LYME DISEASE ASSOCIATION, INC.*

Lyme Disease Association
Research, Education, & LA4K Grant Awards
(1992- 1st quarter 2009 ) & Status
(all grants may not be listed)

for
Lyme & Other Tick-Borne Diseases

GRANTS AWARDED
INVESTIGATORS
STATUS
RESULTANT PUBLICATIONS
CONFERENCE PRESENTATIONS

Lyme Disease Association, Inc.
PO Box 1438 Jackson, New Jersey 08527
www.LymeDiseaseAssociation.org

LDA was Lyme Disease Association of Central Jersey, then Lyme Disease Association of New Jersey, then Lyme Disease Association.

This document is a work in progress. Grants are awarded based on application submission & LDA Board approval.
Pennsylvania 1992 Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptoms. A PCR Study of 97 Cases Manfred Bayer, MD; Fox Chase Cancer Center (Philadelphia) PUBLISHED

Pennsylvania 1993 Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptoms. A PCR Study of 97 Cases Manfred Bayer, MD; Fox Chase Cancer Center (Philadelphia) PUBLISHED

Massachusetts 1993 Brigham & Woman’s, Paul Duray, MD COMPLETE

Louisiana 1994 Dr. Mario Phillip Lyme Disease Seminar Series at Tulane Regional Primate Center. COMPLETE- resulted in research collaboration with Pat Coyle and introduction of a neurotropic strain of Bb into the monkey studies

Pennsylvania 1994 Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptoms. A PCR Study of 97 Cases Manfred Bayer, MD; Fox Chase Cancer Center (Philadelphia) PUBLISHED

California 1995 Endocrine work. Marylynn Barkley, PhD, MD, University of California, Davis COMPLETE

Pennsylvania 1995 Supplement to Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptoms. A PCR Study of 97 Cases Manfred Bayer, MD; Fox Chase Cancer Center (Philadelphia) PUBLISHED

California 1996 Supplement to Endocrine. Marylynn Barkley, PhD, MD, University of California, Davis COMPLETE

New York ~1996 The Underdiagnosis of Neuropsychiatric Lyme Disease in Children and Adults. Brian Fallon, MD, MPH; Columbia University PUBLISHED

California 1997 Endocrine-Immune System Interaction in Chronic Lyme-Marylynn Barkley, PhD, MD, University of California, Davis COMPLETE


California 1998 Endocrine-Immune System Interaction in Chronic Lyme-Marylynn Barkley, PhD, MD, University of California UNFINISHED

Pennsylvania 1998 PCR Evidence for Borrelia Burgdorferi DNA in Synovium in Absence of Positive Serology. H. Ralph Schumacher, MD, University of Pennsylvania PRESENTED AT NATIONAL SCIENTIFIC MEETING

Pennsylvania 1998 Effects of Low Frequency Magnetic Fields on Borrelia Burgdorferi, Manfred Bayer, MD, Science Center University City (Philadelphia) COMPLETE
New York 1998 In-vivo animal and in-vitro studies to evaluate the effect of Hyperbaric oxygen (HBO) and Potassium Iodide (KI) on Borrelia (Bb) infected animals-Zhaid B.M. Niazi, MD; NY Medical College PRESENTED AT 13th INTERNATIONAL CONFERENCE ON LYME DISEASE & OTHER TICK-BORNE DISORDERS

New Jersey 1998 Molecular Confirmation of Infection and In-vivo Expressed Borrelia Antigens in Chronic Lyme Disease, Steven Schutzer, MD, Elizabeth Raveche, MD, UMDNJ-NJ Medical School PUBLISHED

New Jersey 1998 Borrelia burgdorferi Persists in the Gastrointestinal Tract of Children and Adolescents with Lyme Disease, Martin Fried, MD, Director, Pediatric Gastroenterology and Nutrition, Jersey Shore Medical Center; 2002 PUBLISHED

New York 1998 Structural and Functioning Imaging of Post Lyme Encephalopathy: A controlled exploratory study Brian Fallon, MD; Columbia University/NY Psychiatric Institute DATA USED TO APPLY FOR/RECEIVE $4.7M NIH GRANT

New Jersey 1998 Autoimmune role in chronic Lyme disease, Immune Complexes as a marker of active infection in chronic Lyme disease, & Molecular confirmation of infection and in vivo expressed Borrelia antigens in chronic Lyme disease- Steven Schutzer, MD; University of Medicine and Dentistry NJ PUBLISHED AS PART OF OTHER RELATED STUDIES

California 1999 Host and Borrelia Burgdorferi: (Bb) Interaction: The Dynamics of Persistent Infection, Marylynn Barkley, MD, PhD, University of CA, Davis UNFINISHED

Rhode Island 1999 Biological Control of Ixodes Scapularis with Metarhizium Anisopliae Using Remote Applicator, Elyes Zhioua, PhD, University of Rhode Island COMPLETE

New York 1999 Lyme Disease and Other Spirochetal and Tick-borne Disease: A Two Day Discussion of the Most Recent Developments in Research and Clinical Management. Bard/LDA Lyme Disease Conference CME’S AWARDED

