PRESENTATION FRIDAY APRIL 9, 1999

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Novel Features of Rabbit Infection and Immunity in the Study of Lyme Disease

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No abstract available.

Notes:

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Potential Role of the UHB Gene Family of the Lyme Disease Spirochetes in Immune Evasion

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Evidence suggests that the Lyme disease spirochetes evade destruction by the immune system in part through antigenic variation in outer surface proteins. While the *vls* gene family has been demonstrated to contribute to antigenic variation, the overall process is likely multi-factorial. We have conducted extensive analyses on a series of lipoprotein encoding genes that form a super gene family. All members of this gene family exhibit homology with each other, particularly in the N terminal region of their deduced amino acid sequences and are flanked at their 5' end by a conserved upstream, promoter carrying sequence element called the upstream homology box (UHB).

Hence we have designated this gene family as the UHB gene family. We have demonstrated that this gene family contains 3 distinct sub-families (*ospE*, *ospF* and *pG* groups). Members of these subfamilies exhibit significant variation. PCR analyses revealed the presence of highly polymorphic domains in the coding sequences of both the *ospE* and *ospF* sub-families. In the *ospE* related genes these variable domains are flanked by direct repeat elements (up to 38 bp) and computer analyses predict this domain to be hydrophilic, surface exposed, and antigenic. To determine if immune pressure drives rearrangement or sequence changes in the UHB flanked genes we have analyzed the stability of these genes over an infection period in mice of 2 months.

While plasmid composition changed over the course of infection, gross gene rearrangements in the *ospE* and *ospF* related genes were not detected through PCR analyses. We are currently sequencing the amplicons to determine if point mutations have arisen during the course of infection. In addition to the analyses outlined above we are also assessing the transcriptional expression of UHB flanked genes under different environmental conditions and are characterizing the humoral immune response to these proteins. The characterization of the UHB gene family among Bbsl species will prove important in attempts to decipher its role in the biology and pathogenesis of the Lyme disease spirochetes.

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Borrelia burgdorferi Lipoproteins and the Control of Inflammation in Lyme Disease.

P. K. Murthy, V. A. Dennis, B. Lasater, and M. T. Philipp*

Borrelia burgdorferi lipoproteins are known to induce local and systemic production of proinflammatory cytokines such as IL-6, IL-1-beta and TNF-alpha in macrophage/monocytes. These cytokines have been implicated in the pathogenesis of Lyme disease.

We have reported that heat-killed *B. burgdorferi* spirochetes (Bb) and lipidated outer surface protein A (L-OspA) but not unlipidated OspA (U-OspA) are able to stimulate not only the production of inflammatory cytokines but also that of the anti-inflammatory cytokine IL-10 in peripheral blood mononuclear cells from uninfected humans and rhesus monkeys. Monocytes are the cells that transcribe both types of cytokines (Giambartolomei et al., Infect. Immun. 1999, 67, 140-147). We have now demonstrated, in a kinetic study, that in the monocytic cell line THP-1, stimulation with Bb, L-OspA, or LPS but not U-OspA induces the production of IL-10, IL-6 and IL-12 at about 8 h post-stimulation (PS). However, while the peak production of IL-10 occurred between 8 and 16 h PS, that of the other two cytokines took place much later, at 48 h PS. Recombinant IL-10 (rIL-10) added to L-OspA- or LPS-stimulated THP-1 cells completely inhibited IL-12 production using as little as 0.1 ng/ml of rIL-10. The inhibitory effect of rIL-10 on IL-6 production was dose dependent. The addition of anti-IL-10 antibody markedly enhanced IL-6 and IL-12 production.

These results show that IL-10 induced by *B. burgdorferi* lipoproteins can downregulate proinflammatory responses similarly induced by lipoproteins. They further suggest that IL-10 induced by the spirochete may contribute to control inflammation in Lyme disease and that exogenous rIL-10 might be therapeutically useful.

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A Novel Toxin (*Bb* Tox 1) of *Borrelia burgdorferi*

Mark J. Cartwright, Ph.D.*, Suzanne E. Martin, Ph.D. and Sam T. Donta, M.D.

