tick-borne diseases, TBD.

This year, CHPPM was required to submit an annual report to Congress, which is titled DoD Research and Surveillance Activities Regarding Lyme Disease and Other Tick-Borne Diseases, since Congressman Smith and Senator Dodd were able to get an attachment for TBD monies to the Strom Thurman National Defense Authorization Act for Fiscal year 1999. Congressman Smith was also successful several years ago in attaching Lyme disease monies to the defense appropriations.

Not really knowing the extent of Army involvement, we were surprised to find that the Army takes TBD very seriously. We were shown laminated tick cards designed especially for the Balkan theater where Lyme is transmitted through infected sheep ticks. We were given tick removal kits that are distributed to the Department of Defense (DoD) health clinics, so that ticks removed from soldiers can be submitted to USACHPPM for identification and testing. The DoD has a 3 prong Insect repellent system which they heavily promote: permethrin on uniform, DEET on exposed skin, and properly worn uniform = maximum protection. The DoD has developed a permethrin impregnation kit that soldiers can use to treat their uniforms. The treatment offers protection for the life of the uniforms. We were also amazed to find the DoD has now made available uniforms that are actually impregnated with permethrin at time of manufacture, so that applications do not need to be done by the soldiers. They also use a

state-of-the-art, long-acting DEET skin cream that is commercially only available through Amway.

The most exciting research was being done in the area of technology. In the lab, we saw how the Army has developed a prototype “in the field” PCR test kit, a virtual lab in a suitcase, to be able to perform testing for the presence of Borrelia burgdorferi right where the action is. It has been designed so that soldiers with limited training can operate it successfully. Individuals utilizing these kits could amass tick data including species, density, location (using a Graphic Information System, GIS), and results of PCR testing, which are then transmitted directly from the field to computers via a portable satellite uplink.

The development of a “heads up” display for tick populations is certainly some of the best use of technology in tick prevention that I have ever seen. If you are not familiar with this terminology, you are not alone. A soldier in the field wears a special helmet with a special “heads up display” visor. The soldier is also equipped with a Global Positioning System (GPS) receiver, which is able to pinpoint his/her exact location on earth, and also a small transceiver linked via satellite to the DoD’s GIS computer. The GIS computer tracks the soldier’s position and transmits critical information, including tick population densities, to the “heads up” display visor. This high tech system provides soldiers in the field with a real time assessment of the risks posed by ticks in the potential troop deployment area and offers guidance during maneuvers, so that if possible, personnel shifts can be made to avoid dense tick populations.

The mapping of tick populations has already started and the density overlays are reported to a military map. The map overlay image is transmitted via secure satellite links to whomever requests it. On the example shown to us, the graphic shows the “risk of infection with Lyme disease from ticks occupying this area” from 0% to 100%. Additionally, tick infection rates are being determined at all major military installations and this data is being used to create overlays and analyze tick densities to protect those who are employed at these installations. This feat is accomplished by coupling GIS to field collected data.

The CHPPM officials were extremely cooperative. We had discussions on how these army developments can benefit the civilian population, and more importantly, how can this information be relayed to the civilian sector in a timely basis? We felt that this visit would be a first step in "opening up" communications. We, of course, can both benefit by us helping to promote monies in the Defense Authorization Act, as we have already done through Congressman Smith, and us ensuring that they receive monies through the Lyme Disease Initiative 1999 (current DoD appropriation in bill-$30M/5years). I have had preliminary discussions with Congressman Smith's office about the possibility of inserting language into the LD Initiative that would require DoD tick-borne illness projects to be made public within a specified time period after their development. It is too early to determine if this is a viable proposal.

Space limitations prevent me from printing the Report to Congress here, but I have selected several paragraphs that I feel reflect the tone of the report. The first three paragraphs of Section I of the report state: FINDINGS: Ticks are among the most important of all arthropod vectors of disease. There are over 850 recognized species worldwide. Ticks rank second only to mosquitoes in the number of life-threatening and debilitating diseases they transmit to humans. In the United States, ticks are responsible for more human disease than any other arthropod group. Tick-borne diseases represent potentially serious health threats to troops, their family members, DoD civilian employees, and other residents at military installations in many parts of the world.

In recent years, data indicate that tick-borne disease transmission has been increasing in the United States, both in terms of incidence of some diseases and the number of known pathogens transmitted by ticks. Tick-borne pathogens appear to be in the vanguard of a group of newly emerging diseases. Since 1957, at least 14 new disease agents have been discovered worldwide. Ticks transmit four of these, or almost 30%. They cause Lyme disease, human monocytic ehrlichiosis, human granulocytic ehrlichiosis, and human babesiosis. Deaths have been associated with some of these. To further complicate matters, there is increasing evidence that individual ticks can carry and transmit two or more infectious agents simultaneously, thereby increasing the severity and complexity of

symptoms, and compounding the difficulty of diagnosis and treatment.

Lyme disease is now the most prevalent vector-borne disease in the United States, with approximately 100,000 cases reported to the Centers for Disease Control and Prevention (CDC) since it became a nationally reportable disease in 1991. It is estimates that the actual number of cases may be as high as one million or more….

I have always been an individual with a lot of questions, but this report has raised many more in my mind. Why are Lyme and other TBD's seriously considered threats to the troops who defend our country, yet not seriously considered threats to the civilian population? Why are military installations mapped and rated for tick densities and rates of infection, while public parks are not even posted with warning signs? Why would PCR's be reliable "in the field" and not at commercial labs? Why is the government impregnating uniforms with permethrin, when we all know that the civilian population is creating a climate of "Lyme hysteria" and that Lyme is "overdiagnosed and overtreated?" To quote the report: "In addition to directly transmitting disease, the adverse impact of psychological factors associated with tick attack, including fear, discomfort, and distraction, as well as indirect medical complications such as secondary infections, dermatitis or allergic reactions, should not be overlooked." The army has not labeled this "hysteria" but normal "complications" of tick attacks.

Why is the vaccine promoted to the civilian population yet the report states "…questions and concerns linger regarding the new vaccines safety…; effectiveness…; age restrictions…; frequency of boosters…; and the known limitation that it is ineffective against European strains of the Lyme disease agent. Confident decisions as to its value and use within the military cannot yet be made…." Why does this double standard exist? I do not have all the answers, but I think we need to work more closely with government and the military to get all the answers so that we can solve this enigma that has been called Lyme disease.