

2010 Annual Scientific Conference: The Science & Clinical Implications

Co-sponsored by Columbia University & Lyme Disease Association, Inc.

Held Saturday & Sunday – October 2 & 3, 2010

Hyatt Regency Penns Landing, Philadelphia, PA

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Conference Summary Prepared by Columbia University:

This remarkable two-day conference featured speakers from around the country – representing both basic science and clinical medicine. As in previous years, this conference enabled clinicians, other health care providers and the medically-interested public to learn about the latest research in tick-borne diseases. The speakers generously volunteered their time to participate and the Lyme Disease Association generously provided all administrative back-up and planning. As many speakers presented material that has not yet been published, only information authorized for release by the speakers is summarized below.

Dr. Madeleine Cunningham, Professor of Microbiology & Immunology at Oklahoma University, discussed her research on molecular mimicry, autoimmunity, and infection in inflammatory heart disease and in behavioral and movement disorders, particularly as related to sequela of group A strep infection. Autoantibodies triggered by strep infection can cause damage to the heart and to the brain, a mechanism which is thought to result in neuropsychiatric disorders such as TIC disorders and OCD among susceptible patients. She has begun to study whether patients with chronic symptoms after Lyme disease also have evidence of Bb-induced antibody mediated neuronal cell signaling.

Dr. Diego Cadavid, Associate Director of Experimental Neurology at Biogen Idec and Consultant in Immunology and Inflammatory Diseases at Massachusetts General Hospital in Boston, discussed his work with mice demonstrating that the relapsing fever

spirochete, *Borrelia turicatae*, release lipoproteins that are tissue tropic and can disseminate from the periphery and cross the blood brain barrier to cause inflammation in the brain. The results from these remarkable studies counter the prevailing view in medicine that bacteria must enter the brain to cause inflammation – in this case of *Borrelia turicatae*, the spirochete itself doesn't need to cross the BBB but rather the neurotropic Vsp1 lipoproteins are sufficient to induce a local CNS reaction.

Dr. Armin Alaedini of Cornell Weill Medical College, reported that approximately 50% of patients with chronic Lyme disease have evidence of elevated anti-neuronal antibodies and that the intensity of these antibodies is comparable to that seen in Lupus but much greater than that seen among recovered Lyme patients. Whether these anti-neuronal antibodies are directly related to chronic Lyme symptoms is an area of future investigation.

Dr. Peter Burbelo from the National Institute of Craniofacial Research at NIH, described the development of a novel diagnostic technique applicable to Lyme disease – LIPS (luciferase immunoprecipitation systems) antibody profiling. Using a synthetic protein, designated V0V0, consisting of a repeated antigenic peptide sequence, VlsE-0spC-VlsE-0spC, this assay had 98% sensitivity and 100% specificity, performing similarly to the C6 ELISA, but with a much larger dynamic range for the detection of Ab than the C6 ELISA. This appears to be a high throughput, rapid, and highly sensitive and specific technique for both early and later stages of Lyme disease.

Dr. Ben Luft, Professor of Medicine at SUNY Stonybrook, discussed the conundrum of chronic Lyme disease and the problems with serologic tests that are based on only one strain of Bb. His recent work, which includes the sequencing of 13 strains of Bb with Claire Fraser and other collaborators, expands the antigenic profile available for test development from the focus on one strain to the expression of 13 strains.

Dr. Satish Raj, Assistant Professor at Vanderbilt University and cardiologist at the Vanderbilt Autonomic Dysfunction Center discussed postural tachycardia syndrome (POTS) – an autonomic disorder that can accompany or be triggered by Lyme disease. Characterized by orthostatic tachycardia in the absence of orthostatic hypotension, POTS can be associated with a high degree of functional disability. Patients with POTS complain of symptoms of tachycardia, exercise intolerance, sleep disturbance, lightheadedness, extreme fatigue, headache and mental clouding. Patients with POTS

demonstrate a heart rate increase of ≥ 30 bpm with prolonged standing (~10 minutes), often have high levels of upright plasma norepinephrine (reflecting sympathetic nervous system activation), and many patients have a low blood volume. Therapies aimed at correcting the hypovolemia and the autonomic imbalance may help relieve the severity of the symptoms.

Dr. Steven Schutzer, Professor of Medicine at UMDNJ, reported on the results of his polymicrobial study, in collaboration with IBIS, Inc, of what else might be contained in ticks. Ticks that are known to carry *Borrelia burgdorferi* have been shown to carry other microbes (e.g., *Babesia microti*, *Borrelia miyamotoi*, *Anaplasma*) and multiple genotypes of *B. burgdorferi* even in the same tick. These findings were made possible by technological advances that enable the identification of all microorganisms in a specimen without prior knowledge of the likely organism.

Ellen Stromdahl, MS, entomologist at the U.S. Army Public Health Command's Entomological Sciences Program at the Aberdeen Proving Ground, discussed the army's Tick-borne Diseases Laboratory which both identifies and tests ticks from DOD personnel and disseminates educational materials. Her particular area of interest is the other pathogens found in their most frequently received tick – lone star tick, *Amblyomma Americanum*. PCR analysis of these ticks from MD (APG) revealed a very high prevalence of a spotted fever group (SFG) rickettsia. Restriction fragment length polymorphism (RFLP) and sequence analysis identified "*Rickettsia amblyommii*". This organism is not yet described or well studied, and its pathogenicity is unknown; however, investigations of the organism are warranted because of its high prevalence in *A. americanum*. High *R. amblyommii* prevalence in populations of *A. americanum* presage co-infection with other *A. americanum*-borne pathogens. *A. americanum* nymphs and adults from APG were found to be co-infected with *R. amblyommii* and *Borrelia lonestari*, *Ehrlichia chaffeensis* and *Ehrlichia ewingii*, respectively, and larval pools were infected with both *R. amblyommii* and *B. lonestari*. Co-infections can compound effects and complicate diagnosis of tick-borne disease.

Dr. Edward Breitschwerdt from the College of Veterinary Medicine at NCSU described new findings related to *Bartonella*. The genus "*Bartonella*" is currently comprised of at least 26 species and subspecies of vector-transmitted, fastidious, gram-negative bacteria that are highly adapted to one or more mammalian reservoir hosts. Most *Bartonella* species have been discovered in the last 15 years. The clinical and diagnostic challenges posed by *Bartonella* transmission in nature may be much more complex than is currently appreciated in either human or veterinary medicine. Based

upon the annual increase in publications related to Bartonella infections during the past decade, it is clear that members of this genus are receiving increased scrutiny by the medical and scientific communities. The recognized clinical profile of Bartonellosis includes hepatitis, angiomas, endocarditis, myocarditis, arthritis, vasculitis, and seizures; viewed as a silent epidemic, new diagnostic assays enable the organism to be more readily cultured thereby enabling the disease impact on humans to be accurately described.

Dr. Beth Winkelstein, Associate Professor in Bioengineering at University of Pennsylvania addressed “Glia, Inflammation, and Pain”. Pain is a complicated cascade of local and central mechanisms including a wide array of cell types, including the neurons and their supporting glia. Inflammation has an important and potent role in initiating pain via local mediating factors and centrally-modulating synaptic circuits leading to maintenance of chronic pain. In fact, research findings suggest that leveraging inflammatory responses may help in the development of effective treatment and diagnosis of chronic pain states.

Dr. Eugene R Shippen, practitioner in family practice and endocrinology in Shillington PA, spoke on “Vitamin D, Regulatory Hormone of Immunity and Inflammation – Implications in Chronic Infectious Diseases.” Vitamin D deficiency is widespread in the northern latitudes where Lyme disease/co-infections are most prevalent. Because well over 800 genes are modulated by Vitamin D, Dr. Shippen concluded that it was not surprising that most major organ systems and diseases are adversely affected by inadequate or deficient vitamin D status. Vitamin D activity is associated with a) activating the initial “innate” immune response to all new infections increasing resistance to any new infectious invaders; b) reducing inflammatory cytokines and increasing the secondary “adaptive” immunity that helps with antibody formation as well as the autoimmune controlling Treg cells that inhibit autoimmune diseases; and c) increasing production of cellular antimicrobial peptides, the cathelicidins and defensins, that help the body control bacterial, viral and fungal infections both acutely and chronically. Chronic infections frequently increase resistance to vitamin D activities. This makes deficiency worse and increases the need to maintain higher intake or production of vitamin D through sunlight, UVB exposure. Dr. Shippen concluded that research is needed to determine the beneficial effects of higher dose vitamin D in the treatment of patients with chronic infections, like Lyme disease.

Dr. Brian Fallon of Columbia University provided an update on the Lyme and Tick

Borne Diseases Research Center – biomarker studies, the establishment of a specimen bank, and most recently, the completion of a large community study in Lyme endemic areas to compare established and novel diagnostic assays. The focus of this talk was on two studies of diagnostic tests. One study examined whether three well-known Lyme specialty labs had greater sensitivity or specificity than one well-known national commercial laboratory in the correct detection of patients vs. healthy controls. The second study reported on a community-based study of 450 patients from Lyme endemic areas in the Northeast to determine whether two new diagnostic approaches imported from Europe and adapted for the U.S., resulted in greater sensitivity or specificity than currently available tests.

The second day of this conference featured presentations from experienced clinicians. Highlights from selected presentations are offered below.

Dr. Dirk Elston, Director of Department of Dermatology at Geisinger Medical Center in Pennsylvania, presented a visually powerful and humor-filled but serious talk. Tick-borne illnesses remain a significant risk to public health. Cutaneous signs of illness can be helpful in establishing an early diagnosis. These include erythema migrans, acral petechiae, and retiform purpura. In areas endemic for Rocky Mountain spotted fever, tetracycline should be started in patients presenting with fever and headache. Therapy should not be delayed because of absence of rash.

Dr. Darrin Wiggins, Chairman of the Department of Emergency Medicine at Southampton Hospital on Long Island spoke about the recognition and diagnosis of acute tick-borne diseases in the emergency room, placing special emphasis on MD-examination of peripheral blood smears.

Dr. David Hardesty, movement disorder neurologist from Columbia University, presented an overview of movement disorders phenomenology with videos of tics, generalized dystonia, focal dystonias, and Parkinson's disease. He mentioned drug-induced movement disorders, and the role of diagnostic testing to determine the etiology of myoclonus. The role of the basal ganglia in psychiatric illness and movement disorders was reviewed. A video of 'amphetamine-like high' caused by deep brain stimulation of the sub thalamic nucleus at settings that improved motor control in PD was presented.

Dr. Ernest Visconti, pediatrician and infectious disease specialist from Lutheran Medical Center in Brooklyn, NY presented a talk on differential diagnosis of patients with chronic symptoms, highlighting the importance of careful and thorough

examination of patients for missed diagnoses. Of particular concern were those patients who presented with previously undetected Mannose Binding Protein deficiency – a deficiency that would impair clearance of infections.

Dr. Sam T. Donta, infectious disease specialist, consultant at Falmouth Hospital on Cape Cod, and retired Professor of Medicine from Boston University, reviewed strategies and considerations in making antibiotic decisions in Lyme disease. He reported very favorable open label clinical experience for the treatment of patients with biaxin and plaquinyl as well as with tetracycline.

Dr. Cheryl Ortel, OB-GYN in private practice, spoke about Women's Health and Lyme Disease. Dr. Ortel reviewed the frequency of tick-borne disease in private practice and the particular concerns for women during pregnancy.

Dr. James Dillard, MD, DC, Lac in clinical practice in Manhattan and East Hampton, gave a sweeping review of acupuncture, herbs, nutrition & other integrative medicine approaches to managing chronic pain among patients with chronic Lyme symptoms.

Dr. Amiram Katz, neurologist and Assistant Professor of Neurology at Yale University, discussed his finding that autonomic neuropathy is not uncommon in the context of the late manifestations of Lyme disease. It usually accompanies ganglionic and small fiber neuropathy. To date, autonomic malfunction could be demonstrated only by tedious, expensive, and not always reproducible battery of autonomic testing. He and his colleagues have recently been able to diagnose autonomic neuropathy and quantify its degree, by counting sweat gland nerve fiber density. In a preliminary analysis with this technique, he has shown that IVIG treatment repairs autonomic neuropathy, and this repair might sometimes antedate recovery of small fiber neuropathy.