The mechanisms responsible for many of the symptoms of Lyme disease remain to be delineated. Because many of the symptoms involve the nervous system, we postulated that the Lyme spirochetes produce a toxin that interferes with normal neurophysiological function. We have identified and cloned a gene of *B. burgdorferi* which encodes a protein that is a neurotoxin.

Initially, degenerate primers were designed to highly conserved regions within various toxin groups. These primers were used for amplification of DNA extracted from *B. burgdorferi* strain 2591 to identify genes that express proteins analogous to existing toxins. Degenerate primers designed to the highly conserved catalytic domains of diphtheria and pertussis toxins yielded an amplification product. The product was cloned, sequenced, and subsequently identified in The Institute of Genomic Research (TIGR) database as BB0755, a 37 kD protein of unknown function. The full length gene for BB0755 was cloned, expressed and purified using epitope tags in the pET30a expression system, and the resultant recombinant protein renamed Bbtox1. Using the synthetic target agmantine, Bbtox1 exhibited ADP-ribosyltransferase activity. No ADP-ribosyltransferase activity was detected using elongation factor 2 as the target. In tissue culture, Bbtox1 affected the morphology (rounding) of Y1 mouse adrenal cells and C6 rat glial cells. Bbtox1 induced cell death in both Y1 and C6 cells. C6 glial cells responded to Bbtox1 in a dose and time dependent manner. Brefeldin A, an inhibitor of the trans-golgi network, accelerated the onset of action of Bbtox1 an Y1 adrenal cells.

The effects of Bbtox1 are consistent with a mechanism of action similar to that of botulinum C2 and other cytoskeletal toxins. Studies are underway to identify the cellular target of Bbtox1 and its role in Lyme Disease. In addition, a homologous gene in *Treponema pallidum* of undefined function is being analyzed to determine if it codes for a toxin similar to Bbtox1

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Quantitative Spirochetal DNA in Dog Tissue

Reinard K. Straubinger, D.V.M., Ph.D.

Background: *B. burgdorferi* is known to establish a persistent infection in the mammalian host. However, little is known about the number and the tissue preference of the spirochete. Quantification of *B. burgdorferi* organisms by culture or staining methods is either impossible or not practical. Current DNA amplification methods are labor intensive and only a limited number of samples can be processed.

Objective: Determine the absolute number of *B. burgdorferi* organisms by a new method of DNA amplification in a large number of canine tissue and buffy coat samples collected over a 500-day period.

Design: Sixteen specific-pathogen-free beagle dogs were infected with *B. burgdorferi* by tick challenge. Starting at day 120 after tick exposure, 12 dogs were treated with antibiotics for 30 consecutive days (4 dogs, azithromycin, 25 mg/kg daily, po; 4 dogs, ceftriaxone, 25 mg/kg, daily, iv; 4 dogs, doxycycline, 10 mg/kg, BID, po). The remaining four dogs received no antibiotic therapy. Over a 500-day period, blood samples were taken at two-week intervals and skin punch biopsy samples at monthly intervals. Twenty-five tissue samples were collected during necropsy. DNA of all samples was recovered by phenol/chloroform extraction. Detection and quantification of *B. burgdorferi* DNA was carried out in 96-well plates in an ABI7700 Sequence Detection System. Primers and a fluorescent-labeled probe designed to bind specifically to the ospA gene of *B. burgdorferi* strain N40 were used for DNA amplification and quantification. The intensity of fluorescent signal for test samples was compared to a standard curve, generated with DNA in a ten-fold dilution series of a known number of culture-derived low-passage *B. burgdorferi* organisms suspended in canine buffy coats.

