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Lyme & Other Tick-Borne Diseases Conference: What Clinicians Need to Know About An Expanding Epidemic

Jointly Provided by:



COLUMBIA UNIVERSITY
College of Physicians
and Surgeons



LYME DISEASE ASSOCIATION, INC.
A National Non-Profit

Saturday & Sunday, September 23 & 24, 2017
Hilton Penns Landing
Philadelphia, PA

Accreditation, Disclosure, Audience & Learning Objectives

Accreditation: This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the College of Physicians and Surgeons of Columbia University and the Lyme Disease Association. The College of Physicians and Surgeons of Columbia University is accredited by the ACCME to provide continuing medical education for physicians. AMA Credit Designation Statement: The College of Physicians and Surgeons designates this live activity for a maximum 14.5 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure: The College of Physicians and Surgeons must ensure balance, independence, objectivity, and scientific rigor in its educational activities.

Disclosure: All faculty participating in this activity are required to disclose to the audience any significant financial interest and/or other relationship with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in his/her presentation and/or the commercial contributor(s) of this activity. When unlabeled uses are discussed, these will also be indicated.

Target Audience: The target population is physicians from all specialties, nurses, psychologists, scientists, public health, other health related professionals. It is open to the public & Lyme disease educators usually attend. Geographic area is nationwide, no special background required, although those whose practices contain high proportion of Lyme patients and those whose research concentrate on *Borrelia burgdorferi* will receive most benefit.

Learning Objectives: Practitioner should be better able to describe the role of inflammation and autoimmunity in persistent symptoms related to Lyme disease. Practitioner should be better informed about new diagnostic advances. Practitioner should become more knowledgeable about antibiotic treatments for patients with neurologic Lyme disease. Awareness that there are a wide array of new strategies to prevent tick-borne infections. Awareness of how Lyme disease infection can affect cardiac function.

This activity has been submitted to Pennsylvania State Nurses Association for approval to award contact hours. Pennsylvania State Nurses Association is accredited as an approver of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

GIVE The LDA received educational gift support
STEVEN & ALEXANDRA COHEN FOUNDATION for this conference from
Steven & Alexandra Cohen Foundation

The LDA received a donation for commercial support
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SCHOLARSHIPS OFFERED Lyme Disease Association, Inc. (LDA)

is offering scholarships to the conference to eligible medical students, residents, post-doctoral candidates, fellows, veterinarians with equivalent status to the above, and nurse practitioner candidates.



REGISTRATION, HOTEL & CONFERENCE DETAILS go to the LDA website www.LymeDiseaseAssociation.org

Lyme & Tick-Borne Diseases Conference: What Clinicians Need to Know about an Expanding Epidemic

An educational and networking event featuring prominent speakers on tick-borne diseases

Columbia University & Lyme Disease Association, Inc. Conference Faculty

AGENDA - SATURDAY SEPTEMBER 23, 2017

Registration / Exhibits / Continental Breakfast (7:15 - 8:00 a.m.)

Patricia V. Smith, President, BA (8:00 - 8:20 a.m.)

President, Lyme Disease Association, Inc., Jackson, NJ
Conference Planner, Conference Organizing Committee
Welcome, Remarks / Brief Overview of LDA, Lyme & TBD

Introduction of:

Brian A. Fallon, MD, MPH, Course Director, Organizing Committee

Saturday Morning Facilitator

Nicole Baumgarth, DVM, PhD Keynote (8:20 - 9:00 a.m.)

Professor, Pathology, Microbiology, Immunology
Center for Comparative Medicine, University of California Davis, Davis, CA
Borrelia burgdorferi and the Subversion of the Adaptive Immune Response

Garth Ehrlich, PhD, FAAAS (9:00 - 9:35 a.m.)

Professor Microbiology/Immunology
Executive Director, Center for Biofilms & Chronic Infections
Drexel University College of Medicine, Philadelphia, PA
Development of pan-domain diagnostics to provide accurate and comprehensive analyses of Lyme Disease and tick-borne co-infections

Eva Sapi, PhD (9:35 - 10:10 a.m.)

Professor and Department Chair, Director of Lyme Disease Program
Department of Biology and Environmental Science
University of New Haven, West Haven, CT
Biofilms and Lyme Disease

Morning Discussion Panel (10:10 - 10:25 a.m.)

Coffee Break (10:25 - 10:40 a.m.)

Ying Zhang, MD, PhD (10:40 - 11:15 a.m.)

Professor, Dept. of Molecular Biology & Immunology
Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
Persisters

John Aucott, MD (11:15 - 11:50 p.m.)

Asst. Professor of Medicine, Johns Hopkins University School of Medicine
Director, Johns Hopkins Lyme Disease Clinical Research Center, Baltimore, MD
Immune Biomarkers in Lyme Disease

Sheila Arvikar, MD (11:50 - 12:25 p.m.)

Physician Scientist, Rheumatology, Allergy and Immunology and Center for Immunology and Inflammatory Diseases
Massachusetts General Hospital (MGH); Instructor of Medicine at Harvard Medical School, Boston, MA
Autoimmune Disorders Following Lyme Disease

Late Morning Discussion Panel (12:25 - 12:40 p.m.)

Lunch (12:40 - 1:45 p.m.)

Beatrice M. Szantyr, MD

Afternoon Facilitator

Brian A. Fallon, MD, MPH (1:45 - 2:20 p.m.)

Professor of Psychiatry
Director, Lyme & Tick-Borne Diseases Research Center
Columbia University Medical Center
Director, Center Study of Neuroinflammatory Disorders/Biobehavioral Medicine
New York State Psychiatric Institute, New York, NY
Why do Symptoms Persist?

Robert Bransfield, MD, DLFAPA (2:20 - 2:55 p.m.)

Associate Clinical Professor, Rutgers-RWJ School of Medicine
Private Practice in Psychiatry, Red Bank, NJ
The Psychoimmunology of Lyme and Associated Diseases

Diego Cadavid, MD (2:55 - 3:30 p.m.)

Adjunct Associate Professor, Neurology and Neuroscience
New Jersey Medical School, Rutgers, Newark, NJ
Vice President of Clinical Development
Fulcrum Therapeutics, Cambridge, MA
Treatment of Neurologic Lyme Disease

Mid-Afternoon Discussion Panel (3:30 - 3:45 p.m.)

Afternoon Coffee Break (3:45 - 4:00 p.m.)

Sam Telford, III, ScD (4:00 - 4:35 p.m.)

Professor, Infections Diseases and Global Health, Tufts University, Grafton, MA
Babesia microti, B. duncani, & B. miyamotoi

Ed Breitschwerdt, DVM (4:35 - 5:10 p.m.)

Professor of Medicine & Infectious Diseases
North Carolina State University College of Veterinary Medicine
Adjunct Professor of Medicine, Duke
Director, Intracellular Pathogens Res. Lab, Ctr for Comp. Med./Translational Res.
Co-Director, Vector-Borne Diseases Diagnostic Lab
Director, NCSU-CVM Biosafety Level 3 Laboratory, Raleigh, NC
Chief Scientific Officer, Galaxy Diagnostics, Inc.
Bartonella henselae

Saravanan Thangamani, MSc, PhD (5:10 - 5:45 p.m.)

Associate Professor, Department of Pathology
Vice-Chair, Institutional Animal Care and Use Committee
Director, Insectary Services Core
Director, Arthropod Containment Laboratories
University of Texas Medical Branch, Galveston, TX
Powassan Virus: An Emerging Tick-Borne Virus of Public Health Concern in North America

Late Afternoon Discussion (5:45 - 6:00 p.m.)

NETWORKING RECEPTION (6:00 - 8:00 p.m.)

AGENDA - SUNDAY SEPTEMBER 24, 2017

Registration / Exhibits (7:30 - 8:00 a.m.)

John Aucott, MD

Sunday Facilitator

Monica E. Embers, PhD (8:00 - 8:35 a.m.)

Research Assistant Prof., Division Bacteriology/Parasitology
Tulane National Primate Research Center, Covington, LA
The Challenges of Diagnosing and Curing Late Stage Lyme Disease

Safwan Jaradeh, MD (8:35 - 9:10 a.m.)

Professor of Neurology and Neurological Sciences
Autonomic and Neuromuscular Disorders
Stanford University School of Medicine, Stanford, CA
Autonomic Dysfunction in Post-Infectious States

Adrian Baranchuk, MD, FACC, FRCPC, FCCS (9:10 - 9:45 a.m.)

Professor of Medicine, Queen's University, Ontario, CA
Lyme Carditis and Management of High Degree AV Block

Ahmet Z. Burakgazi, MD (9:45 - 10:20 a.m.)

Assistant Professor, Neuroscience Section/Dept. of Neurology
Virginia Tech Carilion School of Medicine, Roanoke, VA
Case Report: Optic Neuritis and Probable Lyme Disease

Food Break (10:20 - 10:55 a.m.)

Morning Discussion Panel (10:55 - 11:15 a.m.)

Lorraine Johnson, JD, MBA (11:15 - 11:50 p.m.)

CEO, LymeDisease.org
Principle Investigator, MyLymeData
Member, Pt Centered Research Outcomes Inst, Expert Panel Open Access
Steering Committee, Consumers United for Evidence-Based Healthcare
MyLymeData: The Value of Using Big Data and Subgroup Analysis in Lyme Disease

Chronic Lyme Panel (11:50 - 12:25 p.m.)

Nicole Baumgarth, DVM, PhD
Beatrice M. Szantyr, MD
Brian Fallon, MD, MPH
Lorraine Johnson, JD, MBA
Challenges in the Study of Chronic Lyme Disease

Maya R. Jerath, MD, PhD (12:25 - 1:00 p.m.)

Associate Professor of Medicine and Pediatrics
Associate Chief of Clinical Allergy, Division of Rheumatology, Allergy & Immunology
Director, Allergy and Immunology Clinic, University of North Carolina, Chapel Hill, NC
Alpha-gal Meat Allergy

BREAK (1:00 - 1:15 p.m.)

Christopher D. Paddock, MD, MPHTM (1:15 - 1:50 p.m.)

Medical Officer, Rickettsial Zoonoses Branch
Centers for Disease Control and Prevention, Atlanta, GA
The Evolving Mosaic of Tick-Borne Rickettsioses in the United States

Beatrice M. Szantyr, MD (1:50 - 2:25 p.m.)

Internal Medicine, Pediatrics and Adolescent Medicine, Lincoln, ME
Prevention: Tick-Bite Management, Personal Protection, Vaccine Development - What's Known & What's New

Afternoon Discussion Panel (2:25 - 2:45 p.m.)

Challenges in the Study of Chronic Lyme Disease

Moderator: Monica Embers PhD

Panel Members:

Nicole Baumgarth, DVM, PhD
Bea Szantyr, MD
Brian Fallon, MD, MPH
Lorraine Johnson, JD, MBA
Diego Cadavid, MD

**THANK YOU
FOR JOINING US!**

SYNOPSIS OF LECTURES



Nicole Baumgarth, DVM, PhD, Keynote — *Borrelia burgdorferi* and the Subversion of the Adaptive Immune Response

Borrelia burgdorferi is capable of establishing persistent infections in a wide variety of species, particularly rodents. Infection is asymptomatic or mild in most reservoir host species, indicating successful co-evolution of the pathogen with its natural hosts. Infected humans and other incidental hosts, however, can develop Lyme disease, a serious inflammatory syndrome characterized by tissue inflammation of joints, heart, muscles, skin and CNS. While *B. burgdorferi* infection induces both innate and adaptive immune responses, they are ultimately ineffective in clearing the infection from reservoir hosts, leading to bacterial persistence. The goal of our work is to document evidence of immune suppression and to identify the exact immune targets of *Borrelia* such immune suppression. Here I will present studies conducted in our laboratory using mouse models of infection that identify the adaptive immune response, and particularly, "T cell dependent antibody responses" as a particular target. This type of immune response usually provides high affinity antibodies against pathogens and provides the host with long-lasting "memory" and immune protection in response to an infection. Ineffective immunity would result in a lack of bacterial/pathogen clearance and allow for repeat infections to occur. A better understanding of the mechanisms causing persistence in rodents may help to increase our understanding of the pathogenesis of Lyme disease and ultimately aid in the development of therapies that support effective clearance of the bacterial infection by the host's immune system.



Garth Ehrlich, PhD, FAAAS — Development of Pan-Domain Diagnostics to Provide Accurate and Comprehensive Analyses of Lyme Disease and Tick-Borne Co-Infections

Lyme disease, strictly speaking, is defined as infection by the tick-borne spirochete, *Borrelia burgdorferi*. *B. burgdorferi* itself reveals extensive genomic plasticity which manifests itself clinically as highly variable disease symptoms in infected individuals. These include great variations in the severity and the chronicity of the disease, and the tissue tropism. However, this complexity is combinatorially amplified as there are both several other tick-transmitted *Borrelia* species that cause similar symptoms; and in a high proportion of cases the transmitting tick bite will also result in infection with one or more other pathogens which can be viral, bacterial (including *Rickettsia* and other obligate intracellular bacterial pathogens), or even eukaryotic parasites. Thus, both the epidemiological characterization of region-specific endemic tick populations and the diagnosis of tick-borne infections requires multiple pan-domain technologies to determine the spectrum of co-infections, as well as strain specific diagnostics once the species are determined. Only then will it be possible to provide adequate therapeutic and prognostic information for the management of affected persons. Toward these ends we have been developing pan-domain, species-specific rRNA gene-based diagnostics for both bacterial and eukaryotic pathogens using the third generation, long-read DNA sequencing system produced by Pacific Biosciences (PacBio). This platform provides for circular consensus sequencing of entire genes. It is possible for the first time to perform error correction on single molecule sequencing which provides highly accurate species-specific analysis. Co-incident with the development of the laboratory methods we also developed and validated a multi-step data processing algorithm which eliminates the over-calling of the number of taxa present, and constructed new databases to support the long-read technology.



Eva Sapi, PhD — Biofilms and Lyme Disease

Lyme disease patients are treated with various antibiotics though the rates of relapse and recurrence of the disease are frequent after discontinuing the antibiotic treatment. It was proposed earlier that the observed antibiotic resistance and reoccurrence of Lyme disease might be due to the formation of defensive morphological forms of *Borrelia burgdorferi*. In addition to its familiar spirochete form, *B. burgdorferi* can transform from motile spirochetes into round body and biofilm forms in the presence of unfavorable environmental conditions including the presence of antimicrobial agents. Our laboratory has demonstrated that *B. burgdorferi* biofilm formation enhances the antibiotic resistance of the organism to various antimicrobial agents, which previously showed some success against the spirochete and round body forms of *B. burgdorferi*. This data strongly suggests that *Borrelia* biofilm could play significant role in their survival in diverse environmental conditions by providing refuge to individual cells. However, the question remains if these structures can be found *in vivo* and whether these biofilm structures hold significant relevance for the survival strategies for *Borrelia* spp. in infected tissues. We provide evidence of *Borrelia* biofilm presence in various human organs obtained from autopsy tissues of a well-documented Lyme disease patient who died despite of multiple rounds of antibiotic treatments. Findings of the role of *Borrelia* biofilm in inflammatory processes will be also discussed as well as our recent metagenomics findings indicating potential co-infection in *Borrelia* biofilms



Ying Zhang, MD, PhD — Persisters

In this presentation, the causes as to why some patients continue to suffer from post-treatment Lyme disease syndrome (PTLDS) despite antibiotic treatment will be discussed. In particular, the relevance of *Borrelia* persistence in animal models and *in vitro* to the PTLDS condition in patients will be addressed. Different strategies for treating persistent infection will be presented in terms of drug combination treatment as compared to pulse dosing. In addition, an update on the search for practical and effective drug combinations that eradicate round bodies and biofilm-like structures *in vitro* will be presented. A path for translating these findings for more effective treatment of persistent Lyme disease will be discussed.



John Aucott, MD — Immune Biomarkers in Lyme Disease

Progress in molecular immunology combined with a focus on translational research has resulted in a unique opportunity for discovery of immune biomarkers for Lyme disease. The SLICE study at Johns Hopkins has enrolled hundreds of patients with well validated and meticulously characterized Lyme disease at all stages of illness. The careful clinical analysis of these patients allows the formation of distinct subgroups of patients with unique characteristics. These subgroups have more homogenous features that increase the ability to find biologic markers of illness. The SLICE studies large biorepository of blood samples is analyzed by different methods in order to identify different types of immune biomarkers. The types of biomarkers include the genetic blueprints for the immune response, the immune proteins themselves as well as the immune cells in our blood. This talk will review several immune biomarkers that may be important for diagnostic, prognostic and treatment guidance for the future



Sheila Arvikar, MD — Autoimmune Disorders following Lyme Disease

One of many challenges in Lyme disease is the symptoms which may persist despite treatment. Musculoskeletal complaints are prominent among these symptoms, and may range from arthralgia (joint pains without inflammation) seen in Post-Treatment Lyme disease Syndrome to frank arthritis with inflammation and swelling as in Lyme arthritis. There may be multiple mechanisms for these phenomena, including immune dysregulation and autoimmunity. With Lyme arthritis, an immune-mediated inflammatory arthritis may persist after antibiotic treatment. However this is usually confined to a single previously infected joint, without systemic symptoms. We have recently described a cohort of 30 patients who developed new-onset rheumatoid arthritis, psoriatic arthritis or peripheral spondyloarthritis, a median of 4 months after antibiotic treatment for Lyme disease. In the majority, the rheumatic disease followed an early manifestation of Lyme disease such as erythema migrans. These patients often had distinguishing clinical features from Lyme arthritis patients including family history of autoimmunity, involvement of many joints, involvement of the spine and entheses (tendon insertion sites), and the onset of skin psoriasis. They also had distinguishing laboratory features from Lyme arthritis patients such as rheumatoid arthritis-specific biomarkers, significantly lower titers of antibodies to *B. burgdorferi* and lower frequency of Lyme-associated autoantibodies. The patients were treated with typical inflammatory therapies which the standard of care for these diseases, resulting in improvement. In addition to this cohort, we have seen other types of systemic autoimmune diseases follow Lyme including systemic lupus and thyroid disease. Autoimmune neurologic conditions have also been reported. Although systemic autoimmune diseases may follow Lyme disease by chance, onset within months suggests that *B. burgdorferi* infection may be a pro-inflammatory trigger. Clinicians need to be aware of this possibility when evaluating patients with post-infectious symptoms. Although this may not be a common outcome, given that Lyme is now epidemic in parts of the U.S., awareness of autoimmune disease in the spectrum of post-Lyme syndromes is essential in preventing delays in appropriate diagnosis and treatment.



Brian A. Fallon, MD, MPH — Why do Symptoms Persist?

Persistent symptoms after a course of antibiotic therapy can cause considerable distress, functional impairment, and controversy between patients and doctors and between doctors themselves. This talk will review the evidence in support of several potential causes of symptom persistence: persistent infection, tissue damage from prior infection, altered immune activation, altered brain neural networks, altered microbiome, unrecognized other diagnoses.



Robert Bransfield, MD, DLFAPA — The Psychoimmunology of Lyme and Associated Diseases

Attention to psychoimmunology helps us understand the pathophysiological sequence that begins as a tick-borne or other infection and results in psychiatric symptoms. The nervous system and immune system communicate with each other and have many similarities—both have innate and adaptive capabilities, both involve complex communication between cells, both have similar pathophysiological processes. Many genes associated with mental illness involve immune functioning. Although there are multiple other contributors that provoke and weaken the immune system, acute and persistent infections are a major cause of pathological immune reactions resulting in disease progression. Adaptive functioning involves recognition of danger and early inflammation followed by adaptive immunity. *Borrelia burgdorferi* has the capacity to evade and suppress the immune system. In pathophysiological processes, this can result in persistent infection, persistent inflammation with cytokine effects without adaptive immunity, sometimes accompanied with autoimmune reactions. Persistent infection in the body can result in persistent immune effects that cross the blood brain barrier and result in neuropsychiatric symptoms. Sickness syndrome associated with interferon treatment and autoimmune limbic encephalopathies are models to understand inflammatory and molecular mimicry effects upon neuropsychiatric symptoms. Progressive inflammatory reactions have been proposed as a model to explain disease progression in other mental illnesses. Pathophysiological changes have been associated with oxidative stress, excitotoxicity, changes in homocysteine metabolism and altered tryptophan catabolism. Lyme disease has been associated with the proinflammatory cytokines IL-6, IL-8, IL-12, IL-17, IL-18, IL-10 and interferon-gamma, the chemokines CXCL12 and CXCL13, CRP, CNS gliosis, Bb impacting neuronal and Schwann and glial cells, proinflammatory lipoproteins, increases in quinolinic acid, Bb surface glycolipids and flagella antibodies eliciting anti-neuronal antibodies and anti-neuronal antibodies and dissemination of immune reactions from the periphery to inflame the brain. Immune mediated effects of Lyme and other tick-borne diseases contribute to cognitive impairments, dementia, depression, anxiety, autism, violence and other psychiatric illnesses. Autism spectrum disorders associated with Lyme/tick-borne diseases may be mediated by a combination of inflammatory and molecular mimicry mechanisms.



Diego Cadavid, MD — Treatment of Neurological Lyme Disease

In humans, *Borrelia burgdorferi* causes Lyme disease. People become infected when bitten by ticks carrying the bacterium. The person may experience symptoms in the joints, skin, muscles, and nervous system (peripheral nerves (nerves outside the brain and spinal cord), the brain, and the spinal cord). Without antibiotic treatment, neurological Lyme either may resolve or cause long-term problems. Neurological Lyme differs between Europe and the United States, probably because of differences in *B. burgdorferi*. Limited information exists about which antibiotics are better for the treatment of neurological Lyme. A recently completed Cochrane review of the existing evidence found seven trials studying antibiotic treatments for neurological Lyme disease. All but one trial compared different antibiotics. The other trial compared the treatment effects of oral amoxicillin to placebo following initial ceftriaxone treatment. The trials included 450 Europeans. The antibiotics tested were penicillin G, doxycycline, ceftriaxone, and cefotaxime. One of the trials involved children only, while the others included mostly adults. We only selected studies in which treatment allocation was determined by chance (randomly), as such studies provide the best information for comparing the effects of different treatments. Most studies were not blinded. We could not find any studies of antibiotic treatments for neurological Lyme disease from the U.S. No studies assessed the effects of delaying the start of treatment. The 7 studies were too different for their results to be combined, so they were analyzed individually. The results showed that none of the studies provided clear evidence that one antibiotic was better than another. One study failed to find evidence that a second and longer treatment with an oral antibiotic (amoxicillin) offered any extra benefit following initial treatment with ceftriaxone. As none of the other studies used a placebo, the extra benefit offered by antibiotic treatment over recovery that occurs naturally is unknown. Generally, the treatment was tolerated well, although the quality of adverse event reporting in most studies appeared to be low. This systematic review of the existing literature indicate that treatment with penicillin G, doxycycline, ceftriaxone, and cefotaxime produced similarly good outcomes for treatment of neurological Lyme disease in Europe. A 2nd treatment with amoxicillin does not appear to provide added benefit to ceftriaxone. We found no trials of antibiotics for treatment of neurological Lyme disease in the U.S. that met our inclusion criteria.



Sam Talford, III, ScD — *Babesia microti, B. duncani, & B. miyamotoi*

I will review the epidemiology, clinical picture, diagnosis, and treatment of human babesiosis, particularly with respect to the northeastern U.S. Babesiosis is increasing in prevalence and distribution after having lagged that of the co-transmitted Lyme disease. Elsewhere in the U.S. and globally, babesiosis remains a rare and sporadic infection usually affecting only severely immunocompromised individuals. Babesiosis is the most important protozoal transfusion risk because infection tends to be subclinical in healthy younger individuals and donors cannot be excluded based solely on questions about exposure history. Even with treatment, case fatality rates can approach 5%; new treatment regimens need to be developed, particularly for patients who are immunocompromised. Risk of acquiring babesiosis may be reduced by preventing tick exposure or by the many modalities to reduce environmental contamination by ticks. Vaccine development remains a challenge, a perspective that follows from the difficulties faced by the efforts to develop effective vaccines against the related malaria parasites.



Ed Breitachwerdt, DVM — *Bartonellosis: Update on an Emerging Infectious Disease*

Bartonella species are fastidious Gram-negative bacteria that are highly adapted to a mammalian reservoir host and within which the bacteria usually cause a long-lasting intra-erythrocytic and endotheliotropic bloodstream infection. These facts are of particular importance to veterinarians, physicians, diagnosticians and public health officials, as an increasing number of animals have been identified as reservoir hosts for zoonotic *Bartonella* species. Among numerous examples, *Bartonella henselae*, *Bartonella koehlerae* and *Bartonella clarridgeae* have co-evolved with cats. *Bartonella vinsonii subsp. berkhoffii* and *Bartonella rochalimae* have co-evolved with wild canines, and *Bartonella bovis* has co-evolved with cattle. Importantly, the list of reservoir-adapted *Bartonella* species, including a large number of recently identified bat and rodent species, continues to expand exponentially, as new *Bartonella* spp. and additional reservoir hosts are discovered throughout the world. Bartonellosis is a zoonotic infectious worldwide disease, caused by *Bartonella* spp. Of comparative medical importance, *Bartonella* spp. are transmitted by several arthropod vectors, including fleas, keds, lice, sand flies, ticks and potentially mites and spiders. Prior to 1990, there was only one named *Bartonella* species (*B. bacilliformis*), now over 36 species—17 have been associated with an expanding spectrum of animal and human diseases. Recent advances in diagnostic techniques have facilitated documentation of chronic bloodstream infections with *Bartonella* spp. in healthy and sick animals, and in immunocompetent and immunocompromised human patients with vascular, neurological and rheumatologic symptoms..



Saravanan Thangamant, MSc, PhD — *Powassan Virus: An Emerging Tick-borne Virus of Public Health Concern in North America*

Powassan virus (POWV, *Flaviviridae*) is the only N. American member of the tick-borne encephalitis serogroup of flaviviruses. It is transmitted to small- and medium-sized mammals by *Ixodes scapularis*, *Ixodes cookei*, and several other *Ixodes* tick species. Humans become infected with POWV during spillover transmission from the natural transmission cycles. In humans, POWV is the causative agent of a severe neuroinvasive illness with 50% of survivors displaying long-term neurological sequelae. POWV was recognized as a human pathogen in the 1958 index case when a young boy died of severe encephalitis in Powassan, Ontario, and POWV was isolated from a brain autopsy. Two distinct genetic lineages of POWV are now recognized: POWV (lineage I) and deer tick virus (lineage II). Since the index case over 100 human cases of POWV have been reported, with an apparent rise in disease incidence in the past 16 years. This increase in cases may represent a true emergence of POWV in regions where the tick vector species are prevalent or could represent an increase in POWV surveillance and diagnosis. The past 5 years, both basic and applied research for POWV disease has intensified, including phylogenetic studies, field surveillance, case studies, and animal model development. This talk is an overview of POWV, including epidemiology, transmission, clinical disease, and diagnosis of POWV infection. Future priorities and challenges with regard to the disease are will also be emphasized.



Monica E. Embers, PhD — *The Challenges of Diagnosing and Curing Late Stage Lyme Disease*

According to recent estimates, the number of new Lyme disease cases in the U.S. may exceed 300,000 per year. Given the breadth of clinical manifestations that can result from infection with the spirochete *Borrelia burgdorferi*, reliable laboratory diagnostic testing is essential. Currently, the two-tier test, an initial enzyme immunoassay followed by a confirmatory western blot, is the standard. However, this serological testing falls short in sensitivity, especially in the early/acute phase. Another significant issue is the proportion of patients who continue to experience signs and/or symptoms of disease following antibiotic therapy. This phenomenon, known as post-treatment Lyme disease syndrome (PTLDS) may be defined by fatigue, musculoskeletal pain, and cognitive problems that persist for 6 months or more after completion of antibiotic therapy. It is clear that two-tier serologic testing is neither sensitive nor specific enough for diagnosis of PTLDS because of variability in serologic responses after treatment of early Lyme. A multiplex assay that utilizes Luminex® technology has been developed and includes five antigens (OspA, OspC, DbpA, OppA-2 and the C6 peptide). We are using this test to identify differences in serum responses during early disease and in PTLDS. Initial studies indicate a significant improvement over two-tier for detecting exposure in PTLDS patients. While experimental studies in animals have offered evidence of post-treatment persistence of *B. burgdorferi*, variations in methodology, detection methods and limitations of the models have led to some uncertainty with respect to translation to human infection. We sought to mimic human infection and treatment in the closest animal model, namely, the nonhuman primates. Rhesus macaques were inoculated with *B. burgdorferi* by tick bite and a portion were treated with recommended doses of doxycycline for 28 days at four months post-infection. Signs of infection, clinical pathology, and antibody responses were monitored throughout the ~1.2 year study. Our results demonstrate host-dependent signs of infection and variation in antibody responses. We observed evidence of persistent, intact, metabolically-active *B. burgdorferi* and associated foci of inflammation in central and peripheral nervous tissue, joints and heart after antibiotic treatment of the disseminated infection.



Safwan Jaradeh, MD — *Autonomic Dysfunction in Post-Infectious States*

Clinical interests include autonomic disorders, small fiber neuropathies and the development of effective methods of testing and treating these disorders. Prior work has focused on small fiber painful and autonomic neuropathies: syndromes of orthostatic intolerance and syncope; gastrointestinal motility dysfunction; cyclic vomiting; protracted Gastroesophageal Reflux; non-allergic rhinitis syndromes; and the relationship between the autonomic nervous system and normal or abnormal sleep. Additional areas of interest include the neurology of phonation and swallowing disorders, and peripheral nerve injury and repair.



Adrian Baranchuk, MD, FACC, FRCPC, FCCS — *Lyme Carditis and Management of High Degree AV Block*

This presentation will cover all aspects of Lyme carditis with special emphasis on diagnosis and management of electrical disturbances. Very little information is available on how to handle these particular cases, and quite frequently, extrapolation from other cardiac causes of electrical disturbances is applied. This is particularly disturbing as most of Lyme carditis patients are young and they may completely recover from the heart infection and inflammation. The presentation will be illustrated with 2 local cases in the endemic region of Canada and show how the management of these cases requires a different approach than the one provided for most of cardiac patients.



Ahmet Z. Burakgazi, MD — *Case Report: Optic Neuritis and Probable Lyme Disease*

Optic neuritis (ON) is one of the most common manifestations of central nervous system involvement caused by various etiologies. Lyme ON is an exceedingly rare ocular manifestation of Lyme disease (LD) and only a few cases have been published in the literature. Lyme ON is very rare but should be included in the differential diagnosis in unexplained cases, particularly in Lyme endemic areas. Careful and detailed examination and investigation are warranted to make the diagnosis. I will talk on this case to increase awareness of clinicians to include Lyme disease in differential diagnosis of ON for unexplained cases of ON. I will present a unique case with a unilateral ON caused by LD along with pre- and posttreatment findings and literature review.



Lorraine Johnson, JD, MBA — *MyLymeData: The Value of Using Big Data and Subgroup Analysis in Lyme Disease*

In 2015, LymeDisease.org launched the first national Lyme disease patient centered registry and research platform, MyLymeData. The registry has enrolled over 8,000 patients and is in the top 10% of patient registries in the nation. The registry will be used to answer questions that are important to patients and to track real world treatment effectiveness and quality of care improvement. It will also be used as a framework for clinical trials. This presentation will focus on patient-generated data from Phase 1 of MyLymeData and the value of subgroup analysis using big data. This will be illustrated with examples drawing on chronic Lyme disease case definitions, average treatment effect verses subgroup analysis of treatment effect, and the use, effectiveness, and side effects associated with different alternative therapies.



Maya R. Jerath, MD, PhD — *Alpha-Gal Allergy*

Galactose-1,3-galactose ("alpha-gal") is a newly recognized allergen that is responsible for a broad array of allergic reactions. Allergic sensitivity to alpha-gal is believed to be acquired, possibly through a tick bite. Patients who acquire this allergy manifest allergic reactions after eating mammalian food products such as beef hamburgers and pork sausages. We will review food allergies in general – who gets them, what the symptoms are, how the diagnosis is made, and how it is managed. We will then move on to the clinical presentation of alpha-gal allergy and discuss how it is managed. The evidence for the role that ticks play in its onset will be presented. We will discuss how this allergy differs from other food allergies and why unraveling its mechanisms has the potential to significantly change how we view food allergy in general.



Christopher D. Paddock, MD, MPHTM — *The Evolving Mosaic of Tick-Borne Rickettsioses in the United States*

Many fundamental principles regarding tick-borne rickettsioses in the North America have required re-examination since the beginning of the 21st century. As recently 2002, all tick-borne rickettsiosis in the United States and other continents of the western hemisphere was attributable to infection with a single pathogen, *Rickettsia rickettsii*. Unique species or strains of pathogenic *Rickettsia*, including many that were isolated from ticks during preceding decades but remained uncharacterized until the advent of molecular techniques, have now been characterized and are likely to influence the epidemiology of spotted fever group rickettsiosis in various regions of the U.S. Collectively, these processes emphasize the dynamic nature of tick-borne rickettsioses, and the necessity to continuously consider the fluid and varied ecological, social, and temporal interactions among humans, ticks, vertebrate hosts and *Rickettsia* in the emergence and epidemiology of these diseases.



Beatrice M. Szantry, MD, FAAP — *Prevention: Tick Bite Mgt, Personal Protection, Vaccine Development - What's Known & What's New*

The challenges faced in diagnosing and treating later presentations and manifestations of Lyme disease make the importance of prevention strategies clear. Several levels of prevention apply: from the narrowest aspect that is tick bite management, to tick avoidance and personal protection and property management strategies, to the broadest concepts of environmental awareness and management (One Health: diversity, environment, reservoir hosts.) A full working knowledge of prevention methods is crucial for health care providers to have so that they can educate their patients, ideally, before a close encounter with a tick occurs or more commonly, at the time of a tick attachment, to prevent subsequent ones. The evidence base for prevention strategies has been growing in recent years and some recommendations have increasing strength of support. Still, a number of issues remain unsettled, and conflicting recommendations exist. This session will present the evidence base for management of *Ixodes* tick bites in preventing Lyme disease. It will also address specific personal protection methods to reduce the possibility of tick attachments, progress in vaccine development for people, domestic animals and wildlife, property management techniques, and follow-up on an innovative genetic approach to environmental-level management.

REGISTRATION, HOTEL & CONFERENCE DETAILS go to the LDA website www.LymeDiseaseAssociation.org