

Other Conferences

[2001 LDA & Columbia University Annual Scientific Conference](#)

Lyme and Other Tick-Borne Diseases: A 21st Century View

Held on November 10, 2001

Dorral Forrestal

Princeton, New Jersey

To [View Brochure](#) : List of Speakers, Agenda, Program Accreditation and Miscellaneous

{simplecaddy code=TP010}

{simplecaddy code=TP011}

Note: Dr. Stephen C. Davison NASA Headquarters, replaced Dr Joshua J. Zimmerberg in the faculty of this program.

[2000 LDA Annual Scientific Conference](#)

Lyme and Other Tick-Borne Diseases: Focus on Children and Adolescents

Held on November 4, 2000

Doral Forrestal

Princeton, New Jersey

To [View Brochure](#) : List of Speakers, Agenda, Program Accreditation and Miscellaneous

{simplecaddy code=TP008}

{simplecaddy code=TP009}

[1999 LDA Annual Scientific Conference at Bard College](#)

Lyme and Other Spirochetal and Tick-Borne Diseases: A Two Day Discussion of the Most Recent Developments in Research and Clinical Management

Held on November 13 &14, 1999

To [View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

{simplecaddy code=TP007}

2003 Annual Scientific Conference: Current Strategies & A Map to the Future

LDA & Columbia University 4th Annual Scientific Conference

**Lyme and Other Tick-Borne Diseases: Current Strategies & A Map to the
Future**

Held on November 14, 2003

Hyatt Regency at Penn's Landing

Philadelphia, Pennsylvania

[View Brochure](#)

: List of Speakers, Agenda, Program Accreditation and Miscellaneous.

[View Video Clips](#)

{simplecaddy code=DVD110}

Note: Dr. Ray Stricker, San Francisco, California, replaced Dr. Jackie Springer in the faculty of this program.

2004 Annual Scientific Conference: Technology Leading the Way

LDA & Columbia University 5th Annual Scientific Conference

Lyme and Other Tick-Borne Diseases: Technology Leading The Way

Held on October 22, 2004

Hilton Rye Town

Rye Brook, New York

[View Brochure](#): List of Speakers, Agenda, Program
Accreditation and Miscellaneous

{simplecaddy code=COMP2004}

2005 Annual Scientific Conference: Emerging Tick-Borne Diseases

LDA & Columbia University 6th Annual Scientific Conference

Lyme and Other Tick-Borne Diseases: Emerging Tick-Borne Diseases

Held on October 28, 2005

Crowne Plaza

Philadelphia, Pennsylvania

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

[View Video Clips](#)

{simplecaddy code=DVD115}

{simplecaddy code=COMP2005}

{simplecaddy code=DVD114}

2006 Annual Scientific Conference: Seeking Answers through Science

LDA & Columbia University 7th Annual Scientific Conference

**Lyme & Other Tick-Borne Diseases: Seeking Answers through
Science**

Held on October 20, 2006

Crowne Plaza

Philadelphia, PA

[View Brochure](#): List of Speakers, Agenda, Program Accreditation
and Miscellaneous

[View Video Clips](#)

{simplecaddy code=DVD117}

2007 Annual Scientific Conference: Bridging the Medical Chasm

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

Held on October 26, 2007

Marriott Newton, Boston, Massachusetts

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

{simplecaddy code=DVD118}

2008 Annual Scientific Conference: Solutions Through Cutting Edge Science

Held on October 17, 2008

Cathedral Hill Hotel

San Francisco, California

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

DVD of conference – not available

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

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

{simplecaddy code=DVD2009Conf}

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.

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

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

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.

2011 Annual Scientific

Conference: Update for Scientists, Clinicians & Health Officials

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

12th Annual Scientific Conference

Held Saturday & Sunday – October 1 & 2, 2011

Hyatt Regency Penns Landing, Philadelphia, PA

[View Brochure](#): List of Speakers, Agenda, Program Accreditation and Miscellaneous

ngg_shortcode_0_placeholder

Click on picture to link to photo gallery

Conference Summary Prepared by Columbia University:

Scientific Chairs:

Brian Fallon, MD, Columbia University

Richard Marconi, PhD, Virginia Commonwealth University

This year's conference was once again an exciting and stimulating meeting bringing together researchers, clinicians, community leaders, patients, and public health officials. Below we summarize the talks for the benefit of those who were not able to attend.