Results: All 16 dogs became infected after tick challenge. In skin biopsy samples of untreated dogs, spirochete numbers peaked at day 60 post infection ($< 4 \times 10^6$ organisms per 100 ng extracted DNA) and decreased by 100- to 1000-fold during the following six months. Antibiotic treatment did not eliminate the infection, but reduced the number of spirochetes in skin tissue by a factor of 1000 or more. Buffy coat samples were rarely positive (1.6% of 576 buffy coat samples of all dogs). More than 500 days after infection, *B. burgdorferi* was detectable at low levels (10^2-10^4 organisms per 100 ng extracted DNA) in multiple tissue samples in all untreated dogs and in eight of 12 antibiotic-treated dogs. However, more tissue samples were positive in untreated dogs than in antibiotic-treated dogs.

Conclusions: This DNA detection system facilitates the precise and rapid quantification of *B. burgdorferi* in a large number of tissue and blood samples. Data generated with this technique provide evidence that during the first two months after infection the number of spirochetes increased in the skin of infected dogs and declined thereafter. Interestingly, peak numbers of organisms coincided with the development of the first clinical signs. Antibiotic treatment did not eliminate the infection but decreased the number of organisms.

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Antimicrobial Agents that Target DNA Gyrase in *Borrelia burgdorferi*

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The only DNA topoisomerase that can catalyze the introduction of supercoiling into a DNA molecule is the prokaryotic enzyme DNA gyrase. DNA gyrase is an A_2B_2 tetramer: the A subunit binds DNA, generating a double-stranded break and then resealing it, while the B subunit uses ATP to drive the reaction. DNA gyrase is the target of several groups of antimicrobial agents. Coumarin antibiotics, including coumermycin A_1, bind to the B subunit, blocking ATP binding and inhibiting enzyme activity. Fluoroquinolone antibiotics, such as ciprofloxacin, bind to the A subunit after it has generated the double-stranded break in DNA and prevents the resealing reaction. We have examined the effects of several DNA gyrase inhibitors on the cell growth and DNA conformation of *B. burgdorferi* . We found that *B. burgdorferi* is highly susceptible to growth inhibition and plasmid relaxation (loss of supercoiling) by coumermycin A_1 treatment. Although coumermycin A_1 is not a clinically useful antibiotic for a variety of reasons, we have used it to develop a genetic system for *B. burgdorferi* . We have shown that *B burgdorferi* is fairly resistant to ciprofloxacin, and another fluoroquinolone moxifloxacin, but more susceptible to the fluoroquinolones Bay-Y3118 and sparfloxacin. We will test other, more potent fluoroquinolone antibiotics, including trovafloxacin, clinafloxacin and sitafloxacin. Most recently we have used the fluoroquinolone antibiotics to map the sites on DNA where DNA gyrase (or the homologous enzyme topoisomerase IV) prefers to bind.

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Update on Tick-Associated Human Histopathology

Paul H. Duray, M.D., Xiadu Guo, M.D., Ph.D.

Recent technical laboratory approaches have contributed to the understanding of human and mammalian tissue models in infections induced by tick vectors. PCR has been one of the major approaches due to the feasibility of appropriate infectious agent classification and linkage for a given histopathologic condition.

Tissue lesion classifications prior to PCR, tissue immunoblotting with quantitative protein analysis, and animal infection models were fraught with guess-work and supposition. Established and generally accepted histologic spectrum includes the inflammatory and fibroinflammatory dermal, adipose, and fascial tissue lesions, myositis, myocarditis, expansile skin erythematous dermatitis, synovitis with some joint erosion if recurrent, peripheral neuritis, autonomic gangliitis, ocular vitreitis, and some degree of lymphoreticular hyperplasia. Still unclear are the histopathologic lesions directly involved with Borrelia and Ehrlichia infections.

Recent studies have shown borrelial spirochetes to be directly present in the degenerative synovial surface deposits and in relatively high numbers as compared to the underlying sub-synovium in patients with Lyme synovitis prior to antibiotic therapy. We have now observed spirochete clustering in the hair follicle adventitial layer of lymphocytoma cutis-like lesions in humans and in erythema migrans-like lesions rabbit models. Lymphocytoma may be very rarely seen in U.S. cases of undiagnosed Borreliosis, but when present, spirochetes can be identified. Relapsing fever borrelia are linked to pleuritis and are demonstrable in the pleura of rodent models. Some lesions that extended experience permits decreasing links to Borrelia are lichen sclerosis of skin, plasmacytic panniculitis, and cutaneous vasculitis. Gaps in our knowledge will inevitably exist regards the important CNS questions.