Connecticut 1999 Steven Phillips, MD- equipment lease for research COMPLETE

New Jersey 2000 Absence of Borrelia borgdorferi-specific immune complexes in chronic fatigue syndrome, Steven Schutzer, MD, UMDNJ PUBLISHED

New Jersey 2000 Borrelia Driven Inflammation. Steven Schutzer, MD, Elizabeth Raveche, PhD, UMDNJ PUBLISHED

Pennsylvania 2000 Effects of Low Frequency Magnetic Fields on Borrelia Burgdorferi, Manfred Bayer, MD, Science Center University City (Philadelphia) COMPLETE

**Pennsylvania 2000** Combination Therapy Tinidazole/bicillin vs. Monotherapy Bicillin. Steven Burke, MD Kennett Square, PA  INCOMPLETE

**New Jersey 2000** Isolation of Lyme Spirochetes in Cervical Tissue of Women Seropositive for Lyme Disease. Andrea Gaito, MD Basking Ridge NJ  COMPLETE

**US Dept. of Agriculture 2000** Efficacy of Entemopathogenic Nematodes in Field Trials Against Ixodes Scapularis (deer tick) and Amblyomma Americanum (lone-star tick) Replete Females. Dolores E. Hill, PhD, USDA  COMPLETE, REPORT RECEIVED

**New York 2000** Lyme Disease and Babesiosis: A Retrospective Community Survey on the Role of Co-infections and Long Term Antibiotic Treatment. Richard Horowitz, MD Hyde Park, NY  ONGOING

**Colorado 2000** Lyme Disease and Babesiosis in Multiple Sclerosis. Mark E. McCaulley, MD Steamboat Springs, CO  COMPLETE

**Maryland 2000** Beyond Antibiotics: A New Approach to Treatment of the Chronic Neurotoxic Syndrome of Chronic Lyme Disease Using Cholestyramine, with Monitoring by Visual Contrast Sensitivity. Ritchie Schoemaker, MD Pocomoke City, MD  COMPLETED Presented at various conferences

**New Jersey 2001** Lyme Disease Network of New Jersey, Inc., Bill Stolow, Director. Maintaining Lymenet.org.  COMPLETE

**Pennsylvania 2001** Effects of Low Frequency Magnetic Fields on Borrelia Burgdorferi, Manfred Bayer, MD, Science Center University City (Philadelphia)  COMPLETE

**New Jersey 2001** Comparative Genetic Study. Steven Schutzer, University of Medicine and Dentistry New Jersey  ONGOING, TO DATE, 3 PUBLICATIONS RESULTED FROM WORK; PRESENTED AT INTERNATIONAL CONFERENCE IN 2006.

**New Jersey 2002** Confirmation of Chronic Lyme by PCR of Intestinal Biopsies. Martin Fried, MD; Jersey Shore Medical Center  CANCELLED BY RESEARCHER

**New Jersey 2002** Borrelia Burgdorferi--Specific Immune Complexes in Acute Lyme Disease. Steven Schutzer, UMDNJ Medical School  PUBLISHED

**Pennsylvania 2002** Supplement to Effects of Low Frequency Magnetic Fields on Borrelia Burgdorferi, Manfred Bayer, MD, Science Center University City (Philadelphia)  ONGOING

**New York 2002** Lyme Disease Retreatment Study. Daniel Cameron, MD  COMPLETE, Presented at the 6th Lyme & Other Tick-Borne Diseases Conference, Philadelphia.  2005 AWAITING PUBLICATION

**Illinois 2002** Species Identification of a Lone Star Tick-Associated Spirochete from Southeast Missouri and Development of a PCR-Based Assay for testing of Patient Samples. Maria M. Picken, MD, PhD  CANCELLED BY RESEARCHER
**New York 2002** Columbia University, New York. Endowment fund contribution for the proposed Columbia Lyme Disease Research Center, as per agreement. **COMPLETE**

**Massachusetts 2002** Binding and Uptake of *Borrelia burgdorferi* into Nervous System Cells. Sam Donta, MD **INCOMPLETE, Cancelled by researcher**

**New York 2002** *A Retrospective Study of Lyme Disease Patient Records, phase 1.* Joseph Burrascano, MD **COMPLETE, PATIENT DATA BASE DEVELOPED**

**New York 2002** The Neurochemical impact of Lyme disease on the Brain: An In-vivo study using MR Spectroscopy. Columbia (Brian Fallon) **start date TBA**

**New York 2002** Mass Spectrometry and Proteomic Diagnosis of Lyme Disease. Columbia (Brian Fallon MD, Steve Schutzer, MD) **ONGOING**

**New York 2002** Brain SPECT imaging in Lyme disease, Brian Fallon, MD **UNDERWAY**

**Maryland 2003** International Lyme & Associated Diseases Society (ILADS) education. **COMPLETE**

**New Jersey 2003** Lyme Disease Network of New Jersey, Inc. Bill Stolow, Director. Maintaining Lymenet.org. **COMPLETE**

**Maryland 2003** ILADS education & support grant **COMPLETE**

**Kansas 2003** Lyme Disease Association of Greater Kansas City, packets for school nurses; LDA provided grant for material. **DISTRIBUTED**


**New York 2003** Columbia University, *Identification of labs with greatest sensitivity and specificity for chronic Lyme disease.* Brian Fallon **COMPLETE Conference presentation**

