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Put Patients First, Follow Best Science

Lyme Disease Exploding in U.S., Around the Globe

Africa, Global Health and Human Rights Subcommittee
Excerpts of Remarks by Chairman Chris Smith
July 17, 2012

Good afternoon, and welcome to our witnesses and to everyone who is joining us for this first ever congressional hearing examining the global challenges in diagnosing, treating and managing Lyme disease.

My personal commitment to combating Lyme disease is longstanding—going back 20 years when one of our witnesses Pat Smith attended one of my townhall meetings in Wall Township, New Jersey and asked me to get involved. I did.

On September 28, 1993 I offered an amendment to establish a Lyme Disease Program through the Environmental Hygiene Agency of the U.S. Department of the Army. It passed and became law.

On May 5, 1998 I introduced a comprehensive, bipartisan Lyme Disease bill—H.R. 3795 Lyme Disease Initiative Act of 1998—which had at its core, the establishment of a task force—an advisory committee—to comprehensively investigate Lyme with at least four things in mind—detection, improved surveillance and reporting, accurate diagnosis and physician knowledge.

I reintroduced the bill again in 1999, 2001, 2004, 2005, 2007, 2009 and 2011.

(I would note parenthetically that that same year, I also introduced a comprehensive law to combat Autism. Despite significant opposition in Congress and at NIH and CDC that paralleled the Lyme bill struggle, it became law in 2000. Last year I authored the Combating Autism Reauthorization Act of 2011 which was signed into law in the Fall—with the support of

NIH and CDC. If only we had done the same with Lyme Disease legislation in the late 90s—a missed decade on Lyme.

As I have met scores of patients suffering the devastating effects of Chronic Lyme—who only got well after aggressive treatment by a Lyme-literate physician—I have been dismayed and angered by the unwillingness of some to take a fresh, comprehensive look at this insidious disease.

My current bill—H.R. 2557—simply establishes a Tick-Borne Disease Advisory Committee with the requirement of ensuring diversity of valid scientific opinion—a "broad spectrum of viewpoints"—on the committee.

In Europe, Lyme disease syndromes were described as early as 1883, and by the mid-1930s neurologic manifestations and the association with *Ixodes* ticks were recognized and known as tick-borne meningoencephalitis.

In the United States, Lyme disease was not recognized until the early 1970s, when a statistically improbable cluster of pediatric arthritis occurred in the region around Lyme, Connecticut. This outbreak was investigated by Allen Steere, MD, and others from Yale and stimulated intense clinical and epidemiologic research. In 1981, Dr. Willy Burgdorfer, an NIH researcher at the Rocky Mountain Laboratories, identified the spiral-shaped bacteria (or spirochetes) causing Lyme disease and made the connection to the deer or black-legged tick, *Ixodes scapularis*.

Lyme disease is the most common vector-borne illness in the U.S. and is also endemic in parts of Europe and Asia, and recently has been confirmed to be endemic in the Amazon region of Brazil. In Europe, the highest rates are in Eastern and Central Europe. Recent surveillance studies have described growing problems in Australia and Canada.

In the US, Lyme disease has been reported in 49 states and is most common in the northeastern and north central states, and in Northern California into Oregon. Over 30,000 confirmed cases were reported to the Centers for Disease Control and Prevention (CDC) in 2010, making it the 6th most common reportable disease in the US and the 2nd most reportable in the northeast. CDC has estimated that actual new cases may be 10 times more than the reported number – indicating roughly 300,000 new cases in 2010 alone. About 85,00 cases were reported annually in Europe as of 2006 according to the WHO, but that was recognized as a gross underestimate.

In North America, the only *Borrelia* species to cause Lyme disease is *Borrelia burgdorferi* (or B. burgdorferi); in Europe, *B. burgdorferi* and at least four other species of *Borrelia* cause the disease. Different species are associated with different manifestations of disease. There also are numerous strains of *Borrelia*, which may effect the ability to evade the immune system, the ability to invade certain organs or tissues, and the response to antibiotics.