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Ehrlichiosis, Babesiosis, and Borreliosis

Edwin J. Masters, M.D.

Human granulocytic ehrlichiosis (HGE), Lyme borreliosis and Babesiosis are a clinical triad with a common tick vector, *Ixodes scapularis*. This triad occurs mainly in the Northeast and north central states. Human monocytic ehrlichiosis (HME); a new Babesiosis, MO1, and a borreliosis causing clinical erythema migrans are found in the lower Midwest and South.

Human babesiosis in the U.S. has been associated in the northeastern and upper midwestern states with *Babesia microti* and *Ixodes scapularis* ticks, in California and Washington State with WAI-type piroplasms and in the Southeast Missouri with a related but distinct intraerythrocytic piroplasm MO1. Human monocytic ehrlichiosis (HME) caused by *Ehrlichia chaffeensis* has been associated with *Amblyomma americanum* (lone star) ticks in the Midwest and *phagocytophylia*-like organism has been found in the upper Midwest and Northeast. Ehrlichiosis has also been recently found in California. Atypical *Borrelia burgdorferi* have been found in Missouri ticks and a new species, *Borrelia lonestari*, has been discovered in lone star ticks. Additionally, erythema migrans cases have been documented in the lower Midwest and other borrelia appearing spirochetes that stained with H5332 have been observed in lone star ticks. Furthermore, ticks simultaneously harboring *Borrelia* and *Babesia* as well as *Borrelia* and *Ehrlichia* have been reported.

Are there parallel paths of pathogenicity between lone star and *Ixodes* deer ticks? Geographic and temporal histories of the evolving knowledge and awareness of Babesiosis, Ehrlichiosis, and Lyme Disease are compared.

Given this history of the evolving geographic association of Borreliosis, Babesiosis and Ehrlichiosis (although different species or strains may be involved), when there is evidence for the presence of two of these ticks vectored illnesses, a high index of suspicion for the third is warranted, along with the possibility of co-infection.

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Clinical and Pathogenetic Studies of HGE

J. Stephen Dumler, M.D.

Human granulocytic ehrlichiosis (HGE) is an acute febrile tick-borne zoonotic illness caused by obligate intracellular bacteria of the Ehrlichia phagocytophila group, that infect cells of myeloid derivation in mammalian hosts. Recent advances have improved understanding of bacterial and host components involved in HGE. In humans, fever, headache, myalgias, and malaise characterize HGE in most patients and involvement of the gastrointestinal and respiratory systems and skin is less frequent. Definite CNS involvement has not been documented. Laboratory abnormalities include thrombocytopenia, leukopenia, and elevations in serum hepatic aminotransferase activities. Most infections are asymptomatic or subclinical; however, a sepsis-like syndrome, adult respiratory distress syndrome, rhabdomyolysis, hemorrhage, peripheral neuropathies, severe opportunistic and nosocomial infections, and death may occur. Severity appears to be related to initial burden of the infectious agent and delays in diagnosis and treatment.

A chronic or persistent phase of HGE has not been documented, and coinfection with other tick-borne agents has not been proven to adversely affect outcome. Most patients recover rapidly in association with a TH1 response and high titers of antibodies. Animal models, especially horses, are good mimics of human disease; mice do not develop any clinical signs of disease and have TH2 responses, but do develop pathologic lesions similar to those observed in humans and other animal models. In vitro and experimental infections in horses and mice indicate that infection is established in myeloid precursors of bone marrow or other hematopoietic tissues and is mediated via ehrlichial MSP adhesins and leukocyte CD15-associated receptors, after which bacterial infection may control some host cell functions and responses. Later, infected neutrophils are released into the peripheral circulation and adhere to endothelial surfaces, particularly in the spleen, liver, and lung. In vitro, infected neutrophils secrete high levels of chemokines, but not proinflammatory cytokines.