**New York 2003** Contribution to Columbia University as part of the endowment agreement for the endowed chronic Lyme disease research center discussed above. **CENTER OPENED**


**New York 2003** Columbia University. *PET Imaging of 8 patients with history of well-documented Lyme disease who have persistent cognitive impairment but who are now seronegative.* Brian Fallon **HOLD**

New Jersey 2004 Lyme Disease Network of New Jersey, Inc. (Lymenet), Upgrading www.Lymenet.org, support of LymeDiseaseAssociation.org. COMPLETE


Maryland 2004 International Lyme & Associated Diseases Society, Inc. (ILADS). Educational grant for physicians to receive original reprints of peer reviewed guidelines for management of Lyme disease. PRINTED & DISTRIBUTED


New York 2004 *Anti-inflammatory Effects of Antimicrobial Agents*. Brian Fallon, MD, Columbia University. ON HOLD BY RESEARCHER

New York 2004 Research Foundation for Mental Hygiene. Lyme disease research through Dr. Brian Fallon; brain imaging work with Lyme disease patients. ONGOING

New Jersey 2004 *Supplement to Borrelia Sequencing Project: microarrays*. Steven Schutzer, MD, New Jersey Medical School. ONGOING

New Jersey 2005 *Co-infections in Lyme Disease*; Steven Schutzer New Jersey Medical School. ONGOING This project is being done in conjunction with Columbia University and portions are also being funded by Time for Lyme.

Maryland 2005 *Isolation of pathogens of a lone star tick borne Lyme-like illness by human tissue culture and study of the molecular mechanisms of these pathogens*. Joshua Zimmerberg, MD, National Institutes of Health (NIH) for a joint NIH/NASA (National Aeronautics & Space Administration) project awarded through Foundation for Advanced Education in the Sciences, Bethesda. ONGOING


New Jersey 2005 Awarded to the non profit Lyme Disease Network of NJ, East Brunswick for continued upkeep of the Lymenet.org and LymeDiseaseAssociation.org websites. COMPLETE
New Jersey 2005 Hackettstown Regional Medical Center to support their Lyme disease fully accredited continuing medical education (CME) activity for physicians in February 2006, entitled, Lyme Disease in New Jersey. COMPLETE, CMEs AWARDED

New York 2005 Columbia University, New York. Contribution to be used as part of the endowment fund for the proposed Columbia Lyme Disease Research Center as per agreement. COMPLETED

California 2005 California Lyme Disease Association, Inc. CALDA, Ukiah. For the revamping of the most widely distributed lay journal for Lyme disease, Lyme Times. Supported the publishing of the special issue, Lyme Times: Children’s Issue (summer 2005) by the non-profit California Lyme Disease Association, Inc. (CALDA). PUBLISHED


Kansas (and Missouri) 2005 Lyme Association of Greater Kansas City (LAGKC), Overland Park. To continue to prepare educational packets including Handbook for Prevention of Lyme & Other Tick-Borne Diseases to school nurses in the Kansas and Missouri schools. COMPLETED

Florida 2005 Florida Advocacy Network for expenses relating to educational meetings. COMPLETED

New York 2006 Dr Benjamin Luft, Stony Brook. Profiling the Humoral Response to Bb Infection with Protein Microarrays. LDA awarded this grant in conjunction with California Lyme Disease Association and Time for Lyme. COMPLETED

New York 2006 Dr. Alan MacDonald, Smithtown for equipment purchased by LDA/TFL (microscope attachment) related to study of Lyme and Alzheimer’s. This grant is awarded by LDA in conjunction with Time for Lyme in Connecticut. COMPLETED

California 2006 California Lyme Disease Association, Inc. (CALDA), Ukiah. Educational grant. COMPLETED

California 2006 California Lyme Disease Association, Inc. (CALDA), Ukiah. Educational grant for Lyme Times Children’s Education issue. COMPLETED

California 2006 California Lyme Disease Association, Inc. (CALDA), Ukiah. Educational grant. COMPLETED

Connecticut 2006 Time for Lyme (TFL), Greenwich. Education/curriculum project. COMPLETED

Maryland 2006 Mid-Shore Lyme Disease Association- for an education symposium. COMPLETED
**Maryland 2006**  International Lyme & Associated Diseases Society, Bethesda. For CME scientific meeting in Philadelphia.  COMPLETED

**New Jersey 2005**  Lyme Disease Network of NJ, East Brunswick. For continued upkeep of the Lymenet.org and LymeDiseaseAssociation.org websites  COMPLETED

**New York 2007**  Neurology Research Foundation, New York University. Neuromuscular center, David Younger, MD  CANCELLED BY RESEARCHER

**New York 2007**  Neurology Research Foundation, New York University. Lyme disease educational coordinator.  COMPLETED

**Texas 2007**  Texas Lyme Disease Association. Educational grant for Texas Lyme disease brochure publication  COMPLETED

**Pennsylvania 2007**  Southeastern Pennsylvania Lyme Disease Association, Inc. Education grant for educational booklets, The Basics.  COMPLETED

**New Jersey 2007**  University of Medicine & Dentistry NJ. Cyst form project, Steven Schutzer, MD  ON HOLD

**New Jersey 2007**  Lyme Disease Network of NJ, East Brunswick. For continued upkeep of Lymenet.org and LymeDiseaseAssociation.org websites.  COMPLETED