Clinical manifestations of Lyme are usually divided into three stages, although the descriptions of the stages vary. According to the US Army Surveillance System - which may have a greater variety of systems because they have both domestic and international surveillance components - during the first stage, 70 percent of patients display the characteristic erythema

migrans (EM). Other symptoms of stage one include profound fatigue, fever, chills, headache, sore throat, sore and aching muscles and joints, and swollen glands.

The second stage is marked by migratory musculoskeletal pain, neurological complications in 10 – 20 percent of patients, and heart inflammation or heart block in 6 to 10 percent of patients that appear 4 to 6 weeks after infection. Symptoms include severe headache and stiff neck, facial paralysis, weakness and/or pain of the chest or extremities, rarely optic atrophy with blindness and coma. Acrodermatitis Chronics Atrophicans (ACA) is a cutaneous manifestation that may occur during the second stage to several years after disease onset.

The third stage typically involves the onset of arthritis characteristic of rheumatoid arthritis, affecting primarily the knees and other large joints. During this stage, a small percentage of patients also suffer from sleepiness, loss of memory, mood swings, and an inability to concentrate.

The "Lyme Wars"

Few diseases have aroused such a high level of emotion and controversy among the public, physicians, and researchers than Lyme disease. There are two distinct views of Lyme disease, each citing scientific evidence to support its claims, while outcomes research is limited and conflicting. One view – promoted by the Infectious Diseases Society of America (IDSA) - is that the disease is "hard to catch and easy to cure" and denies the existence of chronic Lyme disease or persistent infection with the Lyme bacteria. Any treatment other than a short course of antibiotics is considered too risky. Patients' who do not fit the paradigm may have few options outside of psychiatric evaluation.

The alternative view - promoted by the International Lyme and Associated Diseases Society (ILADS) and also by numerous academic researchers in the US and around the globe - says that the science is too unsettled to be definitive and there can be one or more causes of persistent symptoms after initial treatment in an individual who has been infected with the agent of Lyme disease. These causes include the possibility of persistent infection, or a post-infectious process, or a combination of both. These are not "academic" concerns however because the patients' health is at stake. Unfortunately, some academic researchers believe some of their colleagues are more interested in winning arguments then moving the science forward.

Three areas central to the controversy are: the quality of diagnostics, post-treatment persistence of *Borrelia,* and available treatment options in light of clinical guidelines.

DIAGNOSTICS

Current diagnostic tests commonly used do not detect the spirochete that causes Lyme disease, rather, they detect whether the patient has developed antibodies to the pathogen (serological testing). CDC recommends two-tier serological testing, but cautions that the 2-tier system should be used only for surveillance purposes and not for diagnosis. Part of the difficulty in clinically managing suspected Lyme disease is that the CDC protocol is frequently not only used, but required for diagnosis.

A study in the Netherlands of eight commercially available ELISAs and five immunoblots found that they had widely divergent sensitivity and specificity and a very poor concordance, and concluded that "their high variable sensitivity and specificity further puts the much-advocated two-tier testing strategy into question."

In addition, two of the authors of a July 3, 2007 article on an antibiotic resistance element in *B. burgdorferi*, were Julie Boylan and Frank Gherardini of NIAID's Rocky Mountain Laboratories, stated that, "It is a multistage disorder that is difficult to diagnose at any stage of the disease as well as being difficult to treat during the later symptoms."

Dr. Mark Eshoo, the head of new technology at the IBIS Biosciences Division of Abbott Laboratories will tell us today some exciting information regarding the development of diagnostic tools that, hopefully, will move us past a lot of the controversy.