Thus, the localized secretion of chemokines allows recruitment and activation of mononuclear inflammatory cells that in turn release proinflammatory cytokines and induce localized tissue injury. In mice, a kinetic relationship between ehrlichial burden, IFNK release, and pathologic index is observed, suggesting that E. phagocytophila bacteria drive a potentially deleterious inflammatory response but do not directly mediate substantial cell injury. Although not proven, it is suspected that poorly controlled proinflammatory cytokine release may be related to systemic manifestations and increased severity of disease. Continued study of the ehrlichiae and infected hosts will contribute greatly to our understanding of HGE and help to devise better management and treatment strategies.

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Development of Tick Transmission Models for Infections with *Borrelia*, *Babesia*, and *Ehrlichia*

Edward M. Bosler, Ph.D.

Since *I. scapularis* is the vector *for Borrelia burgdorferi*, *Babesia microti* and the agent of Human Granulocytic Ehrlichiosis it stands to reason that a single tick is capable of harboring and transmitting multiple pathogens and that human co-infection may arise from a single tick bite. Our previous field data demonstrates that co-infection occurs in both mammals and ticks on Long Island. These data also indicate the need to establish laboratory tick-animal transmission models to study transfer of multiple pathogens.

We currently maintain infection in C3H mice with the three *B. burgdorferi* genospecies that cause human disease (*B. burgdorferi* sensu stricto, *B. afzelli* and *B. garinii*) via tick transmission. We recently established pathogen infection profiles for the agents of HGE and Babesiosis in 4 inbred mouse strains when the organisms were singly inoculated at 2 dosages via 2 routes of inoculation. In the case of HGE infection three distinct patterns (self limiting, chronic and intermittent) emerged from the different mouse strains used. Patterns of *B. microti* infection were less defined and to produce consistent murine infection the organism had to first be "mouse adapted".

Non-infected larval ticks were fed on HGE infected mice as well as *Babesia* infected mice in order to obtain infected nymphs for subsequent tick to mouse transmission. HGE infection rates in nymphs ranged between 20-50% and appeared to be dependent on the host mouse strain. Currently only SCID mice appear to efficiently infect larval ticks with *B. microti*.

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Vectors of *B. Burgdorferi* and Related Pathogens

John F. Anderson, Ph.D.

Ixodes scapularis in eastern United States and *Ixodes pacificus* in western United States are the primary vectors of *Borrelia burgdorferi* in the New World. The closely related species *Ixodes ricinus* and *Ixodes persulcatus* are the main vectors in the Old World. All four tick species feed on blood three times in their lives, and all feed on many different types of host (lizards, birds, and mammals). All feed on humans as larvae, nymphs, and adults, but most humans acquire infections of *Borrelia burgdorferi* in eastern United States from bites of nymphal *I. scapularis*. Nymphs normally need to be attached for 40 or more hours for *Borrelia* to be transferred from the tick to its host. Most humans acquire their infections in late spring and early summer when nymphs actively seek hosts. The continued increase in numbers of *I. scapularis* is related to the continued increase in abundance of the white-tailed deer, the primary host animal for the adult tick.

We have been identifying ticks sent in by citizens and testing them for the presence of *Borrelia burgdorferi* since 1990. Sixteen species have been identified of which 13 were off humans and six were not native to Connecticut. The most common species received were *I. scapularis, Dermacentor variabilis,* and *Amblyomma americanum.* Of the 25,463 *I. scapularis* tested by culture, IFA, or PCR, 5226 or 22% were infected with *B. burgdorferi.* Ticks attach to humans literally from head to toe; therefore it is important for humans to examine themselves thoroughly for attached ticks and to remove them promptly.

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Personal and Property Prevention Against Lyme Disease

Kirby C. Stafford III, Ph.D.

Objectives: Lyme disease is considered primarily a peridomestic disease. The use of acaricides, vegetative management, deer exclusion, and the acaricidal treatment of deer were evaluated for the control of the tick, *Ixodes scapularis*, at residential landscapes in Lyme and Old Lyme, Connecticut.