**California 2007**  California Lyme Disease Association. Educational projects and sponsorships (Lyme Times).  COMPLETED

**New Jersey 2007**  University of Medicine & Dentistry NJ. Sequencing project. Steven Schutzer, MD  ON GOING

**New Jersey 2007**  University of Medicine & Dentistry NJ. Proteome project. Steven Schutzer, MD  ON HOLD

**Kansas 2007**  Lyme Association of Greater Kansas City. Educational projects in the schools in Kansas and Missouri.  COMPLETED

**North Carolina 2007**  North Carolina Lyme Disease Foundation. Educational projects.  COMPLETED

**Oregon 2007**  Oregon Lyme Disease Network website upkeep

**New Jersey 2008**  University of Medicine & Dentistry of NJ. Dr. N. Parveen. Equipment loan for Lyme research (in conjunction with TFL).  ONGOING

**Maryland 2008**  Harford County LDSG, Inc. Education grant.  COMPLETED

Kansas 2008  Lyme Association of Greater Kansas City. Educational projects in the schools in Kansas and Missouri COMPLETED

New York 2008  Lyme Rights. COMPLETED

Florida 2008  Florida Lyme Advocacy, Inc. Education website. ONGOING


New York 2008  Rockefeller University. *Dermatologic manifestations of Lyme*. ONGOING

New York 2008  Columbia University. Lyme & Tick-Borne Diseases Research Center. ONGOING

New York 2008  Columbia University. Research expenses. ONGOING

Pennsylvania 2009  Southeastern Pennsylvania Lyme Disease Association, Inc. Education grant for educational booklets, The Basics AWARDED

Florida 2009  Dr. Kerry Clark, MPH, PhD AWARDED

LymeAid 4 Kids fund  LymeAid 4 Kids is an LDA fund which provides assistance to children whose families have no insurance coverage for Lyme disease diagnosis or treatment. Funds can be provided through any doctor in the US after certain criteria are met by the families and the physician has certified them as eligible. Criteria include: Applicants under the age of 21 are eligible to apply for up to $1,000 if they have no medical insurance coverage for Lyme disease and/or receive no government assistance for medical treatment for Lyme disease; the applicant/guardian signs a certified statement testifying that they are suffering from financial hardship and has a signed & dated doctor recommendation that the applicant is suffering from financial hardship, and that based on symptoms and history, Lyme & other tick-borne disease testing and/or treatment is necessary. The LDA retains the right to obtain the tax records and medical bills of the applicant and/or guardian. Over $135,000 has been awarded through 2008.

In 2004, 10 applicants in the following states received funds:
1 West Virginia for a total of $1,000
3 Texas for a total of $3,000
3 Connecticut for a total of $3,000
1 Massachusetts for a total of $1,000
1 Illinois for a total of $1,000
1 North Carolina for a total of $1,000

In 2005, 26 applicants in the following states received funds:
2 Rhode Island for a total of $2,000
1 Texas for a total of $1,000
2 New Jersey for a total of $2,000
In 2006, 19 applicants in the following states received funds:
1 Connecticut for a total of $1,000
3 Pennsylvania for a total of $3,000
8 Massachusetts for a total of $8,000
3 New York for a total of $3,000
1 California for a total of $1,000
1 Arizona for a total of $1,000
1 Maryland for a total of $1,000
1 Illinois for a total of $1,000

In 2007, 45 applicants received funds:
1 California for a total of $1,000
6 Connecticut for a total of $6,000
1 Florida for a total of $1,000
2 Georgia for a total of $2,000
4 Illinois for a total of $4,000
3 Indiana for a total of $3,000
1 Iowa for a total of $1,000
2 Massachusetts for a total of $1,200
3 New Hampshire for a total of $3,000
1 New Mexico for a total of $1,000
5 New York for a total of $5,000
2 Ohio for a total of $2,000
8 Pennsylvania for a total of $8,000
1 Rhode Island for a total of $1,000
1 Texas for a total of $1,000
1 West Virginia for a total of $1,000
1 Wisconsin for a total of $1,000
2 Canada, (US doctors) for a total of $2,000

In 2008, 36 applicants received funds:
1- Newark, OH
1- Ashaway, RI
1- Rockland, ME
1- S Weymouth, MA
1- Dover, MA
1- Fall River, MA
2- Monroe, NY
1- Rochester, NY
1- Riverhead, NY
2- Poughkeepsie, NY
1- Chattanooga, TN
1- Rocklin, CA
PUBLICATIONS RESULTING FROM LDA FUNDING/CONFERENCE PRESENTATIONS

   ABSTRACT Lyme disease is a tick-borne illness caused by the spirochete Borrelia burgdorferi. Reported throughout the United States, the greatest incidence of Lyme disease occurs in certain areas, such as the Northeast, the upper Midwest, and the Pacific Coastal states. It has been dubbed "The New Great Imitator" because, like another spirochetal illness neurosyphilis—the original Great Imitator, Lyme disease has a vast array of multisystem manifestations, including neuropsychiatric ones. Failure to recognize Lyme disease early in its course can result in the development of a chronic illness that is only temporarily or partially responsive to antibiotic therapy. The goal of this article is to present the typical and atypical manifestations of Lyme disease in children and adults in order to help the clinician more rapidly unmask the correct diagnosis behind the puzzling presentations of some patients.