PERSISTENCE

IDSA has repeatedly stated that there is no "convincing" evidence that the Lyme Borrelia persists after standard antibiotic treatment. "Convincing is clearly a subjective term; however, there is substantial evidence of the persistence of *B. Burgdorferi* after treatment with antibiotics. There are numerous documented case studies of persistence in humans after antibiotic treatment, and our witnesses may comment on additional evidence for post-treatment persistance in humans. Additionally, one of our speakers today is Dr. Stephen Barthold, one of the top experts in the country and I am sure in the world on animal models. Dr. Barthold, will describe published and yet to be published experimental studies that provide compelling evidence for *B.burgdorferi* persistence following antibiotic treatment in animal model systems and their potential significance for human medicine.

Numerous studies have been conducted of the mechanisms by which *Borrelia* may evade the immune system and antibiotics. Studies have suggested that resistance to antibiotics might be due to formation of different morphological forms of *B. burgdorferi*, including cell wall deficient forms and biofilm-like colonies. Research also indicates that *Borrelia* can exchange genetic material, possibly contributing to its ability to avoid detection by the immune system. Several other distinct technical mechanisms are well known by which *Borrelia* can evade the immune system.

Contrary to known scientific evidence, in a March 21, 2008, letter to Members of Congress, IDSA stated, "Not only is this assertion [the notion that some spirochetes can persist despite conventional treatment courses] microbiologically implausible, there are no convincing published scientific data supporting the existence of chronic Lyme disease." It is problematic that IDSA would write to congress trying to discourage support of legislation saying that post treatment persistence is microbiologically implausible.

Additionally, in an article, "A Chronic Appraisal of 'Chronic Lyme Disease'" published in the October 4, 2007, New England Journal of Medicine, several IDSA physicians and a CDC colleague made the statement that "Chronic Lyme disease, which is equated with chronic B. Burgdorferi infection is a misnomer, …"

While this statement has been referred to repeatedly in other correspondence, calling "chronic Lyme" a misnomer does not seem reasonable or supportable since it goes far past expressing uncertainty. It seems clear that the intent of the statement was to firmly slam the door on the notion that there possibly could be chronic Lyme.

TREATMENT GUIDELINES

The final major area of controversy is the significance of the IDSA's treatment guidelines which directly impact patients and their ability to get treatment. Guidelines should be developed based on the best science, and there has been extreme controversy regarding the restrictive nature of the IDSA guidelines. The guidelines do not allow for the possibility of chronic infection and severely limit physician discretion on treating the disease.

Supporters of the IDSA guidelines point to dangers of the prolonged use of antibiotics and the possibility of treating when an infection has not been established. They also frequently point to alternative therapies which are unproven and may be dangerous; however, such alternative therapies are in the background for many diseases – perhaps most well recognized for cancer. Critics of the guidelines contend that they are based on highly selective science and that guidelines panelists had significant conflicts of interest. A 2009 review of the IDSA guidelines did not result in any changes.

IDSA and supporters place heavy weight on certain clinical trials of Lyme treatments supported by NIH. There has been much controversy of the quality of those trials and their generalizability to broad populations of patients. It is disturbing to the lay bystander that the controversy has ensued for so long without resolution. Certainly there are numerous unknowns about the bacteria and the disease; however, the public questions why the "experts" can't even agree on whether these small numbers of clinical trials are well designed, well executed, and of sufficient power (whether they have a large enough number of patients), and the degree to which they can be generalized to other patient populations.

IDSA supporters have been adamant in the quality of the studies and the validity of their use to guide treatments for broad patient populations. In fact, several other researchers have been highly critical of the studies, pointing to specific perceived deficiencies, such as selection criteria that almost guaranteed failure, not appropriately defining endpoints, and, significantly underpowering the studies. One journal article from the Netherlands states, "The randomized studies that have been performed have been of questionable quality and were heavily underpowered to detect potential effects."

Many who recognize the shortcomings of clinical trials to date, stress the importance of conducting more well-designed treatment studies with a sufficiently large and representative number of patients, and at least some such efforts are underway around the globe. I am pleased that Dr. Raphael Stricker, a practicing physician who sees many Lyme patients, will guide us through some of the vast amount of literature on Lyme disease.