Dr. J. William Costerton's riveting talk on "The Role of Biofilms in Chronic Bacterial Infections" reviewed the history of the discovery of biofilms, demonstrating that these biofilms enable micro-organisms to resist host defenses and antibiotics, enabling infections to become chronic. Biofilm forms when bacteria adhere to surfaces in moist environments by excreting a slimy, glue-like substance. Sites for biofilm formation include natural materials, metals, plastics, medical implant materials—even plant and body tissue. Biofilms are held together by sugary molecular strands, collectively termed "extracellular polymeric substances" or "EPS." The cells produce EPS and are held together by these strands, allowing them to develop complex three-dimensional, resilient, attached communities. Biofilms can

be as thin as a few cell layers or many inches thick, depending on environmental conditions. Over 500 bacterial species have been identified in typical dental plaque biofilms. Dr. Costerton described how the capillary bed in the knee is a trap for bacteria, pointing out that septic arthritis in children settles in the knee (not the hip) and *Treponema denticola* (from periodontitis) also settles in the osteoarthritic knee (not the hip); this raises questions about the potential role of biofilms in chronic Lyme arthritis. Finally, emerging knowledge on biofilm dispersants was reviewed. For more information about biofilms, check out www.erc.montana.edu.

Dr. Eva Sapi's talk on "Killing *Borrelia* – an impossible job?" addressed various mechanisms associated with *Borrelia burgdorferi* that may help it to survive despite antibiotic treatment. *B. burgdorferi* is a known pleomorphic species, able to adopt alternative, defensive morphologies to evade the immune response and perhaps to increase antibiotic resistance. One of these morphologies is a cyst form, which Dr. Sapi's research suggests is resistant to the front line antibiotic treatment; alternative antibiotics were suggested. Another possible explanation for persistent symptoms might be the formation of a biofilm. Her group has employed several modes of microscopy to characterize biofilm morphology. Among optical microscopy techniques, dark field microscopy was used to observe the interaction of peripheral spirochetes with the biofilm, DIC microscopy revealed the heterogeneity of the biofilm matrix, and fluorescence microscopy enabled observation of the sessile internal biofilm population in a GFP-expressing population. A relatively new technique, atomic force microscopy, was used to directly scan the topography of the biofilm. The ability of *B. burgdorferi* to assume a biofilmic morphology may partly explain the continuing presence of symptoms in chronic Lyme sufferers. Dr. Sapi's group is examining different agents that may help to reduce biofilms, such as the antibiotics doxycycline and tinidazole as well as the herb Bamberol. Dr. Sapi concluded with the hypothesis that the *B. burgdorferi* biofilm likely provides a refuge for chronic Lyme infection, and offers an additional avenue of attack for potential treatments for Lyme disease.

Dr. Jason A. Carlyon's talk focused on *Anaplasma phagocytophilum*, the agent of human granulocytic anaplasmosis (HGA). This emerging tick-borne pathogen demonstrates stealth trickery, enabling it to avoid and even subvert immune cells. In the United States, HGA is endemic in the Northeast, the upper Midwest, and Northern California, where the disease's tick vector is prevalent. HGA presentation varies from sub-