Methods: A survey of tick control practices by licensed pesticide applicators was conducted. Various combinations of landscape modifications and pesticides were tested at residential home sites from 1995-1998. Trials of USDA-patented, pesticide self-application deer feeders ('4-posters') were begun in 1997 with monitoring of corn consumption and usage of the devices by deer. The abundance of questing ticks was measured for all studies at both treatment and control sites.

Results: The pesticides carbaryl, chlorpyrifos, and cyfluthrin were the most widely used materials for tick control in 1994 and 1995. The experimental trials found that synthetic pyrethroid insecticides generally reduced nymphal tick abundance by over 90%. Clearing leaf litter and wood chip barriers at the lawn perimeter can reduce nymphal abundance by an average of 42% - 88%. Certain combinations of natural pyrethrin, piperonyl butoxide, and insecticidal soap or silicon dioxide can reduce tick abundance by 71% - 97%, although some combinations of these materials were less effective and produced more variable results. Over 90% of the local deer population were observed utilizing the '4-posters' during the first year of the study, although usage declined in fall 1998 with competing food sources (i.e. acorns).

Conclusions: Acaricides are extremely effective for the control of *I. scapularis* and some less toxic materials may offer an alternative to synthetic chemicals for tick control at individual homes. On a larger scale, the acaricidal treatment of at least 90% of the local deer population could potentially reduce tick abundance community-wide, but the treatment regime will need to be improved.

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The Work-up of Suspected Lyme Disease

Anthony Lionetti, M.D.

Perhaps one of the greatest stumbling blocks to the accurate and consistent diagnosis of Lyme Borreliosis has been the relative failure of the clinical laboratory in confirmation of disease. This is based on the biology of the causative organism, Borrelia burgdorferi and issues in laboratory performance. These issues will be discussed in detail, as well as their impact on clinical research and individual patient management.

Attendees will learn the elements of the History and Physical Examination which may assist them in the diagnosis of the patient with suspected Lyme Borreliosis. Emphasis will be placed on the Differential Diagnosis including Fibromyalgia and Chronic Fatigue Syndrome.

A diagnostic algorithm incorporating the History and Physical examination, along with the use of Special Studies and the Clinical Laboratory will be presented.

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Neuropsychiatric Lyme Disease in Children and Adults

Brian Fallon, M.D.*, Felice Tager, Ph.D. Ron Rykiel, Ph.D.
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While encephalopathy is not recognized in the CDC's Surveillance Case Definition of Lyme disease, cognitive disturbance due to Lyme Disease is common in adults and accounts for much of the long-term disability. Psychiatric disturbances, such as changes in mood, anxiety, paranoia, mania, psychosis, also may emerge during Lyme disease, in some cases as a reaction to having a serious disabling illness and, in other cases, as an organically induced disorder which improves when appropriate antibiotic treatment is given. Recently, published reports indicate that children also may have severe neuropsychiatric problems related to Lyme disease. This talk will review current knowledge about neuropsychiatric Lyme disease in adults and children, focusing upon one recent controlled study of neuropsychiatric problems in children with Lyme disease.

Methods 22 children with Lyme disease and 27 healthy age- and sex-matched controls between the ages of 8 and 18 were recruited. Measures of psychopathology included the Child Behavior Checklist (parent and child form), the DuPaul Attention Deficit Hyperactivity Disorder Rating Scale, the Child Depression Inventory, and a comprehensive neuropsychiatric symptom checklist. In addition, parents and children with Lyme disease were interviewed using the Diagnostic Interview Schedule for Children to obtain DSM Axis I disorders.