The UK has suffered under a contentious environment among different Lyme disease stakeholders very much like that of the US. We are told however that the UK may be making progress in developing a more cooperative environment. I am pleased that Stella Huyshe-Shires,

the Chairman of Lyme Disease Action, in the United Kingdom, will be able to share with us some of the perspectives on efforts to manage Lyme disease in Europe. I think we would all like to hear about the collaboration, funded by the National Institute for Health Research, with the Jack Lind Alliance to identify the uncertainties faced during consultations between patients and physicians, to then identify the top unanswered questions about diagnosis and treatment of Lyme, and to prioritize research.

This cooperative approach contrasts with the environment in the U.S. A recommendation regarding Lyme disease made during a May 2005 meeting of CDC's National Center for Infectious Diseases Board of Scientific Counselors, attended by the then President of the IDSA, that CDC should focus on science and not on the concerns of patient groups and that others may need to step in to assist CDC with public interface. Collaboration between the IDSA and government agencies on strategies to deal with the public can be seen in various statements and documents.

The September 2011 article, "Antiscience and ethical concerns associated with the advocacy of Lyme disease" reflects the degree of hostility toward patients, treating physicians and the Lyme charities that were formed to support education and research on behalf of patients.

Wouldn't it be much better if instead of belittling, insulting, and smearing patients, treating physicians and advocates, the authors of that study had asked themselves and posed the question to others, "what can we do to better understand and address the needs and concerns of patients, physicians and advocates."?

Two of our witnesses today will focus on the needs and concerns of patients and the non-profit organizations fighting on their behalf – namely, Evan White a former Lyme disease patient, and Ms. Pat Smith, the President of the Lyme Disease Association, who will provide their important perspectives. What we should never lose sight of is that the goal of all of our efforts and the science is to help patients regain health.

There are numerous Lyme disease non-profit organizations, some of them less informed than others. To cast a wide net and say that that they are well-intentioned, but ignorant and ill-formed is not an accurate portrayal. Many of them are intelligent, savvy people, who established medical and scientific advisory boards to advise their organizations. Two that I am most familiar with have funded millions of dollars in Lyme disease research, providing grants to a Who's Who of Academic Researchers.

Efforts to discredit research because it was partially funded by Lyme disease charities are therefore disturbing. Such efforts led some researchers to initially submit research studies and to leave off some funding sources. Researchers have also reported that when they have presented research findings to government officials or other scientists, there has been more interest in the funding sources than the research itself. Without speculating whether such intimidation is intentional, it is most unfortunate because academic scientists and very critical studies have been, and continue to be, supported by several of the Lyme charities, some of whom have raised millions of dollars and have invested every penny into research.

At the end of their "Antiscience …." tirade, the article's authors state that the public's health will be endangered "unless responsible physicians, scientists, government leaders, and the media firmly stand up for an evidence-base approach to this infection that is based on high-quality scientific studies."

That is a perfect ending for my opening remarks because that is precisely what the Lyme community wants; however, it will be necessary for the physicians, scientists, government leaders, and media to be discerning – to evaluate the evidence to see if it is based on the best science and to scrutinize the studies and the critiques of those studies to determine whether they are of high quality. We need scientists to speak out in an unfettered way. We need government agencies to show leadership and to forcefully say what we know and what we don't know based on the best available evidence.

Thankfully, we can be confident that science will prevail: research has been progressing – we are greatly increasing knowledge of pathophysiology, and we seem to be on the cusp of breakthroughs in diagnostics that hopefully will solve questions of persistence and active vs. past infection.

I am looking forward to hearing the valuable perspectives that each of our witnesses brings to this hearing. I regret that, today, we will not be hearing from NIH, CDC, nor a representative from the IDSA. They all were invited, but declined – the IDSA expressing that their potential witness had a scheduling conflict.

I will reissue an invitation to them—and expect they will testify before our subcommittee.