clinical to mild or severe disease. Though rare, HGA can be fatal. Symptoms include fever, chills, headache, myalgia, leucopenia, thrombocytopenia, and elevated serum levels of liver enzymes. The risk of mortality is increased when patients are elderly or, have complicating opportunistic infections or prior immunocompromise and when therapy is delayed. Patients generally respond to the antibiotic doxycycline, the treatment of choice. *A. phagocytophilum* is an obligate intracellular pathogen, which means that it cannot survive freely in the environment. Therefore, it must parasitize certain cells in its tick vector and in its mammalian/accidental human host to obtain nutrients. While the obligate intracellular lifestyle is shared among many bacterial species, *A. phagocytophilum*'s chosen host cell in humans and animals – the neutrophil – makes it unusual. That *A. phagocytophilum* effectively invades and subverts the very cell meant to destroy microorganisms presents a striking paradox and brings forth the question of how it accomplishes this task. A major focus of Dr. Carlyon's laboratory is to understand the means by which *A. phagocytophilum* manipulates neutrophil functions to enable bacterial survival. Dr. Carlyon's lab has identified an Achilles' Heel that *A. phagocytophilum* exploits to convert its host cell into a Trojan Horse. Host cell proteins called Rab GTPases are membrane traffic regulators that orchestrate the series of events that culminate in microbial killing machinery assembly on the phagosomal membrane as well as phagosome-lysosome fusion. These proteins also control the trafficking of cargo – nutrients, cellular components, and waste material – to their appropriate sub-cellular locations. After binding to the surface of a neutrophil or other host cell, *A. phagocytophilum* tricks the cell into engulfing it into a vacuolar compartment. Once inside, the pathogen selectively hijacks Rab GTPases that are involved in "recycling" cellular material. The bacterium redecorates its host cell-derived vacuolar membrane with the hijacked membrane traffic regulators as a means of molecular disguise. By masking itself as a "recycling compartment", the *A. phagocytophilum*-occupied vacuole is able to remain undetected within host cells. The organism also blocks the actions of membrane traffic regulators that would normally destine the engulfed bacterium for destruction. Thus, *A. phagocytophilum* remodels its host cell-derived vacuole from an inhospitable vessel marked for destruction to a protective safe haven for replication. Deciphering how *A. phagocytophilum* facilitates its survival inside neutrophils provides an avenue to better understand how different agents of disease manipulate their host cells to evade the immune response and cause disease. This knowledge has broad-reaching implications, as it will aid in development of treatments and preventative measures for not only the agent of HGA, but also a battery of pathogens that employ similar intracellular

survival mechanisms.

Dr. Richard Marconi's talk on "C-Di-GMP" described research demonstrating that the cyclic nucleotide, c-di-GMP, plays a critical role in regulating several important cellular processes. The levels of c-di-GMP in the cell were manipulated by deletion or overexpression of genes that encode proteins involved in c-di-GMP synthesis and breakdown. High levels of c-di-GMP inhibit the ability of *B. burgdorferi* to pass from ticks to mammals while low levels interfere with the passage of spirochetes from mammals to ticks. The molecular basis of the observed phenotypes was demonstrated to be due at least in part to aberrant motility and chemotaxis patterns. These studies provide unique insight into the molecular mechanisms that control the ability of the Lyme disease spirochetes to complete the enzootic cycle.

Dr. Chris Earnhart's talk described work developing a novel next-generation Lyme disease vaccine based on outer surface protein C. Osp C is expressed by all Bb species and strains and is expressed in the human host for several weeks before being down-regulated. The first generation OspA vaccine killed Bb in the mid-gut of the tick and was only 68-76% effective, requiring very high antibody titers in the human to maintain its effect, thus requiring frequent boosters. The OspA vaccine also raised considerable fears because of the putative autoimmunogenic T cell epitope that might trigger a type of arthritis. Other groups have tried to revise the OspA vaccine by changing amino acids within this immunogenic epitope. Dr. Earnhart then went on to report progress in developing an OspC polyvalent chimeric vaccine. This work appears highly promising and may soon lead to animal trials to test its effectiveness.

Dr. Robert S. Lane gave a brief overview of his research team's long-term studies of the ecology and epidemiology of Lyme disease in California, and then summarized some exciting recent findings regarding the genospecies and genotypes of *Borrelia burgdorferi* s. l. that infect the western black-legged tick and humans in this region. In particular, he and members of his research team reported in the March issue of the *Journal of Clinical Microbiology* that *Borrelia bissettii*-like spirochetes occasionally infect humans. This is the first time that this Lyme disease-group spirochete has been demonstrated to infect people in North America. Previously, it was known as a human pathogen only in central and southern Europe. Dr. Lane also pointed out that northwestern California is highly endemic for Lyme disease, that *Ixodes pacificus* has at least 108 vertebrate hosts, and that some of the highly invasive strains of Bb found in the Northeast were not detected in CA ticks.

Dr. Karen Newell Rogers presented a talk about novel ways to target chronic inflammation and chronic immune activation among patients with chronic Lyme disease.

The primary controversy with Lyme disease has been whether the disease is the result of long-lasting bacterial infection or whether long-term symptoms result from a post-infectious, uncontrolled autoimmune response. By working with inbred strains of genetically identical mice, several researchers have found that mice with different genetic backgrounds display a broad range of symptoms when infected with the same amount of *Borrelia*. Recent studies have found that inflammation is involved in some symptoms of chronic Lyme disease, including Lyme arthritis. Some researchers would argue that chronic inflammation requires the continuous presence of bacteria, whereas others would suggest that continuous presence of bacteria does not always result in inflammation and that exacerbations of chronic symptoms could result from infection with a different organism—or that chronic symptoms could re-cure from unrelated pro-inflammatory events. Potentially reconciling these seemingly conflicting perspectives on the mechanism of Lyme disease may be the effect of *Borrelia burgdorferi*'s bacterial by-products on Toll Like Receptors, (TLR)-mediated immune activation. TLR appear to be the “gate-keepers” of an inflammatory response. Bacteria, including *Borrelia*, produce products that, by binding to TLRs on the cell surface, promote leukocyte activation, cytokine production, and acute inflammation. In some genetic backgrounds of mice, acute inflammation is sufficient to fight off infection and resolve disease. In other mouse strains, the pathogens, or in this case the bacteria, get past TLR-induced inflammation and remain symptomatically undetectable in cells and tissues (Barthold, etc); Barthold et al. have found that no matter how severe or mild the disease in any of the genetically inbred strains of mice, there was no more inflammatory disease when the bacteria were eliminated. If bacteria find a new disguise, and then come out of hiding, does the process start over again, resulting in chronic, or relapsing remitting, symptoms of inflammation, until the pathogen finds a new disguise or a new hiding place? Or, even if the *Borrelia* remain dormant, does exposure to a different pathogen that also produces TLR agonists re-trigger the expansion of latent pro-inflammatory cells that were initially stimulated by *Borrelia* TLR binding proteins?

Dr. Newell's research is aimed at determining how *Borrelia* infection, accompanied either by acute response and resolution, or by chronic response and chronic inflammation, is influenced by TLR dependent activation of polyclonally expanded B cells and expression of an individual's immune response genes (specific Major Histocompatibility Complex encoded gene products) (Newell et al. JLB, Oct. 2010).

Dr. Robert Yolken's talk on “Infections and Human Neuropsychiatric Diseases” focused

on the Stanley Center's work at Hopkins which has examined infectious triggers of psychosis. He emphasized that schizophrenia is a major neuropsychiatric disorder with massive medical, social, and economic consequences. Epidemiological studies indicate a role for infectious agents contributing to many cases of schizophrenia, often in individuals who are susceptible due to genetic factors. *Toxoplasma gondii* in particular has a number of biological properties which suggest that it is one infectious agent contributing to schizophrenia risk. Of particular interest is that embedded within the genes of *T. gondii* is the code for tyrosine hydroxylase which leads to an increase in dopamine, thus providing one possible mechanism for the association between psychosis and *T. gondii* infection. He concluded by emphasizing that an increased understanding of the role of infectious agents might lead to new methods for the prevention and treatment of severe neuropsychiatric disorders, such as schizophrenia.

Dr. Josep Dalmau's talk on "The Clinical Spectrum and Cellular Mechanisms of Autoimmunity in NMDA and other synaptic receptors". His pioneering work studying anti-NMDA receptor encephalitis shows how an immune response triggered by a tumor (e.g., ovarian teratoma) or perhaps an infectious process, results in antibodies that can attack critical receptors and synaptic proteins in the Central Nervous System involved in memory, behavior, cognition, and psychosis. Dr. Dalmau's early work in this area was with patients who have cancer, and others who have benign tumors, who develop immune responses that attack the brain; these are called paraneoplastic syndromes. His recent work has led to the identification of new mechanisms of disease, as well as treatments for some previously untreatable diseases. Specifically his group demonstrated that there is a subgroup of patients with limbic encephalitis who have antibodies against the glutamate AMPA receptor, and that these antibodies modify the levels of this receptor – they are no longer on the cell surface, where they do their job, but are internalized or pushed away from the synapses to extrasynaptic sites; this had never been so clearly demonstrated before. Dr. Dalmau showed stunning videotapes of patients with limbic encephalitis with profound neurobehavioral disturbances (e.g., extreme terror) whose symptoms reversed after receiving treatment that interfered with the autoimmune process. He noted that the abnormal movements seen in these patients are not classifiable using currently accepted descriptions of defined movement disorders. Background on the NMDAR hypofunction hypothesis of schizophrenia may be helpful. The descending glutamatergic pathway projects from cortical pyramidal neurons to dopamine neurons, and normally acts as a brake on the mesolimbic dopamine pathway by communicating

through an inhibitory GABA interneuron. Antibodies that decrease the levels of NMDA receptors on GABA inhibitory interneurons may then lead to reduced GABA release. This could then disinhibit post-synaptic excitatory transmission and lead to the release of excessive glutamate in the prefrontal/subcortical structure. The resulting glutamate and dopamine dysregulation may contribute then to the symptoms of psychosis and unusual dyskinesias. Psychiatrists should be aware of these autoimmune encephalitides as 77% of these patients are first seen by psychiatrists (23% by neurologists); 88% are eventually admitted to the ICU and 90% have a CSF pleocytosis. Treatments vary, but include IV Ig, plasma exchange, cyclophosphamide, and rituximab (monoclonal Ab against CD20). This work may be of relevance in the field of Lyme disease given findings that patients with chronic Lyme disease have elevated levels of anti-neuronal antibodies which have been shown in vitro to target neurons in the cerebral cortex and dorsal root ganglia; it remains to be demonstrated however whether these antineuronal antibodies are associated with the chronic clinical symptoms in post-antibiotic treatment Lyme disease.

Dr. John Aucott's talk on "Early Lyme disease" reported from the SLICE prospective cohort and his Maryland studies. He indicated that 75% of patients with early Lyme disease will have the telltale skin lesion within the first 1-4 weeks of infection that lasts from days to weeks and expands in size. He emphasized that the classic description of a "bull's eye rash" occurs only 20% of the time – it is not the most common manifestation of the Lyme rash. Rather, a uniformly red or reddish-blue rash, round or oval in shape, with sharply demarcated borders is most common. Most often the rash develops in places such as the knee, groin, or arm pit, occurring at prime tick season, such as the late spring and early summer. The rash is usually accompanied by fever, chills, and muscular pain in the neck and extremities; these rashes are not extremely painful and are not markedly pruritic. Preliminary evaluation of immunologic responses to early infection with *Borrelia* show interesting patterns of cellular immune response. These may eventually shed light on the differing clinical outcomes that are seen during the two year study follow up after initial antibiotic therapy.

Dr. Reinhard K. Straubinger's talk on "Canine and Equine Lyme Borreliosis" focused on Lyme borreliosis in animals, especially in dogs and horses. There is no transfer of *Borrelia* from pets to humans. Epidemiological data generated with animal populations can help to monitor the geographical distribution of Lyme borreliosis (e.g., dogs are excellent sentinels). In experimentally induced infections, not all animals develop disease; for example, in one study up to 75 % of all infected dogs developed disease, while none of the experimentally exposed ponies showed clinical

signs. Regarding clinical disease in naturally infected dogs and horses, no broad epidemiological data are available so far. Contrary to common belief, the presence of serum antibodies does not correlate with clinical signs and infected dogs can seroconvert and stay asymptomatic. In dogs and horses the first signs of clinical disease are mild fever, general malaise, lameness and swelling of local lymph nodes; this stage may go unnoticed, waning after a few days. An erythema migrans has not been described in dogs and horses. With dissemination, local inflammatory reactions can cause pain, swelling and lameness. As shown after experimental tick exposure, dogs became lame 2 to 6 months post infection, with severe lameness lasting for 2 to 5 days (mono- or oligoarthritis). The lameness is an intermittent limping and sometimes recurs 2 to 3 weeks later in the same or another limb. In naturally infected dogs, a glomerulonephritis with protein loss has been described for certain breeds (Labrador Retrievers, Golden Retrievers or Bernese Mountain Dogs); progressive renal disease can also occur, with death or euthanasia 1 day to 8 weeks after onset of the disease without demonstration of viable Bb. Neuropathological findings in infected dogs and horses were described as an asymptomatic encephalitis, mild perineuritis or meningitis. The two-tiered ELISA and Immunoblotting system is the method of choice for LB serodiagnosis in dogs and horses using either whole-cell preparations of borrelial antigens or with recombinant antigen from borrelia. Whole-cell preparations provide intrinsic high sensitivity, but cross-reactivity with non-specific antibodies occurs frequently. The use of recombinant proteins, especially in commercial tests, is now well standardized. In veterinary medicine, IgM detection is not common and recommended, because clinical signs develop weeks after tick exposure when detectable IgG are already present. These IgG antibodies persisted for years; even after successful antibiotic treatment these antibodies were detectable for years in otherwise healthy individuals. The highly variable surface protein VlsE is, according to current knowledge, exclusively expressed in the mammalian host. The invariable region IR6, and even a shorter peptide sequence of IR6 called C6 were found having a high potential as specific antigenic components in serologic test systems. This was shown by evaluating sera from infected humans, dogs, monkeys and mice. In experimentally infected dogs, C6-specific IgG antibodies appeared 3 weeks post infection; hence almost one week earlier than antibodies detected with ELISA based whole-cell preparations. Additionally, another benefit became clear when testing sera of people and dogs before and after antibiotic treatment. Contrary to antibodies against whole-cell components, research demonstrates that C6-antibodies declined substantially a few months after treatment. However, in animals with low C6-antibody levels prior to treatment, the decline obviously was minimal post treatment. Despite their high specificity for borrelial contact, C6-antibodies do not necessarily correlate with clinical signs in dogs and false-positive results may result from maternal antibodies in puppies born to infected bitches. Treatment of C6-positive dogs independent of the presence of illness should be considered carefully. Still, the use of C6-antibody testing in veterinary practice is recommended in order to clarify whether lameness seen in patients is the result of an infection with *B. burgdorferi* or by other tick-transmitted organisms such as *Anaplasma phagocytophilum*.

Dr. James Moeller presented a talk on "Immunologic aspects of neuropsychiatric illness: Lyme disease as model". In this talk, Dr. Moeller reported analyses demonstrating that the level of anxiety and depression among patients with chronic Lyme encephalopathy was highly correlated with a clinical index combining Bb-specific serologic & CSF status and brain metabolism. This represents the first time that psychiatric symptoms in Lyme disease have been directly linked to objective measures of Bb specific immunity & brain function.

Dr. Brian Fallon presented a talk on "Models of Chronic Lyme Disease". The talk started with a review of the terms that refer to chronic symptoms and

recommendations on how the the IDSA's definition of Post-treatment Lyme Syndrome could be improved. This talk reviewed the evidence regarding models of persistent infection and/or persistent immune activation. This talk also described the results of a recent collaborative study conducted by Dr. Steven Schutzer (PloS-One, 2011) with Dr. Fallon's samples at Columbia, Dr. Nadelson's samples from NJ, and the Pacific Northwest Lab's Proteomics team (Tao Lui, Richard Smith, and Tom Angel) which revealed several important findings: a) that there are approximately 700 unique proteins distinguishing the patients with chronic neurologic post-Lyme syndrome from the patients with chronic fatigue syndrome, clearly demarcating them as different disorders; b) both PTLs and CFS had elevated levels of complement in the CSF proteome, highlighting what appears to be an aberrantly functioning immune system in both disorders, compared to normals; and c) compared to controls, PTLs patients had reduced levels of proteins considered important for the maintenance of CNS cellular architecture, such as axon, neurite, and dendritic spine growth and organization, supporting the neurologic basis for chronic Lyme encephalopathy. He highlighted that these discovery phase results require replication before conclusions can be drawn, but may lead to invaluable diagnostic and treatment marker insights. This talk concluded with reference to other chronic illnesses, such as chronic fatigue syndrome and fibromyalgia, discussing the close interplay with the neurologic, immune, and endocrine systems, and the potential importance of the emerging literature on "Central Sensory Sensitization" to patients with chronic symptoms.

Dr. Andrew Walter reported on Ehrlichiosis and Hemophagocytic Lymphohistiocytosis (HLH) in cases of children diagnosed in Delaware. Ehrlichiosis is an uncommon tick borne disease seen in the mid-Atlantic area and therefore clinicians need to maintain a heightened vigilance. Ticks in the MD/Delaware/PA area carry *A. phagocytophilum* which causes HGA. *Amblyoma americanum* ticks in the mid-west carry *E. chaffeensis* and cause Human Monocytic Ehrlichiosis (HME). The elderly have the highest rate of illness due to Ehrlichiosis although more than 20% of children in endemic regions have evidence for past infection with TBRD. Doxycycline is the drug of choice for treatment of Ehrlichiosis since patients sick with Ehrlichiosis may be co-infected with other TBRD which are effectively treated by doxycycline. HLH is a rare complication of infectious diseases including Ehrlichiosis. Hemophagocytic lymphohistiocytosis (HLH) is a disease with major diagnostic and therapeutic difficulties. Primary HLH is an autosomal recessive illness that is fatal with a median survival among infants of less than 2 months. Secondary HLH may result from a

strong immunological reaction from a severe infection; most patients are not immunosuppressed. The most typical findings of HLH are fever, hepatosplenomegaly, lymphadenopathy, skin rash, jaundice, cytopenias, as well as hypertriglyceridemia, coagulopathy with hypofibrinogenemia, liver dysfunction, and elevated levels of ferritin and serum transaminases. Neurological symptoms may be associated with a spinal fluid hyperproteinemia and a moderate pleocytosis. Patients who are very ill with Ehrlichiosis or other infection should be immediately screened for HLH with LFT, CBC, ferritin with other specialized tests to follow as needed.

Dr. Andrea Gaito provided an update on the clinical evaluation and treatment of Lyme Arthritis from an autoimmune perspective. Lyme arthritis occurs in sixty percent of patients with untreated Lyme disease. The arthritis may be mono, oligo or polyarticular and is frequently migratory in nature. The spirochete rapidly disseminates to joints by inducing the production of cytokines which then induce vascular permeability, allowing further infiltration of spirochetes into the synovial tissue. The presence of the bacteria can then trigger an autoimmune response in susceptible patients. The musculoskeletal evaluation of a patient with Lyme disease involves a physical exam focused on determining the mechanical and inflammatory state of the involved joint. Both serologic tests and diagnostic x-rays are often required to assess the joint pathology. Evaluation of joint fluid for blood count, viscosity and cell type, along with testing for the presence of the Lyme bacteria is essential if an effusion is present. MRIs and synovial biopsies may be helpful in advanced cases. Many rheumatologic disorders may be associated with Lyme disease. These include Rheumatoid Arthritis, Systemic Lupus, Sjogren's syndrome and hyperviscosity syndromes, such as antiphospholipid antibody disease. The management of autoimmune disorders in a Lyme patient may require additional therapy with disease modifying agents along with an antibiotic regimen. The use of steroids should be limited due to concerns of immunosuppression. Autoimmune disorders with accompanying inflammation should be considered and managed as aggressively as bacterial coinfections in a complex patient, as both can play a significant role in propagating the disease process.

Dr. Ingeborg Dzedzic presented an interesting (and at times entertaining) overview of how Lyme disease impacts the eye, emphasizing that the eye is in part like the skin and in part like the brain. Diseases, like Lyme disease, that affect skin and brain can thus potentially affect eyes. The embryonic connection between eyes and other ectoderm and mesoderm derived organs predisposes them to developmental disorders and infectious diseases. Lyme disease has many clinical forms but they are all related to it being firstly an infectious disease and secondly to inflammation. Eye manifestations that relate to infection with *B. burgdorferi* tend to be acute and can be recurrent conjunctivitis, keratitis, iritis, retinal vasculitis, retinitis, and optic neuritis. Presenting symptoms for "ITISES" are as follows. Keratitis: visual discomfort, gritty feeling, increased dry eye, cannot keep the eyes open, pain, glare. Iritis: photophobia and eye pain. Vasculitis: may be asymptomatic. Retinitis: decreased vision. Optic neuritis: loss of peripheral vision first,

central vision later or in more aggressive cases, acute loss of vision and it is an eye emergency. Lyme disease eye-related symptoms are as varied as they are seen systemically. These issues should be taken seriously & treated so the patient can function better & recover sooner.

Dr. Vijay Thadani presented an overview of seizures and non-epileptic seizures, showing videos of both. Brain infections such as Lyme disease can lead to the development of epilepsy. This happens as a result of inflammation of the surface of the brain and the formation of scar tissue. Such damaged areas of brain can act as foci from which seizures begin and spread through the brain. Epilepsy is not however a common complication of Lyme disease, and if it occurs it can usually be treated successfully with anti-epileptic drugs. Epilepsy that is resistant to drugs can occur, but when encountered should be investigated thoroughly to rule out other causes of seizures. These include lack of blood and oxygen, and metabolic problems such as low or high blood sugar. The consequences of any brain disease, or any traumatic life experience, include mental stress that can manifest as a conversion disorder with non-epileptic psychogenic seizures. About 25% of patients with seizures refractory to anti-epileptic medication do not have epilepsy but have non-epileptic psychogenic seizures. A few patients have both. Long-term video-EEG recording is the best way to capture events and make a definite diagnosis. Correct treatment depends on correct diagnosis.

Dr. Steve Bock addressed complementary and integrative medicine approaches to the treatment of chronic Lyme disease. Dr. Bock's talk started with the notion that most patients with chronic symptoms don't just suffer from Lyme disease but they also may have other diseases, perhaps triggered by other co-infections. Dr. Bock then proposed that the treatment needs to address multiple symptoms of the "Chronic Lyme Disease Complex" as well as the accompanying dysfunction. He then reviewed the "Wheel of Function" which included a multisystem assessment approach – inflammation, GI function, endocrinology, immune deficiency, nutritional deficiency, stress, sleep disturbance, neurotransmitter disturbance, food allergies, heavy metal toxicity, coinfections. Dr. Bock concluded by discussing various testing and treatment approaches.

Dr. Elizabeth Maloney addressed studies of antibiotic treatment of Lyme disease, providing a thoughtful and critical review of the literature to identify lessons, gaps, and future research needs. This presentation examined the evidence from prospective studies conducted in the U.S. with regards to adequacy of design,

success rates and lessons learned. The evidence from many clinical trials was found to be inadequate due to small sample sizes with high non-completion rates, poor trial designs and limited antibiotic regimens; success rates were unacceptably low. The review also found that the efficacy of prophylaxis studied in the single dose doxycycline trial pertained only to the development of an EM at the bite site; success rates in the EM trials ranged from 60 – 80%. The design of the largest of the chronic post-treatment Lyme trials (Klempner et al, 2001 study – reporting no benefit from retreatment) was limited in that the high bar set for clinical improvement increased the likelihood of a Type II error in a study sample of this size. Additionally, the review called attention to the fact that the retreatment trials by both Krupp and Fallon demonstrated positive treatment effects.