

2009 10th Annual Scientific Conference: 34 Years, From Lyme, CT, Across the Nation

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

Held on October 23, 2009

Gaylord National Hotel & Convention Center, National Harbor, Maryland

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Conference Summary Prepared by Columbia University:

Scientific Program Chairs:

Brian Fallon, MD (Columbia University)

Richard T. Marconi, PhD (Virginia Commonwealth University)

Speakers from many disciplines were represented at this annual meeting co-sponsored by the Columbia University Lyme & Tick-Borne Diseases Research Center and the Lyme Disease Association. Outstanding presentations were given on Lyme and other tick-borne diseases: their distribution, pathogenesis, genetics, vaccine development and treatment. The keynote lecture was given by **Dr. C. Ben Beard** (Chief, Bacterial Diseases Branch of the Division of Vector Borne Infectious Diseases at the Centers for Disease Control) on the topic "Lyme Disease in the United States". His lecture emphasized that Lyme disease reported cases have steadily increased over the last 15 years, that the geographic distribution has broadened, that prevention and control activities are hampered by the absence of a "silver bullet" and by a number of other complicated factors, including community education and awareness. He stated that studies over the last 20 years

indicate that under-reporting is a problem, suggesting that there are actually 3-12 times more cases than actually reported to the CDC. Using the new reporting criteria, the number of definite cases for 2008 was 28,921 and, if probable cases were included, the number increased to 35,198. He concluded by emphasizing that effective prevention and control require the collaborative efforts of numerous stakeholders including universities, industry, advocacy groups, and public health agencies. A new memorial lecture was established in honor of Dr. Ed Masters – the pioneering family physician and clinical researcher from Missouri who focused national attention on an outbreak of erythema migrans in the southern U.S. and stimulated a national search for its cause. **Dr. Kerry Clark** (University of North Florida) delivered the Dr. Ed Masters Memorial Lecture: “Southern Tick-Borne Infections”. He reported that an overview of published research findings during the past 20 years reveals extensive evidence of *B. burgdorferi sensu lato* in ticks and wild vertebrates in the southern United States. Evidence of infection in humans is less extensive due to fewer studies in the South. However, studies of patients with Lyme-like illness (LLI) in several southern states do provide some evidence of human infection with Lyme *Borrelia*, while evidence implicating *B. lonestari* as a cause is represented by a single case. New evidence presented showed that over 40% of human patients with LLI across the country tested positive with a flagellin gene PCR specific for Lyme group species. Also, a genetic group of strains distinct from *B. burgdorferi sensu stricto* appears to be responsible for a significant number of infections detected by PCR and DNA sequencing, and these strains appear to be widely distributed among patients across the United States. **Dr. Susan E. Little** (Oklahoma State University): “Dogs as Sentinels of Tick-Borne Infection” Dogs are affected by many tick borne diseases that affect humans. Because millions of dogs are routinely tested for these diseases each year, data on rates of infection can be used to provide information about geographic and temporal trends of these diseases in the human population. Surprisingly, foci of active transmission from dog studies have been identified even in areas where Lyme and other TBD are not endemic. In response to questions, Dr. Little indicated that the canine vaccine is 50-85% effective. **Dr. Christopher Earnhart** (Virginia Commonwealth University): “Lyme Disease Vaccine Development: An Update on Recent Progress”. There have been marked advances in the development of a broadly protective Lyme vaccine in recent years. While Osp-A based vaccines continue to be promising candidates, their acceptance in the market may be limited. Dr. Earnhart provided impressive findings regarding recombinant, chimeric

OspC-based vaccines which he described as the newest candidates for the next generation of Lyme vaccine; these have shown great potential in early trials. With rapid progress being made in vaccine development, there is reason to expect that one or more effective and broadly protective Lyme vaccines will be in clinical trials in the near future. **Dr. X. Frank Yang** (Indiana University): "Genetic Regulation of Borrelia Genes" This talk revealed more about the genetic regulation of spirochetal transmission – controlled by genetic inactivation of the two sets of two-component systems in *B. burgdorferi*. One set controls spirochetal transmission from ticks to mammals and is essential for Borrelia to establish infection in mammals, whereas the second set is important for spirochetal survival in the tick vector. A number of environmental factors contribute to genetic activation of Bb in mammals, including pH and temperature. **Dr. Richard Marconi**(Virginia Commonwealth University): "Immune Evasion Mechanisms of Pathogenic Spirochetes" Most spirochetal infections of humans can be chronic and in the absence of treatment can persist indefinitely. In this presentation, recent advances in our understanding of the molecular mechanisms employed by the Lyme disease, Relapsing fever and periodontal disease associated spirochetes to evade the innate immune system and complement mediated destruction were presented. The discussion focused on the role of specific bacterial membrane proteins (such as Factor H binding protein) that bind negative regulators of the complement cascade and then exploit this interaction for the purpose of survival and persistence in mammals. **Dr. Amiram Katz** (Yale University): "IV Immunoglobulin and Autoimmune Disease in Lyme Peripheral Neuropathy" Although IVig therapy is not routinely indicated for persistent symptoms associated with Lyme disease, it may be indicated in certain cases when Lyme is complicated by immune deficiency or for neurological conditions of an autoimmune nature. Dr. Katz reported on a series of 26 patients with painful neuropathy attributed to either the OspA vaccine (Latov, Wu et al. 2004) or Borrelia infection who had persistent symptoms post-antibiotic treatment. Patients had serologic evidence of OspA and either nerve-conduction study confirmed neuropathy or diminished epidermal nerve fiber density. After open label non-randomized treatment with intravenous immunoglobulin, there was a significant mean increase in epidermal nerve fiber density on repeat testing and all patients reported an improvement in their neuropathic symptoms. **Dr. Robert Dantzer** (University of Illinois at Urbana-Champaign): "From Inflammation to Sickness Behavior: The Role of Cytokines" Lyme disease patients often present with non-specific symptoms that include pain, fatigue, sleep disturbances, mood disorders and concentration problems. These symptoms are often viewed as the result of persistent psychological distress caused by the disease. However, there is now evidence that

the organism itself or inflammation caused by tick bites and *Borrelia* can either directly or indirectly induce the expression of inflammatory mediators in the brain. These mediators are responsible for the development of the non-specific symptoms of disease of which the intensity and duration can be modulated by psychosocial stressors and banal infections. Dr. Dantzer concluded by observing that to be ill is normal as long as you recover from it; the problem is that some patients fail to recover – this may be related to the concept of a “glial scar” – that the initial inflammatory event from years earlier (due to infection or trauma) may be reactivated at a later point and, because of that past event, fail to turn off after being reactivated – causing chronic sickness symptoms. **Dr. Phyllis Faust** (Columbia University): “Tick-Borne Encephalitis-A Fatal Case” A fatal case of deer tick virus encephalitis in a New York State resident was described. The virus identified at autopsy by PCR assay was related to the Powassan virus which can be pathogenic in humans and can cause severe encephalitis. There are 2 distinct lineages of the Powassan virus. Deer tick encephalitis is associated with lineage 2. A preliminary estimate of the infection rate in deer ticks in New England and Wisconsin is 0.6-1.3%. Diagnostic testing for Powassan virus is not routinely done on patients with encephalitis, but would certainly now be recommended for encephalitis of unknown etiology in these tick-infected areas. **Diane M Gubernot, MPH** (U.S. Food and Drug Administration): “Babesia Infection and the US Donor Blood Supply” Babesiosis is a known transfusion-transmitted disease risk and there is no FDA-licensed test for mass donor screening. Approximately 80 transfusion-associated cases have been reported from 1979 through 2008. Eleven transfusion-related Babesiosis fatalities have also been reported, with ten occurring since 2005. Without a licensed screening test, enhanced clinician awareness of the possibility of Babesiosis in febrile transfusion recipients may facilitate prompt diagnosis, improved prognosis, and more timely investigations to interdict extant infected units. Ms. Gubernot concluded by recommending prompt reporting of Babesiosis donor and transfusion-related events to assist the FDA in assessing the scope of this risk and developing appropriate public health control measures. **Dr. Peter Hildenbrand** (Harvard University): “Lyme Neuroborreliosis: The Great Neuroimaging Imitator” Due to enhanced community and medical awareness of Lyme Disease, the number of patients who develop imaging discernable manifestation of Lyme Neuroborreliosis is small. The most frequent neuroimaging finding in LNB is cranial nerve enhancement, particularly the 7th cranial nerve. The imaging pattern of LNB and viral facial neuritis is the same. The white matter pattern of involvement in LNB may be sufficiently similar to that of multiple sclerosis to suggest either a common demyelinating pathway or *Borrelia*

subunits as an indirect MS causative antigen. A broadly accepted serologic and/or neuroimaging biomarker of LNB treatment response warrants further collaborative research. **Dr. John M. Costello** (Harvard University): "Lyme Carditis in Children" Carditis is a rare manifestation of Lyme disease in adults and children, occurring in 0.8% of cases reported to the Centers for Disease Control and Prevention. Of 207 children treated for early disseminated Lyme disease at Children's Hospital Boston between 1994 and 2008, 33 (16%) had carditis. Independent predictive factors for Lyme carditis included older age and cardiopulmonary symptoms. All but one carditis patient had other signs and symptoms of early disseminated Lyme disease; most commonly flu-like symptoms, multiple erythema migrans, meningitis and/or cranial nerve palsy. Variable degrees of atrioventricular block were present in the vast majority of patients, including 15% with second degree heart block and 27% with complete heart block. Advanced heart block resolved in all but one patient within a week. Four of 33 patients presented with depressed myocardial function (severe in 3 cases), which completely recovered in all cases. **Dr. Patrick McAuliffe** (Columbia University): "Neuropsychological Deficits in Children and the School System" Children with post-treatment Lyme disease are at increased risk for long-term problems in cognition and school functioning. Interventions were proposed in terms of minimizing fatigue, modifying the curriculum and providing classroom accommodations for students with post-treatment Lyme disease. **Dr. Brian Fallon** (Columbia University) the Dr. John Drulle Memorial Lecture "A Critique of Treatment Guidelines" Dr. Fallon reviewed evidence from recent U.S. clinical trials for chronic Lyme disease. He emphasized the difference between treatment efficacy and treatment recommendations. Efficacy is based on whether a treatment is shown to be effective compared to placebo. Recommendations are based on a combination of factors that include side effect risk. He concluded that recent studies of post-treatment Lyme fatigue demonstrate efficacy for repeated antibiotic therapy that was sustained to the 6 month end-point, however the risks associated with repeated IV antibiotic therapy led the authors to not recommend this treatment approach. Presumably if an antibiotic treatment could be identified that worked as well as IV ceftriaxone but was not associated with the risks of an indwelling catheter, then that would be an excellent treatment recommendation for patients with chronic Lyme-related fatigue. It's not that repeated antibiotic treatment has been shown to be ineffective. Rather, the problems are: a) the risks of IV ceftriaxone mitigate against recommending their use without a very careful cost-benefit discussion; and b) we do not have biomarkers at present to identify those patients who are most likely to benefit from this treatment.