2. “Borrelia burgdorferi DNA in the Urine of Treated Patients with Chronic Lyme Disease Symptom.” A PCR Study of 97 Cases” M.E. Bayer, MD et al; Infection 24 (1996) #5 Author affiliation Fox Chase Cancer Center, Philadelphia, PA 19111, USA
   ABSTRACT All patients had shown erythema chronica migrans following a deer tick bite. Most of the patients had been antibiotic-treated for extended periods of time. Of the 97 patients, 72 (74.2%) were found with positive PCR and the rest with negative PCR. The 62 healthy volunteers were PCR negative. It is proposed that a sizeable group of patients diagnosed on clinical grounds as having chronic Lyme disease may still excrete Borrelia DNA, and may do so in spite of intensive antibiotic treatment.

   ABSTRACT Chronic fatigue syndrome (CFS) and Lyme disease often share clinical features, especially fatigue, contributing to concern that Borrelia burgdorferi (Bb), the cause of Lyme disease, may underlie CFS symptoms. We examined 39 CFS patients and 40 healthy controls with a Bb immune complex test. Patients and controls were nonreactive. Centers for Disease Control and
Prevention-defined CFS patients lacking antecedent signs of Lyme disease--erythema migrans, Bell's palsy, or large joint arthritis--are not likely to have laboratory evidence of Bb infection.

4. **“Borrelia Burgdorferi--Specific Immune Complexes in Acute Lyme Disease.”** Steven Schutzer, UMDNJ. JAMA, Nov. 24, 1999, Vol.282, No.20

**ABSTRACT**

**Context** Diagnosis of infection with Borrelia burgdorferi, the cause of Lyme disease (LD), has been impeded by the lack of effective assays to detect active infection.

**Objective** To determine whether B. burgdorferi specific immune complexes are detectable during active infection in LD.

**Design, Setting, and Patients:** Cross-sectional analysis of serum samples from 168 patients fulfilling Centers for Disease Control and Prevention surveillance criteria for LD and 145 healthy and other disease controls conducted over 8 years. Tests were performed blinded.

**Main Outcome Measure** Detection of B. burgdorferi immune complexes by enzyme-linked immunosorbent assay and Western blot.

**Results:** The B. burgdorferi immune complexes were found in 25 of 26 patients with early seronegative erythema migrans (EM) LD; 105 of 107 patients with seropositive EM LD; 6 of 10 patients who were seronegative with culture-positive EM; 0 of 12 patients who were treated and recovered from LD; and 13 of 13 patients with neurologic LD without EM. Among 147 controls, B. burgdorferi immune complex was found in 0 of 50 healthy individuals; 0 of 40 patients with persistent fatigue; 0 of 7 individuals with frequent tick exposure; and 2 of 50 patients with other diseases.

**Conclusion:** These data suggest that B. burgdorferi immune complex formation is a common process in active LD. Analysis of the B. burgdorferi immune complexes by a simple technique has the potential to support or exclude a diagnosis of early as well as active LD infection.

**Funding/Support:** This work was supported in part by grants A41518, NS34092, AI31561, and AR40470 from the National Institutes of Health and grant U50/CCU206582 from the Centers for Disease Control and Prevention, and by the Lyme Disease Association of New Jersey.


**ABSTRACT** Patients with chronic Lyme disease who experience persistent cognitive deficits despite having received the recommended antibiotic treatment pose a therapeutic dilemma. This pilot study was designed to assess whether additional antibiotic therapy is beneficial.

Enrolled in the study were 23 patients with complaints of persistent memory problems who had previously received 4-16 weeks of intravenous antibiotic therapy. Patients were tested at baseline and 4 months later. During this interval, the private physician determined treatment (intravenous, intramuscular, oral, or none). Assessments included standardized measures of cognition, depression, anxiety, and functional status.

Between times 1 and 2, 5 patients were given no antibiotics and 18 were given additional antibiotics: 7 intravenously, 4 intramuscularly, and 7 orally. At time 1, there were no statistically significant group differences in cognition, depression, or anxiety between those who later received antibiotics and those who didn't. At time 1, the 23 patients were also functionally disabled. At time 2, compared with patients who received no antibiotics, patients given antibiotics scored better on overall and individual measures of cognition. Patients given intravenous antibiotics showed the greatest functional improvement (pain, physical functioning, energy) and the most cognitive improvement, even when controlling for baseline differences in cognition between the treatment groups. Patients who did not have a reactive Western blot currently or historically were just as likely to improve cognitively as patients with reactive Western blot results.

This uncontrolled study suggests that repeated antibiotic treatment can be beneficial, even among patients who have been previously treated and even among patients who are currently Western blot negative, with the intravenous route of treatment being the most effective. A double-blind placebo-controlled study is needed to confirm these results.
6. **“Preliminary in Vitro and in Vivo Findings of Hyperbaric Oxygen Treatment in Experimental Bb Infection.”** Charles Pavia, PhD, NY Medical College School of Medicine. 13th International Scientific Conference on Lyme Disease and Other Tick-borne Disorders.

**CONFERENCE PRESENTATION**

In these studies, we evaluated repeated HBOT for its ability to kill Bb in vitro, and in vivo, in a murine model of Lyme disease. Several North American tick-derived and recently obtained patient isolates were studied separately in our assay systems. To test for in vitro susceptibility, one-half to one million Bb were cultured in a small volume (0.1 - 0.2 ml) of BSK media using small snap-cap test tubes. With the caps removed, these cultures were then exposed, for one hour (twice daily for 2 consecutive days), to pure, filtered oxygen pressurized to 2-3 times normal atmospheric conditions. This was achieved using a specially constructed, miniaturized cylindrical chamber (length = 12 inches; diameter = 8 inches), equipped to accept any pressurized gas mixture through its portal opening. After the final HBOT, all cultures received an additional 0.5 ml of BSK media (making the final volume now 0.6 - 0.7 ml), and their caps were snapped shut. Matching control cultures received no HBOT. All cultures were incubated at 33° C for 2-3 days and were examined microscopically for live Bb. Our results showed that 14 of 17 strains of Bb had their growth inhibited by 33-94%, while there was little or no inhibition of 3 Bb strains. For the in vivo studies, separate groups of C3H or CO1 mice were infected intradermally with 100,000 Bb. Two to 4 weeks later, one group of infected mice received two, 1.0-1.5 hour HBO exposures, for two consecutive or alternating days. The treated mice were sacrificed one day after the last treatment, and extract cultures of their urinary bladders were prepared in BSK media. It was found that no Bb grew out of 80% of these extract cultures, whereas live Bb organisms were recoverable from 90% of extract cultures prepared from matched, infected control mice not treated with HBO. These data suggest that HBOT may be considered as a clinically useful form of adjunct therapy in the treatment of Lyme disease.


**CONFERENCE ABSTRACT: PCR EVIDENCE FOR BORRELIA BURGDORFERI DNA IN SYNOVIOUM IN ABSENCE OF POSITIVE SEROLOGY.** P. Branigan, Jay Rao, H. Gerard, A. Hudson, W. Williams, T. Arayssi, M. Bayer, S. Rothfuss, G. Clayburne, M. Sieck, HR Schumacher U of Pa, Allegheny University of Health Sciences and VAMC, Phila. PA 19104 and NIAMS, NIH, Bethesda, MD 20892

Although Borrelia burgdorferi have been identified in synovium by several groups using immunohistochemistry, EM Steiner stains and PCR, there is controversy about whether they can infect joints without inducing a serologic response and whether they can persist after antibiotic treatment. We have performed PCR for Borrelia on a series of 185 synovial biopsies and synovial fluid regardless of clinical diagnosis. There were no cases included with known clinical Lyme disease or with positive Lyme ELISA serology. A positive control was from an erythema migrans lesion with known Lyme disease. PCR primers used identified Borrelia burgdorferi Osp A DNA. In 6 PCR positive cases synovium was also studied by Steiner stain and 4 had transmission EM to search for evidence of organisms.

Ten of the 185 cases studied (5, 3%) and the positive control were positive for the Osp A gene of Borrelia burgdorferi. Steiner stains were negative in all 6 studied. EM in no cases revealed any classic organisms but did show several features (including a variety of unusual membranous arrays) that have been reported before in known Lyme disease and other infections. Clinical patterns were reviewed on the Borrelia PCR positive patients. Clinical diagnoses were RA in 4, Adult Onset Stills Disease or JRA in 2, reactive arthritis in 2, psoriatic 1, and unclassified oligoarthritis 1. Four had received extensive antibiotics before the biopsy with improvement in 2.
PCR evidence for Borrelia has been identified in synovial biopsies of patients with clinical pictures that had not initially suggested Lyme disease. All patients were negative for antibodies to Borrelia and some were PCR positive in synovium despite previous treatment with antibiotics.


The findings were that 43% of the males tested carried evidence of the Lyme disease bacterium in semen by PCR DNA testing.

Dr. Bach also presented results of the study at the American Psychiatric Association meeting in November 2000.


ABSTRACT Although neurologic Lyme disease is known to cause cognitive dysfunction in adults, little is known about its long-term sequelae in children. Twenty children with a history of new-onset cognitive complaints after Lyme disease were compared with 20 matched healthy control subjects. Each child was assessed with measures of cognition and psychopathology. Children with Lyme disease had significantly more cognitive and psychiatric disturbances. Cognitive deficits were still found after controlling for anxiety, depression, and fatigue. Lyme disease in children may be accompanied by long-term neuropsychiatric disturbances, resulting in psychosocial and academic impairments. Areas for further study are discussed.


ABSTRACT This study documents the persistence of B burgdorferi DNA in the gastrointestinal tract of pediatric patients who have already been treated with antibiotics for Lyme disease. Ten consecutive patients between the ages of 9 and 13 years presented with an erythema migrans (EM) rash, a positive western blot for Lyme disease, chronic abdominal pain, heartburn, or bright red blood in the stool. Endoscopy assessed the gastrointestinal (GI) mucosa for inflammation and biopsies were examined for B burgdorferi using a Dieterle stain and with polymerase chain reaction (PCR) to the outer surface protein A (Osp A) of B burgdorferi. As controls, 10 consecutive patients with chronic abdominal pain were also tested by GI biopsies and with PCR. B burgdorferi persisted in the GI tract in all 10 patients with Lyme disease as shown by Dieterle stain of biopsies and with PCR. None of the control subjects' biopsies were PCR positive for B. burgdorferi. Chronic gastritis, chronic duodenitis, and chronic colitis were found in Lyme disease patients and associated with the detection of B burgdorferi DNA in the GI tract despite prior antibiotic treatments. We have concluded that the DNA of B burgdorferi persisted in patients with Lyme disease even after antibiotic treatment.


This study examined brain functioning in patients with Lyme encephalopathy. Eleven patients underwent neuropsychological tests and Xenon¹³³-regional cerebral blood flow (rCBF) studies, using
an external detector system. Each rCBF scan was age- and sex-matched to two archival, normal controls. While few differences were noted on gray-matter flow indices (ISI, fg), Lyme patients demonstrated significant flow reductions in white matter index (k2) (p=.004), particularly in the posterior temporal and parietal lobes bilaterally (p=.003). Flow reductions in white matter areas were significantly associated with deficits in memory (r=.66, p=.027) and visuospatial organization (r=.62, p=.041). Results suggest that Lyme encephalopathy may be a disease primarily affecting the cerebral white matter.


ABSTRACT Comparative genomics of closely related bacterial isolates is a powerful method for uncovering virulence and other important genome elements. We determined draft sequences (8-fold coverage) of the genomes of strains JD1 and N40 of Borrelia burgdorferi sensu stricto, the causative agent of Lyme disease, and we compared the predicted genes from the two genomes with those from the previously sequenced B31 genome. The three genomes are closely related and are evolutionarily approximately equidistant (≈0.5% pairwise nucleotide differences on the main chromosome). We used a Poisson model of nucleotide substitution to screen for genes with elevated levels of nucleotide polymorphisms. The three-way genome comparison allowed distinction between polymorphisms introduced by mutations and those introduced by recombination using the method of phylogenetic partitioning. Tests for recombination suggested that patches of high-density nucleotide polymorphisms on the chromosome and plasmids arise by DNA exchange. The role of recombination as the main mechanism driving B. burgdorferi diversification was confirmed by multilocus sequence typing of 18 clinical isolates at 18 polymorphic loci. A strong linkage between the multilocus sequence genotypes and the major alleles of outer-surface protein C (ospC) suggested that balancing selection at ospC is a dominant force maintaining B. burgdorferi diversity in local populations. We conclude that B. burgdorferi undergoes genome-wide genetic exchange, including plasmid transfers, and previous reports of its clonality are artifacts from the use of geographically and ecological isolated samples. Frequent recombination implies a potential for rapid adaptive evolution and a possible polygenic basis of B. burgdorferi pathogenicity.

13. “Evidence of Borrelia Autoimmunity-Induced Component of Lyme Carditis and Arthritis.” Elizabeth S. Raveche, Steven E. Schutzer, Helen Fernandes, Helen Bateman, Brian A. McCarthy, Steven P. Nickell, and Madeleine W. Cunningham. Journal of Clinical Microbiology, February 2005, p. 850-856, Vol. 43, No. 2 DOI: 10.1128/JCM.43.2.850-856. 2005 Departments of Pathology and Medicine, New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, New Jersey, 1 Department of Molecular Genetics and Microbiology, University of New Mexico, Albuquerque, New Mexico, 2 University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma 3. Received 2 January 2004/ Returned for modification 29 March 2004/ Accepted 5 September 2004

ABSTRACT We investigated the possibility that manifestations of Lyme disease in certain hosts, such as arthritis and carditis, may be autoimmunity mediated due to molecular mimicry between the bacterium Borrelia burgdorferi and self-components. We first compared amino acid sequences of Streptococcus pyogenes M protein, a known inducer of antibodies that are cross-reactive with myosin, and B. burgdorferi and found significant homologies with OspA protein. We found that S. pyogenes M5-specific antibodies and sera from B. burgdorferi-infected mice reacted with both myosin and B. burgdorferi proteins by Western blots and enzyme-linked immunosorbent assay. To investigate the relationship between self-reactivity and the response to B. burgdorferi, NZB mice, models of autoimmunity, were infected. NZB mice infected with B. burgdorferi developed higher degrees of joint
swelling and higher anti-\textit{B. burgdorferi} immunoglobulin M cross-reactive responses than other strains with identical major histocompatibility complex (DBA/2 and BALB/c). These studies reveal immunological cross-reactivity and suggest that \textit{B. burgdorferi} may share common epitopes which mimic self-proteins. These implications could be important for certain autoimmunity-susceptible individuals or animals that become infected with \textit{B. burgdorferi}.


METHODS: Data were obtained from a randomized, double-blind placebo-controlled study of patients with recurrent Lyme disease. Patients received either amoxicillin 500mg 3 times/day or placebo for 3 months. The Short Form-36 Health Survey, administered at baseline and at the conclusion, provided a Mental Component Summary (MCS) and a Physical Component Summary (PCS) for HRQOL. Baseline HRQOL scores were compared with the general US and chronically-ill populations. Patients with Lyme disease were divided into the lowest, moderate, and higher initial quality of life as measured by SF-36.

RESULTS: The quality of life of Lyme disease was significantly lower than the US norm and chronically-ill patients on all SF-36 scales. Compared with patients who received placebo, patients treated with amoxicillin showed greater improvement on SF-36 physical function, general health perception, vitality, social function, and emotional health. Lyme disease patient presenting with the best initial quality of life had the highest success rate.

CONCLUSION: Recurrent Lyme disease severe impairs quality of life. Retreatment is effective.


There is controversy regarding the nature and degree of intellectual and memory deficits in chronic Lyme disease. In this study, 81 participants with rigorously diagnosed chronic Lyme disease were administered the newest revisions of the Wechsler Adult Intelligence Scale (WAIS-III) and Wechsler Memory Scale (WMS-III), and compared to 39 nonpatients. On the WAIS-III, Lyme disease participants had poorer Full Scale and Performance IQ's. At the subtest level, differences were restricted to Information and the Processing Speed subtests. On the WMS-III, Lyme disease participants performed more poorly on Auditory Immediate, Immediate, Auditory Delayed, Auditory Recognition Delayed, and General Memory indices. Among WMS-III subtests, however, differences were restricted to Logical Memory (immediate and delayed) and Family Pictures (delayed only), a Visual Memory subtest. Discriminant analyses suggest deficits in chronic Lyme are best characterized as a combination of memory difficulty and diminished processing speed. Deficits were modest, between one-third and two-thirds of a standard deviation, consistent with earlier studies. Depression severity had a weak relationship to processing speed, but little other association to test performance. Deficits in chronic Lyme disease are consistent with a subtle neuropathological process affecting multiple performance tasks, although further work is needed to definitively rule out nonspecific illness effects. (JINS, 2006, 12, 119-129.).

16. \textit{“Identification of Borrelia burgdorferi outer surface proteins.”} Brooks CS; Vuppala SR; Jett AM; Akins DR Department of Microbiology and Immunology. The University of Oklahoma Health Sciences Center, Oklahoma City, OK 73104, USA, Infection and Immunity, January 2006, p.296-304

Several Borrelia burgdorferi outer surface proteins have been identified over the past decade that are up-regulated by temperature- and/or mammalian host-specific signals as this spirochete is transmitted from ticks to mammals. Given the potential role(s) that these differentially up-regulated proteins may
play in B. burgdorferi transmission and Lyme disease pathogenesis, much attention has recently been placed on identifying additional borreliotic surface proteins. To identify uncharacterized B. burgdorferi outer surface proteins, we previously performed a comprehensive gene expression profiling analysis of temperature-shifted and mammalian host-adapted B. burgdorferi. The combined microarray analyses revealed that many genes encoding known and putative outer surface proteins are down-regulated in mammalian host-adapted B. burgdorferi. At the same time, however, several different genes encoding putative outer surface proteins were found to be up-regulated during the transmission and infection process. Among the putative outer surface proteins identified, biochemical and surface localization analyses confirmed that seven (Bb0405, Bb0689, BbA36, BbA64, BbA66, BbA69, and BbI42) are localized to the surface of B. burgdorferi. Furthermore, enzyme-linked immunosorbent assay analysis using serum from tick-infested baboons indicated that all seven outer surface proteins identified are immunogenic and that antibodies are generated against all seven during a natural infection. Specific antibodies generated against all seven of these surface proteins were found to be bactericidal against B. burgdorferi, indicating that these newly identified outer surface proteins are prime candidates for analysis as second-generation Lyme disease vaccinogens.

17. “Wide Distribution of a High-Virulence Borrelia burgdorferi Clone in Europe and North America.” Wei-Gang Qiu,* John F. Bruno,† William D. McCaig,* Yun Xu,† Ian Livey,‡ Martin E. Schriefer,§ and Benjamin J. Luft† Hunter College of the City University of New York, New York, New York, USA; †Stony Brook University, Stony Brook, New York, USA; ‡Baxter Innovations GmBH, Orth/Donau, Austria; and §Centers for Disease Control and Prevention, Fort Collins, Colorado, USA Emerging Infectious Diseases Volume 14, Number 7–July 2008

The A and B clones of Borrelia burgdorferi sensu stricto, distinguished by outer surface protein C (ospC) gene sequences, are commonly associated with disseminated Lyme disease. To resolve phylogenetic relationships among isolates, we sequenced 68 isolates from Europe and North America at 1 chromosomal locus (16S–23S ribosomal RNA spacer) and 3 plasmid loci (ospC,dbpA, and BBD14). The ospC-A clone appeared to be highly prevalent on both continents, and isolates of this clone were uniform in DNA sequences, which suggests a recent trans-oceanic migration. The genetic homogeneity of ospC-A isolates was confirmed by sequences at 6 additional chromosomal housekeeping loci (gap, alr, glpA, xylB, ackA, and tgt). In contrast, the ospC-B group consists of genotypes distinct to each continent, indicating geographic isolation. We conclude that the ospC-A clone has dispersed rapidly and widely in the recent past. The spread of the ospC-A clone may have contributed, and likely continues to contribute, to the rise of Lyme disease incidence.