Results The children with Lyme disease were ill for over 3 years (mean 39.9 months). The mean time between symptom onset and diagnosis was 10.5 months. Nearly two-thirds had received IV antibiotics in addition to oral antibiotic treatment. Among the ongoing symptoms endorsed by over 70% of the Lyme children, the majority were neuropsychiatric (irritability, rage reactions, mood swings, depression, headache, poor concentration, memory loss) and systemic (fatigue, arthralgias, insomnia). Each symptom was reported significantly more frequently by the Lyme sample than the controls. 50% of the children with Lyme disease reported suicidal ideation and 9% reported having made a suicide gesture. After controlling for multiple comparisons, the Lyme children had significantly more anhedonia (CDI), more inattentiveness (DuPaul), and more internalization and externalization (CBCL). On the DISC child interviews, the most common diagnoses were disturbances of: *mood* (major depression 55%, systhymia 15%); *fear* (panic disorder 20%, separation anxiety disorder 20%, overanxious disorder 20%); *cognition* (Attention Deficit Hyperactivity Disorder 25%); and *behavior* (Oppositional Defiant Disorder 25%, Conduct Disorder 20%).

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Fibromyalgia, Lyme Disease, and Gulf War Syndrome

Sam T. Donta, M.D.

Ever since the realization that Lyme Disease can exist in a chronic form, there has been an increasing awareness of the relationship of chronic Lyme Disease to other multi-symptom disorders such as fibromyalgia and chronic fatigue. These chronic multi-symptom disorders, including the newest member, Persian Gulf War Illness, share as their major features fatigue, musculoskeletal pain, and neurocognitive dysfunction. On clinical grounds, there is little basis to separate or distinguish one disorder form the other.

This presentation will review some of the epidemiologic features of the chronic multi-symptom disorders, the clinical symptoms, and possible etiologies. Using chronic Lyme Disease as a model, approaches to the diagnosis and management of the multi-symptom disorders will be suggested.

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Discussion These results suggest that neuropsychiatric problems occur among children with chronic Lyme disease, particularly since the majority of parents reported that these neuropsychiatric problems were new-onset after contracting Lyme Disease. The frequency rates of neuropsychiatric disorders are not generalizable to all children with chronic Lyme disease given the likelihood of referral bias affecting our study. Nevertheless, these findings should alert clinicians and educators to the need to consider Lyme disease when faced with a child from a Lyme endemic area who has new onset neuropsychiatric and systemic symptoms.

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Sam T. Donta, M.D.

Ever since the realization that Lyme Disease can exist in a chronic form, there has been an increasing awareness of the relationship of chronic Lyme Disease to other multi-symptom disorders such as fibromyalgia and chronic fatigue. These chronic multi-symptom disorders, including the newest member, Persian Gulf War Illness, share as their major features fatigue, musculoskeletal pain, and neurocognitive dysfunction. On clinical grounds, there is little basis to separate or distinguish one disorder form the other.

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Monitoring Lyme Disease in the Community - First Sentinel Health Site

Daniel Cameron, M.D., M.P.H.

Hypothesis: New and innovative designs are necessary if we are ever to improve the understanding of chronic Lyme disease.

Design: This sentinel health site is set in a private medical practice in Mt. Kisco, Westchester County, New York, USA, an area hyperendemic for Lyme disease. This sentinel health site evaluated a consecutive case series cohort (n=1181) and followed the cohort prospectively. 962 patients were evaluated and treated for Lyme disease from June 1997 to February 1999. 219 patients (19%) were evaluated, observed, but not treated, thus not included in this analysis.

Results:

1) The majority of the 962 treated patients (83%) presented with chronic Lyme disease, the remaining 17% with an erythema migrans rash.
2) Only 123 patients (13%) presented with a positive ELISA with Western Blot confirmation.
3) The treatment success for an initial presentation of chronic Lyme disease was 80%.
4) The prevalence of relapses was 54%.
5) The one year incidence of a relapse was 19%.
6) The success rate of retreating the first relapse was 85%.

Conclusions: This sentinel health site easily affords a timely response to current research questions. When examined using a sentinel health site a high proportion of chronic Lyme disease is revealed, most not able to be confirmed with a positive Western Blot. Most Chronic Lyme disease can be successfully treated but the success is tempered by the high prevalence and incidence of relapses. If a relapse occurs, a relapse can successfully respond to retreatment.

Notes: