Lyme & Other Tick-Borne Diseases: 20th Annual Scientific Update for Clinicians & Researchers

LYME DISEASE ASSOCIATION, INC.
A national non-profit
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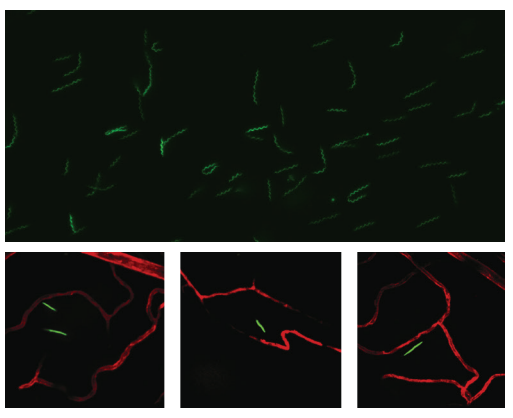


GFP-expressing relapsing fever agent Borrelia hermsii. Rupali Walia and George Chaconas

Intravital imaging of transmigrated B. burgdorferi in the knee joint-proximal tissue of a living mouse. From Kumar et al, PLoS Pathog. 2015 18;11(12):e1005333…

Jointly Provided by:

COLUMBIA
VAGELOS COLLEGE OF PHYSICIANS AND SURGEONS

LYME DISEASE ASSOCIATION, INC.
A National Non-Profit

Sat. & Sun., September 21 & 22, 2019

Philadelphia, PA

Hilton Philadelphia at Penn's Landing

201 S. Christopher Columbus Blvd., Philadelphia, Pennsylvania 19106

Accreditation Statement 2019 Columbia/LDA CME Lyme Conference

AMA Credit Designation Statement: The Columbia University Vagelos College of Physicians and Surgeons designates this live activity for a maximum of 14.25 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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 Columbia University Vagelos College of Physicians and Surgeons and the Lyme Disease Association. The Columbia University Vagelos College of Physicians and Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

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

Target Audience: The target population is physicians from all specialties, nurses, psychologists, scientists, public health workers. It is also open to the public, and Lyme disease educators generally attend. The geographic area being reached is nationwide. No special background is required for effective participation, although those whose practices contain a high proportion of Lyme disease patients and those whose research concentrates on Borrelia burgdorferi will receive the most benefit.

Learning Objectives:
Clinicians should have better ability to use current diagnostic tests and to understand the difference between direct & indirect testing
Clinicians should be able to describe the manifestations and tests for Babesia duncani, spotted fevers, Powassan virus, and anaplasma
Clinicians should be able to explain to patients that changes in the microbiome may impact brain function
Clinicians should be able to describe some of the key immune biomarker findings in Lyme disease
Clinicians should be able to describe the possible ocular, neurologic, and cardiac effects of Lyme disease

GIVE
STEVEN & ALEXANDRA COHEN FOUNDATION

The LDA received educational gift support for this conference from the **Steven & Alexandra Cohen Foundation**

The LDA received a donation for commercial support for this conference from **IGeneX,Inc.**

SCHOLARSHIPS OFFERED
Lyme Disease Association, Inc. (LDA)

Medical student; resident; post-doctoral candidate; fellow; nurse practitioner candidate; doctor or nurse practitioner new to practice, i.e., less than 5 years experience; veterinarian with equivalent status to the aforementioned; physician assistant whose sponsoring physician writes a letter of support on office letterhead; representative from a public health department.

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

Lyme & Other Tick-Borne Diseases: 20th Annual Scientific Update for Clinicians & Researchers

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

AGENDA - SATURDAY September 21, 2019

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

Patricia V. Smith, President, BA (8:00 a.m. - 8:20 a.m.)
President, Lyme Disease Association, Inc., Jackson, NJ
Conference Planning Committee; Organizer
Welcome, Remarks / Brief Overview of LDA, Lyme & TBD

Charles Chiu, MD, PhD/Keynoote (8:20 a.m.-9:00 a.m.)
Professor, Laboratory Medicine and Medicine
Division of Infectious Diseases
University of California,
San Francisco (UCSF) School of Medicine, San Francisco, CA
"Multi-Omics approaches to diagnosis of Lyme disease and other tick-borne infections"

George Chaconas, PhD (9:00 a.m.-9:35 a.m.)
Professor of Biochemistry and Molecular biology, Dept. of Microbiology, Immunology and Infectious Diseases
University of Calgary, Alberta, Canada
"An inside look at the life of a pathogen: Intravital imaging to study hematogenous dissemination of the Lyme disease spirochete"

Emir Hodzic, DVM, MSc, PhD (9:35 am.-10:10 a.m.)
Director, Real-Time PCR Research & Diagnostics Core Facility School of Veterinary Medicine
Department of Medicine and Epidemiology
University of California, Davis, CA
"Post-treatment persistence of antimicrobial tolerant replicatively-attenuated Borrelia burgdorferi in a mouse model"

Morning Discussion Panel (10:00 a.m.-10:25 a.m.)

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

Saturday facilitator Sam Donta, MD

Adrian Baranchuk, MD, FACC, FRCPC, FCCS (10:40 a.m.-11:15 a.m.)
Professor of Medicine (Tenure) Queen's University
Ontario, Canada
"Systematic approach for the diagnosis and treatment of Lyme carditis"

Osama Haddad, MD (11:15-11:50 p.m.)
Department of Thoracic and Cardiovascular Surgery
Cleveland Clinic, Cleveland, OH
"Mitral Valve Endocarditis: A Rare Manifestation of Lyme Disease"

Peter Novak, MD, PhD (11:50 p.m.-12:25 p.m.)
Division Chief, Autonomic Neurology
Director, Autonomic Laboratory
Department of Neurology, Brigham and Women's Faulkner Hospital
Assistant Professor of Neurology, Harvard Medical School
Boston, MA
"Neurological correlates of Post Treatment Lyme Disease Syndrome"

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

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

Holly M. Frost, MD (1:45-2:20)
Assistant Professor
Department of Pediatrics
Denver Health Medical Center
University of Colorado School of Medicine
Denver, CO
"The pitfalls of serologic assays for the diagnosis of tick-borne diseases: a case series and review of the literature"

Robert Naviau, MD, PhD (2:20 p.m.-2:55 p.m.)
Professor of Genetics, Biochemical Genetics and Metabolism Departments of Medicine, Pediatrics, and Pathology; Co-director, Mitochondrial and Metabolic Disease Center
UCSD School of Medicine
San Diego, CA
"Metabolomic Features of Acute and Chronic Lyme Disease—Early Results from the UCSD Lyme-ME/CFS Comparison Study "

Madeleine W. Cunningham, PhD. (2:55 p.m.-3:30.p.m.
Professor, Microbiology & Immunology
Directory, Immunology Training Program
University of Oklahoma Health Sciences Center, OK
"From Bench to Bedside:Anti-Neuronal Autoantibodies in Lyme Disease and Beyond"

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

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

Choukri Ben Mamoun, PhD (4:00 p.m.-4:35 p.m.)
Professor, Microbial Pathogenesis & Medicine
Yale School of Medicine, New Haven, CT
"Continuous in vitro culture of Babsesia duncani in human red blood cells: An inflection point in diagnosis and therapy of human babesiosis

Margaret R. MacDonald, MD, PhD (4:35 p.m.-5:10 p.m.)
Research Associate Professor
Laboratory of Virology and Infectious Disease
The Rockefeller University
New York, NY
"Powassan virus: an emerging tick-borne threat"

Brian A. Fallon, MD, MPH (5:10 p.m.-5:45 p.m.)
Professor of Psychiatry
Director, Lyme & TBD Research Center
Director, Ctr. Study of Neuroinflammatory Disorders
Columbia University, Vagelos College of Physicians & Surgeons
New York, NY
"Clinical Trials: Biologic & Clinical Measures of Change"

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

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

AGENDA - SUNDAY SEPTEMBER 22, 2019

Registration/Exhibits/BREAKFAST ON YOUR OWN (7:30 a.m.-8:00 a.m.)

Sunday Facilitator Elizabeth Maloney, PhD

Daniel Sonnenshine, PhD (8:00 a.m.-8:35 a.m.)
Daniel E. Sonenshine, PhD
Professor (Emeritus) Department of Biological Sciences
Old Dominion University
Norfolk, Virginia 23529
"How Climate Change Affects Range Expansion of Tick Vectors and Spread of Tick-Born Diseases in North America"

Robert Yolken, MD (8:35 a.m.-9:10 a.m.)
Professor, Dept. of Pediatrics, Stanley Neurovirology Laboratory
Johns Hopkins UJniversity School of Medicine
Baltimore, MD
"The brain-immune gut axis: a big new idea in neuropsychiatric disorders"

Joanna Lyon, Pharm D. MEd, MHS, CHES, BCGP (9:10 a.m.-9:45 a.m.)
"The possible aswsociatoion between the human ABCB1 gene and Post Treatment Lyme Disease Syndrom"

Mark J. Soloski, PhD (9:45 a.m.-10:20 a.m.)
Professor of Medicine, Pathology, Molecular Biology and Genetics and Molecular Microbiology and Immunoloogy
Johns Hopkins University School of Medicine
Co-Diredctor for Basic Research, Lyme Disease Research Center, Baltimore, MD
"The host immune response in Lyme borreliosis"

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

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

Paige Armstrong, MD, MHS (11:15 a.m.-11:50 a.m.)
Medical Epidemiologist, Rickettsial Zoonoses Branch
Centers for Disease Control & Prevention
Atlanta, GA
"Rickettsial diseases: Epidemiologic trends, clinical diagnosis and management"

J. Stephen Dumler, MD (11:50 a.m.-12:25 p.m.)
Chair, Department of Pathology Uniformed Services University of the Health Sciences
F. Edward Hébert School of Medicine
Bethesda, MD
"Human Granulocytic Anaplasmosis-Emerging Faster than Lyme"

Eric Storch, PhD (12:25 p.m.-1:00 p.m.)
Professor and McIngvale Presidential Endowed Chair
Vice Chair & Head, Psychology
Menninger Department of Psychiatry and Behavioral Sciences
Baylor College of Medicine, TX
"Obsessive Compulsive Disorder"

BREAK (1:00 p.m.-1:10 p.m.)

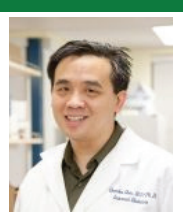
Mid-Morning Discussion (1:10 p.m.-1:25 p.m.)

Lance A. Liotta, MD, PhD(1:25 p.m.-2:00 p.m.
University Professor
Co-Director Center for Applied Proteomics and Molecular Medicine
Medical Director Clinical Proteomics Lab
College of Science
George Mason University, VA
"Shedding of urinary tick pathogen-specific proteins in patients with tick-borne diseases"

Ingeborg Dziedzic, MD, ABAARM (9:10 a.m.-2:35 p.m.)
Pleasant Vision Ophthalmology Practice,
Pleasantville, New York
"Potential late ophthalmic consequences of Lyme Disease"

Afternoon Discussion Panel (2:35 p.m.-3:00 p.m.)

Synopsis of Lectures



Charles Chiu, MD, PhD — *"Multi-Omics approaches to diagnosis of Lyme disease and other tick-borne infections"*

There are approximately 300,000 cases of Lyme disease annually in the U.S., yet accurate and sensitive diagnostic tests for acute infection do not exist. Timely diagnosis is needed to prevent downstream complications of Lyme disease and other undiagnosed tickborne infections. Here I will describe efforts to develop metagenomics and transcriptomic approaches for diagnosis of early Lyme disease. These include development of the TickChip, a sequencing-based platform leveraging a CRISPR-Cas12a technique for comprehensive and multiplexed detection of tickborne pathogens, and the use of globalRNA-Seq transcriptome profiling to characterize host biomarkers for Lyme disease with accuracy exceeding 80%. I will also describe efforts to leverage this research into the validation of implementation of clinical assays in a CLIA (Clinical Laboraotry Improvement Amendments)-certified laboratory for diagnosing early Lyme disease and other acute tickborne infections and for monitoring patients with chronic complications of Lyme disease. Our goal is to validate these assays on a nanopore sequencing platform for real-time analysis and visualization from whole blood and other clinical samples from affected patients. Finally, I will discuss development of a novel platform for comprehensive,genome-wide serological profiling using a phage display approach that can be used to characterize recent and past tickborne infections.

George Chaconas, PhD — *"An inside look at the life of a pathogen: Intravital imaging to study hematogenous dissemination of the Lyme disease spirochete"*

One of the salient features of Lyme borreliosis that makes diagnosis difficult is the multitude of symptoms that can result from the disease. The wide variety of disease manifestations is a consequence of the ability of the spirochete (Borrelia burgdorferi in North America) to disseminate to many locations within the body and to promote pathogenic processes at multiple sites. The disease process starts by inoculation in the skin through the bite of an infected hard-shelled tick (Ixodes species). The first stage of the disease is a localized infection in the skin. The next stage, early disseminated disease, results from invasion of the vasculature by the spirochetes. During this stage B. burgdorferi gets a free ride throughout the body. Finally, when spirochetes exit the bloodstream at an assortment of locations, they can cause a wide variety of physical problems and symptoms. The process by which B. burgdorferi departs from the vasculature into surrounding tissue remains largely unknown and is a focus of studies in my laboratory. This is a complex, multistage procedure that we study using intravital microscopy, a methodology that allows us to see live spirochetes at work in a living mouse, in real time, using spinning disk laser confocal microscopy. The early stages of escape require that a spirochete slows its wild ride in the bloodstream, which is like an ant being swept in a stream of water in a garden hose. This occurs through physical interactions with the endothelium that are mediated by adhesins on the spirochete, proteins that function like Velcro. The spirochetes also promote changes in the blood vessels which allow them to escape to the other side through an as yet uncharacterized mechanism. Intravital videos and data will be presented describing processes involved in both vascular interactions and vascular escape.

Emir Hodzic, DVM, MSc, PhD — *"Post-treatment persistence of antimicrobial tolerant replicatively-attenuated Borrelia burgdorferi in a mouse model"*

A basic feature of infection caused by Borrelia burgdorferi, the etiological agent of Lyme borreliosis, is that persistent infection is the rule in its many hosts. The ability to persist and evade host immune clearance poses a challenge to effective antimicrobial treatment. A link between therapy failure and the presence of persister cells has started to emerge. There is growing experimental evidence that viable, but non-cultivable spirochetes persist following treatment with several different antimicrobial agents. In earlier studies, we have detected a population of B. burgdorferi in tissues after antimicrobial therapy in mice treated with ceftriaxone, doxycycline, or tigecycline at various intervals of infection, and tissues were tested at intervals after treatment. Specific BbDNA was consistently detected in tissues of mice at late at 12 months after treatment, but culture was consistently negative. I will discuss results of that and subsequent study. In the most current study, we utilized a disease-susceptible (C3H/HeN) and disease-resistant (C57BL/6) mouse strain infected with B. burgdorferi strains N40 and B31, to confirm the generality of this phenomena as well as to assess the persisters' clinical relevance. The status of infection was evaluated at 12 and 18-months after treatment. The results demonstrated that persistent spirochetes remain viable for up to 18 months following treatment, as well as being non-cultivable. The clinical relevance of persistent spirochetes and their resurgence beyond 18 months following antimicrobial treatment compels further studies utilizing other animal models.

Adrian Baranchuk, MD, FACC, FRCPC, FCCS — *"Systematic approach for the diagnosis and treatment of Lyme carditis"*

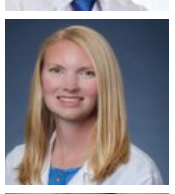
Lyme carditis represents about 2-3% of all Lyme disease presentations. Usually, patients with Lyme carditis are under-recognized in many ER departments. Patients need to visit the ER 2-3 times in average until the diagnosis is suspected. During this presentation, the "Suspicious Index in Lyme carditis (SILC)" will be discussed and its acronym *"COSTAR"* will be presented. This may help physicians to become more familiarized with this type of Lyme disease presentation. A full algorithm on how to treat this condition will be presented. High-degree AV block represents about 90% of all Lyme carditis cases. Failure to recognize this entity may result in preventable fatalities.

Osama Haddad, MD — *"Mitral Valve Endocarditis: A Rare Manifestation of Lyme Disease"*

Lyme Disease affects around 300,000 Americans each year, it is the most common tick-born disease in the northern hemisphere. Lyme disease can lead to death if not treated with antibiotics, it can cause cardiac, neurologic and joint problems with possible permanent tissue damage. Lyme disease is known to affect the heart usually in the form of conduction problems or inflammation of the heart muscle. Involvement of the heart valves is very rare. This case report is the second to be reported in the US and the fourth world wide. The message from the report is the importance of the routine use of the PCR (Polymerase Chain Reaction) to identify DNA of the causative organism in all explanted valve tissues . This will lead to increased awareness of Lyme Disease as a causative agent for Infective Endocarditis disease. The case report was published in the *"Annals of Thoracic Surgery"* journal.

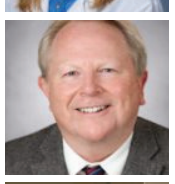
Peter Novak, MD, PhD — *"Neurological correlates of Post Treatment Lyme Disease Syndrome"*

Lyme disease is a transmittable tick-borne infection caused by the spirochete Borrelia burgdorferi. Neurologic sequelae of Lyme disease, termed Lyme neuroborreliosis, occur in 10-15% of patients with untreated Lyme disease. Persistent symptoms despite standard antibiotic therapy of Lyme disease are reported in 10% to 36% of patients. These symptoms, when prolonged for a period of 6 months or longer, are referred to as post-treatment Lyme disease syndrome (PTLDS). Typical symptoms of PTLDS include widespread pain, fatigue, and cognitive disturbances. PTLDS results in considerable impairment of quality of life. The origin of PTLDS symptoms is unclear. Potential mechanisms include direct cytotoxicity by the spirochete, the presence of neurotoxic mediators occurring during host-pathogen interaction, autoimmune reactions or genetic predisposition. The main problem in PTLDS research is lack of the objective biomarker. In our study, we analyzed 10 PTLDS patients (all had history of Lyme disease satisfying CDC criteria) and patients all had evidence of small fiber neuropathy, dysautonomia and abnormal cerebral blood flow. The study suggest that SFN appears to be associated with PTLDS and may be responsible for certain sensory symptoms. Reduced orthostatic CBFv can be associated with cerebral hypoperfusion and may lead to cognitive dysfunction in PTLDS.



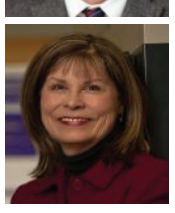
Holly M. Frost, MD — *"The pitfalls of serologic assays for the diagnosis of tick-borne diseases: a case series and review of the literature"*

Lyme disease often presents with non-specific clinical findings that can be confused with other diseases and create diagnostic dilemmas for providers. Despite tremendous research devoted to the development of improved Lyme diagnostic tests, two-tiered Lyme serology remains the mainstay of testing. Unfortunately, significant cross-reactivity exists between Lyme immunoassays and those for other diseases with non-specific clinical findings, including infectious mononucleosis. In this talk we explore the pitfalls of two-tiered Lyme serology to verify or exclude the diagnosis of Lyme disease by examining a case series of patients with clinical presentations and diagnostic tests suggestive of both Lyme disease and infectious mononucleosis



Robert K. Naviaux, MD, PhD — *"Metabolomic Features of Acute and Chronic Lyme Disease—Early Results from the UCSD Lyme-ME/CFS Comparison Study"*

The symptoms of post-treatment Lyme disease syndrome (PTLDS) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) are very similar. Without knowledge of the triggering event, it is not possible to distinguish the two disorders on purely clinical grounds. Both are chronic fatiguing illnesses that lead to long-term pain and disability. Both disorders can display significant post-exertional malaise, disrupted and unrefreshing sleep, headaches, brain fog, autonomic dysfunction with or without postural orthostatic tachycardia syndrome (POTS) and small fiber polyneuropathy (SFPN), GI abnormalities, and joint and muscle pain, with our without fibromyalgia. In this study, we will compare the metabolomic signature of PTLDS to ME/CFS, and to Borreliosis associated with acute Lyme disease. In addition, we will present the first evidence for and against the role of environmental pesticide and other toxicant exposures in regulating innate immune and cell danger responses in patients with PTLDS and controls.



Madeleine W. Cunningham, PhD — *"From Bench to Bedside: Anti-Neuronal Autoantibodies in Lyme Disease and Beyond"*

Molecular mimicry targeting neural tissue has been reported after Borrelia burgdorferi (Bb) infection, and antibody crossreactivity with group A streptococci has been previously suggested in Bb animal models. In this presentation, I will review the results from two recent studies in which we have investigated whether adults with Lyme disease(LD) have an elevation in a group of antineuronal autoantibodies previously found to be elevated in streptococcal infections and persist in Sydenham chorea, the neurologic manifestation of acute rheumatic fever. We have also used a functional assay to examine whether serum from prior LD with erythema migrans signaled a human neuronal cell line (as measured by the activation of calcium calmodulin dependent protein kinase II (CaMKII)). Our studies were conducted among patients with erythema migrans, convalescent erythema migrans, post-treatment Lyme disease, and non-Bb-infected controls. The results of two studies will be reported – one from the Center at Columbia University and other from the Center at Johns Hopkins College of Medicine.

Choukri Ben Mamoun, PhD — *"Continuous in vitro culture of Babesia duncani in human red blood cells: An inflection point in diagnosis and therapy of human babesiosis"*

Human Babesiosis is a malaria-like illness caused by several species of Babesia parasites, two of which, Babesia microti and Babesia duncani are the main causative agents of the disease in the United States and have been associated with severe to fatal clinical cases. The parasites develop and multiply within human red blood cells to cause the pathological symptoms associated with the disease. These protozoan parasites are closely related to other pathogens of the Apicomplexa phylum and are transmitted to humans either through tick bite or blood transfusion. Clinical and experimental data suggest that current diagnostic strategies and treatment regimens are not ideal and new technologies and therapeutic strategies are needed for optimal management of the disease. A major focus of research of Ben Mamoun at Yale is to advance knowledge about the biology and pathogenesis of these parasites and to leverage this knowledge to develop sensitive assays for detection of active Babesia infections and novel therapies for radical cure of the disease. An important first success in this effort was achieved following our completion of the genomic and transcriptomic sequences of B. microti and B. duncani and subsequent annotation of their genes. A second and critical milestone was recently achieved following our successful development of a continuous in vitro culture of B. duncani in human red blood cells. The establishment of this in vitro culture system has paved the path for implementation of unique approaches to antigen and drug discoveries. In this talk, I will present data from our lab on the discovery of a panel of antigens for diagnosis of active Babesia infections and the identification of new classes of drugs and prodrugs that are far more potent than those commended for the treatment of human babesiosis. I will also present our recent data on the use of new mouse models of Babesia infection that we are using to test the sensitivity and specificity of new diagnostic assays, and efficacy of new therapies.

Margaret R. MacDonald, MD, PhD — *"Powassan virus: an emerging tick-borne threat"*

Viruses in the Flavivirus genus of the Flaviviridae Family, including West Nile, tick-borne encephalitis, yellow fever, dengue and Zika viruses cause significant human disease and are global health threats. These arthropod-borne viruses, or Arboviruses, cycle between vertebrate hosts and insect vectors, most frequently mosquitoes or ticks. Powassan virus is a newly emerging tick-borne virus that infects ticks of the Ixodes genus, including Ixodes scapularis, the same tick that transmits Lyme disease. Powassan virus was originally isolated from the brain of a young child from Powassan, Ontario who died from encephalitis. Since then human cases have occurred in Canada, the Northeast and Great Lakes areas of the USA and Far Eastern Russia. Recently cases of encephalitis due to Powassan infection have been increasing in the USA and global warming may be contributing to the expansion of the tick's geographic range. Diagnosis can be difficult since viremia is transient, and there is significant cross-reactivity of antibody responses to other flaviviruses. There is no vaccine and no specific treatment available other than supportive care. Prevention involves avoiding wooded areas, wearing protective clothing, using tick repellent, and carefully inspecting for ticks after potential exposure. Current and future research efforts are important to gain a better understanding of the epidemiology of the enzootic cycle and the prevalence of human infection, to develop improved diagnostic approaches, preventative methods and treatment options, and to explore the potential role in human disease of co-infection with multiple tick-borne pathogens.

Brian A. Fallon, MD, MPH (Conference Director) — *"Clinical Trials: Biologic & Clinical Measures of Change"*

This talk will review biologic and clinical measures that have been used in Lyme disease clinical trials in the past and describe new biologic and clinical measures that should be considered for future clinical trials. Results from a multi-site validation study of the Global Symptom Questionnaire will be presented.

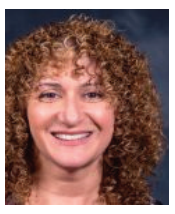
Daniel Sonenshine, PhD — *"How Climate Change Affects Range Expansion of Tick Vectors and Spread of Tick-Borne Disease in North America"*

Ticks are the major vectors of most disease-causing agents to humans, companion animals and wildlife. Moreover, ticks transmit a greater variety of pathogenic agents than any other blood-feeding arthropods. Ticks have been expanding their geographic ranges in recent decades largely due to climate change. Furthermore, tick populations in many areas of their past and even newly established localities have increased in abundance. These dynamic changes present new and increasing severe public health threats to humans, livestock and companion animals in areas where they were previously unknown or were considered to be of minor importance. Here in this review, the geographic status of four representative tick species are discussed in relation to these public health concerns, namely, the American dog tick, Dermacentor variabilis, the lone star tick, Amblyomma americanum, the Gulf Coast Tick, Amblyomma maculatum and the black-legged tick, Ixodes scapularis. D. variabilis has expanded its range northward into southern Canada, where it has been reported to be established in parts of Ontario, Saskatchewan, Manitoba and Nova Scotia. A. americanum northward expansion has progressed to the extent that established population are now reported as far north as Michigan, Pennsylvania, almost all of New York state, and most of New England states almost to the Canadian border. Both biotic and abiotic factors that may influence future range expansion and successful colony formation in new habitats are discussed.

Robert H. Yolken, MD — *"The brain-immune gut axis: a big new idea in neuropsychiatric disorders"*

Serious psychiatric disorders such as schizophrenia, bipolar disorder, and major depression are causes of morbidity and mortality worldwide. The etiologies of these disorders have not been completely defined but are likely to include both genetic and environmental factors. Recent studies point to inflammation as a core process in these disorders and inflammatory changes in the brain have been associated with a range of cognitive and behavioral abnormalities. However the source of inflammation within the central nervous system for most of these disorders has not been identified.

Recently there has also been an increased understanding of the role of the gastrointestinal tract in human brain disorder. The gastrointestinal tract and the brain are linked by a series of inter-connections characterized as the brain-immune-gut axis by means of which inflammatory signals from the gastrointestinal tract are transmitted to the central nervous system. These interactions include direct connections, such as the vagus nerve, as well as chemical mediators such as cytokines and chemokines. There are a number of factors which can stimulate immune activation within the gastrointestinal tract. Among the principal mediators of gastrointestinal inflammation are the micro-organisms which inhabit the mucosal surfaces, collectively termed the microbiome. The microbiome includes bacteria, viruses, fungi, protozoa, and other organisms and is mediated both by genetic and environmental factors. A neonate's microbiome is largely acquired from the mother around the time of birth and is stabilized during infancy and early childhood. I will discuss a number of environmental factors that can alter an individual's microbiome including diet, exposure to cigarette smoke and other toxins, and medications. The microbiome can also be manipulated therapeutically by antibiotic, prebiotic, and probiotic medications all of which promote the development of some microorganisms at the expense of others.

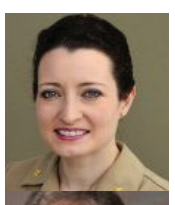


Joanna Lyon, PharmD, MEd, MHS, CHES, BCGP — *"The possible association between the human ABCB1 gene and Post Treatment Lyme Disease Syndrome"*

The high incidence of patients that have been treated for a known Lyme disease infection and yet have not returned to baseline health is a concerning healthcare issue in the United States. Sources cite the incidence of this Post Treatment Lyme Disease Syndrome (PTLDS) from 5% to 17% of individuals treated for an initial Lyme disease infection. There has been an increasing body of research to suggest that individual human genetic differences may be part of the explanation for these residual complications in some patients that experience PTLDS. The ABCB1 gene encodes for a series of efflux pumps in the human body called permeability glycoproteins (P-gp). These P-gps are found in high concentration in many key drug transport regions of the body: epithelial cells of the blood-brain barrier, epithelial cells lining the colon and small intestine, and cells in the kidney proximal tubules. The role of P-gps is to pump or transport a variety of toxins and medications away from vulnerable body organs. It has now been determined that variations in regions of the ABCB1 gene may influence not only how many of these P-gps are found in an individual's tissue, but how well these pumps move toxins and medications through various tissue membranes. In addition, there are a number of medications that can increase and decrease how well these P-gps work in the body. Currently, how P-gp number and function correlates with PTLDS is still poorly understood, but a randomized control trial of 142 patients positively associates several single nucleotide polymorphism variations in ABCB1 gene with the PTLDS disease state. This finding strengthens the view that human genetic variation in the number and/or function of P-gp efflux pumps may be part of the association between PTLDS patients and the chronic, persistent symptoms they experience.

Mark J. Soloski, PhD — "The Host Immune Response in Lyme Borreliosis"

Lyme disease is an inflammatory illness initiated by infection with Borrelia burgdorferi following a bite from an infected tick. Over the last four decades, the number of Lyme disease cases has risen sharply and it is now the most common vector-borne disease in the United States with over 300,000 cases each year. Symptoms of early Lyme disease can range from erythema migrans (EM) alone to systemic toxicity with signs of disseminated infection. Further, a number of patients with undetected and untreated early Lyme disease will develop late-onset musculoskeletal or neurological symptoms. While the acute infection and late-onset disease can be controlled by antibiotic therapy, in a subset of patients, arthritis with inflammation can be antibiotic-refractory. In addition, 10-20% of patients treated for early Lyme disease develop Post-Treatment Lyme Disease Syndrome (PTLDS), a condition with an unknown pathophysiological etiology that may have an immune component. The rising incidence of Lyme disease as well as the complexity of disease outcomes demands a deeper understanding of the immune-mediated process triggered by infection with B. burgdorferi.



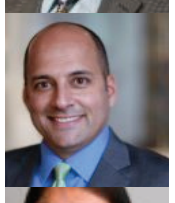
In this presentation the current knowledge of the host immune response to B. burgdorferi in human Lyme disease will be reviewed with particular attention to how variation in host immunity may play a role in driving persistent symptoms versus return to health. Datafrom the study of the Johns Hopkins Slice cohort will also be presented that will address our hypothesis that the nature of the immune response plays a key role in the range of pathophysiological outcomes in human Lyme disease.

Paige Armstrong, MD MHSLCDR — *"Rickettsial diseases: Epidemiologic trends, clinical diagnosis and management"*

Dr. Armstrong's talk on Spotted Fever Rickettsioses (SFR) will discuss the range of diseases that fall within this group, as well as national trends. Rocky Mountain spotted fever (RMSF) is the most severe and well know of the SFR, but there are other emerging species, such as R. parkeri and 364D. The talk will address clinical aspects, diagnostics, treatment, and prevention methods.

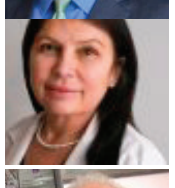
J. Stephen Dumler, MD — *"Human Granulocytic Anaplasmosis-Emerging Faster than Lyme"*

Human granulocytic anaplasmosis (HGA), sometimes called simply human anaplasmosis, is an established, yet increasing cause of disease in the U.S. and worldwide. Among domestic tick-borne infections, reports of HGA have increased to a greater proportion between 2004 and 2016 than any other – 10-fold. This presentation will provide the biological basis for disease and disease severity in humans infected by the causative agent, Anaplasma phagocytophilum, through scientific experimental approaches to evidence-based collection and analysis of data related to its ecology, epidemiology, clinical and laboratory manifestations and complications, old and new diagnostic approaches, and effective as well as ineffective approaches to its treatment and prevention. Additional discussion will also use an evidence-based approach to focus on issues of persistence and contributions to morbidity with co-infections. Additional information regarding potential approaches for novel treatments and
vaccine prevention will also be addressed.



Eric Storch, PhD — *"Obsessive Compulsive Disorder"*

Dr. Eric Storch is Professor and McIngvale Presidential Endowed Chair in the Menninger Department of
There is a well-documented link between obsessive-compulsive symptoms and various immunological conditions, where the latter confers additional burden above and beyond the illness alone. This talk will focus on what is known about the link between immune disorders including Lyme and obsessive-compulsive symptoms. Particular attention will be given to discussing pediatric autoimmune neuropsychiatric disorder associated with streptococcus as a potential model for understanding this linkage. Discussion will be provided regarding the nature of standard therapies as well as more immune- modulating approaches.



Ingeborg Dziedzic, MD, ABAARM — *"Potential late ophthalmic consequences of Lyme Disease"*

Lyme disease starts as an acute infection and then proceeds to change our future health. In acute stage Borreliosis can cause inflammation in the eyes such as uveitis with autoimmune components, conjunctivitis, optic nerve inflammation or papillitis with associated papilledema. It can affect vision through brain disease along the visual pathways. Most patients recover the visual function with treatment and support, but it does not end there. The consequences for the eye can occur decades after the initial infection. These are mediated through many systemic alterations caused by the initial infection and its treatment. We will discuss the influence of microbiome, epigenetics and inflammation on the visual outcomes as related to Lyme disease.

Lance A. Liotta, MD, PhD — *"Shedding of urinary tick pathogen-specific proteins in patients with tick borne diseases"*

Post-treatment Lyme disease syndrome (PTLDS) defines a subset of patients who experience persistent symptoms following antibiotic therapy. The cause of PTLDS, and the appropriate treatment, is highly controversial because direct molecular evidence of pathogen persistence has not previously existed. We utilized mass spectrometry enhanced by nanotechnology to study pathogen-specific proteins shed in the urine of acute Lyme and PTLDS patients (analytical sensitivity = 2.5 pg/mL in urine). We analyzed 415 urine samples comprising 1) acute Lyme disease (LD, Centers for Disease Control and Prevention definition), 2) PTLDS patients defined according to the Infectious Disease Society of America guidelines, 3) diseased negatives (tuberculosis and HIV), and 4) healthy controls. Our target pathogens were Borrelia, Babesia, Anaplasma, Rickettsia, Ehrlichia, Bartonella, Francisella, Powassan virus, encephalitis virus, and Colorado tick fever virus. Specificity was ensured by a 3-tier authentication algorithm requiring 100% amino acid sequence identity with tick-pathogen proteins, evolutionary taxonomic verification for related pathogens, and lack of overlap with human or other organisms.

Elizabeth Maloney, MD
Facilitator

Sam Donta, MD
Facilitator