



Physicians Alert on Lyme (PAL) is a periodic publication of LymeSig/Lyme E-SIG which is a Special Interest Group of American Mensa, Ltd. interested in Lyme disease. The focus of PAL is to provide quick tips about Lyme disease to physicians and health care workers in an effort to increase understanding and dispel common myths associated with Lyme disease that may adversely affect patient care and public health. Comments and correspondence can be addressed to LymeSig, 323 Chapel Ave, Allentown, PA 18103. Current Coordinator is David P. Bartholomew (D.B., also the editor/publisher). Email:JRQR18A@prodigy.com

“A function of intelligence in any species is survival.”

This is the first publication of Physicians Alert on Lyme. The purpose of the publication is to provide current information about Lyme disease (Neuroborreliosis) to physicians and health care personnel that may be helpful to avoid the pitfalls involved in making a proper diagnosis of Lyme disease. Currently, Lyme disease has been found almost world wide: this includes Italy, Russia, Germany, Denmark, China, South America, Japan, Kuwait, and forty-eight States in the United States among many others. With Global distribution being recognized, it has become more apparent that a physician must become familiar with the disease instead of relying on tests which vary considerably among the numerous species and are directly related to the clinical phases and presentations of the disease. Currently, direct detection methods of finding *Borrelia Burgdorferi Sensu Lato* would best serve the physician and patient, but this type of laboratory diagnostics are for the most part unobtainable at present. D.B.

Excerpts From: LYME DISEASE ----- Centers for Disease Control and Prevention Date Last Rev'd: March 9, 1995 GENERAL FACTS ABOUT LYME DISEASE AND ITS TRANSMISSION. (AOL's Lyme disease resources page).

SYMPTOMS OF CHRONIC LYME DISEASE

Chronic Lyme disease may include abnormalities in the skin, the joints, and the nervous system. **Chronic abnormalities in the skin are rare in the United States, but include localized swelling especially in the ear lobe, and nipple areas; and thinning of the skin on hands and feet.** *

Chronic arthritis is the most widely recognized result of untreated Lyme disease. It most often affects one or a few large joints and usually the knee. . It is considered chronic because it recurs in episodes lasting for as long as 6 months. **Unlike most other forms of arthritis, chronic Lyme arthritis does not usually attack the same joint on both sides of the body at once, and does not affect many joints at once. When Lyme disease does affect a joint, it usually causes swelling with redness and accumulation of fluid in the joint.** Lyme arthritis usually responds to antibiotic treatment; however, if severe joint damage has occurred, complete recovery may not occur or may take a long period of time.

Chronic Lyme disease infection of the nervous system most often **produces pain in arms or legs along with weakness and/or numbness in the affected limbs. These problems are caused by Lyme disease infection of the spinal cord.** With infection of the brain, a number of other problems can occur. These include headaches, severe fatigue, impaired vision, double vision, hearing impairment, facial paralysis and difficulties with memory and thinking. It is important for you to know that all these symptoms including those of the skin, joints and nervous system can be caused by many things other than Lyme disease.

* *NOTE*: Chronic skin abnormalities of late lyme disease may be much less rare in the United States than previously presumed. See the following reference for a case history of a patient with Acrodermatitis Chronica Atrophicans in North Carolina not diagnosed from 1989 through 1995 despite dermatological consults:
<http://www.telemed.med.ecu.edu/telcon/patient3.htm> D.B.

In 1996, Alan Barbour discovered an unculturable species of *Borrelia burgdorferi* in the South and in New Jersey. This adds to the already uncertain reliability of tests for antibodies and antigens. Note the next article on PCR and the clinical relationship to tests.

From the Abstract: Identification of an uncultivable *Borrelia* species in the hard tick *Amblyomma americanum*: possible agent of a Lyme disease-like illness.

Abstract: Bites from the hard tick *Amblyomma americanum* are associated with a Lyme disease-like illness in the southern United States. To identify possible etiologic agents for this disorder, *A. americanum* ticks were collected in Missouri, Texas, New Jersey, and New York and examined microscopically. Uncultivable spirochetes were present in approximately 2% of the ticks. *Borrelia* genus-specific oligonucleotides for the flagellin and 16S rRNA genes were used for amplification of DNA. Products were obtained from ticks containing spirochetes by microscopy but not from spirochete-negative ticks. Sequences of partial genes from spirochetes in Texas and New Jersey ticks differed by only 2 of 641 nucleotides for flagellin and 2 of 1336 nucleotides for 16S rRNA. Phylogenetic analysis showed that the spirochete was a *Borrelia* species distinct from previously characterized members of this genus, including *Borrelia burgdorferi*. Gene amplification could be used to detect these spirochetes in ticks and possible mammalian hosts.

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J Infect Dis, 1996 Feb Vol: 173, p 403-409, UNITED STATES

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Article ID: 96162099

A clinical relationship to test results has been found! When serology is negative, PCR's are positive.

Authors: Mouritsen CL, Wittwer CT, Litwin CM, Yang L, Weis JJ, Martins TB, Jaskowski TD, Hill HR

Title: Polymerase chain reaction detection of Lyme disease: correlation with clinical manifestations and serologic responses.

Source: Am J Clin Pathol 1996 May;105(5):647-54

Abstract: The authors have developed a simple, nested polymerase chain reaction (PCR) assay for amplification of an outer surface protein A (OspA) gene fragment of *Borrelia burgdorferi* using rapid temperature cycling and ethidium bromide detection on agarose gels, and applied it to the diagnosis of Lyme disease in humans. With denaturing and annealing temperature spikes instead of holds, cycle times were less than 20 minutes for a 30-cycle amplification. Using this rapid cycle PCR technique, as few as 5 spirochetes per mL of phosphate buffered saline were detected. In addition, *B burgdorferi* DNA was detected from spirochetes that had been spiked into one of several types of human body fluids including serum, synovial fluid, and cerebrospinal fluid (CSF). A number of clinical samples, which had been tested for Lyme immunoglobulin M (IgM) and immunoglobulin G (IgG) antibody were also examined. In 29 serologic positive samples (14 IgG and IgM positive, 9 IgM alone and 6 IgG alone), *B burgdorferi* DNA was not detected. In contrast, nine serum samples and one synovial fluid from patients with definite clinical features of Lyme disease were found to be negative by EIA and Western blot analysis for IgG and IgM antibody, but contained *B burgdorferi* DNA, as detected by PCR. Polymerase chain reaction analysis of serum and synovial fluid may be of significant diagnostic value in Lyme disease, especially in the absence of a serologic response in early, partially treated and seronegative chronic disease. **This is the first study to report an association between PCR positivity and the absence of a serologic response to Lyme borreliosis.**

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Acrodermatitis Chronica Atrophicans: a Late Manifestation of Lyme Disease -Synopsis

The following is provided for information and is quoted from the article "Acrodermatitis Chronica Atrophicans: Historical and Clinical Overview," by Rudolph J. Scrimenti, Associate Clinical Professor of Dermatology, Medical College of Wisconsin, Milwaukee. Remarks added are in parenthesis.

Montgomery and Sullivan from the Mayo Clinic reviewed 45 cases of ACA in 1945, 39 of which occurred in immigrants. (The other six were native-borne Americans).

(ACA has two stages): early infiltration and/or inflammation and, later atrophy.

ACA is an outstanding example of prolonged latency and chronic infection.

Early ACA usually begins in a subtle fashion with infiltration, inflammation, or doughy swelling of an extremity. Ordinarily mildly symptomatic, on rare occasions it may weep.

Patients do not usually associate it with an earlier bite. In some patients, it may be preceded by signs and symptoms of early LB. However, such information is not volunteered readily by patients because a correlation is often not perceived between symptoms separated by long time intervals.

Slow, but definite progression, over months to years, even decades, is the usual course. Central progression toward the torso ensues.

The face rarely is involved and may resemble dermatomyositis, contact dermatitis or collagen disease. The palms and soles participate in this disease process as they do in syphilis, but the lesions are much more confluent.

Eventually, atrophy appears in the involved sites, subcutaneous fat is lost, and inflammation may subside. Now the skin becomes wrinkled, thin, scaling, dry, hypohidrotic and transparent. The underlying venous architecture is readily visible. Alopecia, hyperesthesia, hypo- and hyperpigmentation may occur. Atrophy also may involve nasopharyngeal, lingual, and vaginal mucous membranes. Various stages of inflammation and atrophy may coexist at the same time.

A noteworthy feature of the atrophy is that it may take many years to occur and it is not an absolute requirement for the diagnosis. Also atrophy may be diffuse or localized. Rarely, sac-like formations occur in areas of macular atrophy. Superinfection of erythema migrans in patients with preexisting ACA has been reported in Europe.

Other special distinguishing features noted in European patients are fibrotic bands, fibrous juxta articular nodules, a distinctive arthropathy and pseudosclerodermoid skin changes.

Fibrous nodules appear painlessly over the elbows, knees, hands, fingers, and elsewhere. Ranging in size from one to three centimeters, they may be solitary, multiple and frequently grouped. Their color varies from yellow white to reddish blue.

European observers have reported a sclerosing process of connective tissue as an integral part of the syndrome of idiopathic atrophy. Such lesions vary from moderately infiltrated, yellow, stretched plaques of skin to firmly indurated marble white areas resembling scleroderma.

Deforming arthritis with bone atrophy associated with ACA was first reported in 1924 by Jesner.

Recent studies indicate subluxations, and luxations of small bones of the hands and feet are the most characteristic arthritic features.

A mild, but chronic, motor and/or sensory axonal polyneuropathy is characteristic in a large percentage of patients with chronic borreliosis on both sides of the Atlantic.

ASSOCIATED CONDITIONS . Enthesopathies, periostitis, myositis, myalgias, fasciitis, localized and generalized lymphadenopathy, weight loss fatigue, personality disorders usually with negative cerebrospinal fluid laboratory findings have been reported with ACA.

LABORATORY FINDINGS. Increased erythrocyte sedimentation rates are noted regularly. The organism can be cultured slowly on modified Barbour-Stoener-Kelly medium from skin lesions, even decade-old lesions at temperatures of 32° to 33° C. Focal areas of plasma cells may be present in the deeper dermis. With progression, epidermal thinning, degeneration of elastic fibers and collagen occurs. Eventually after many years, advanced atrophy of the dermis, including all appendages, follows the inflammation. Later, the inflammation disappears, and a pronounced thinning of the entire dermis and subcutis develops. A rich mixture of plasma cells, if present may be the only feature differentiating sclerotic and atrophic ACA from idiopathic scleroderma (morphea) and lichen sclerosus, except for the presence of the spirochete. Immunohistologic staining shows a predominance of CD4 lymphocytes. Most, but not all, studies show no association between the development of ACA and HLA class II alleles. (Newly identified species may not culture and other tests may be negative).

DIFFERENTIAL DIAGNOSIS. The distinctive plasmacytic infiltrate (if present), unique clinical features and serologic findings differentiate ACA from arterial and venous insufficiency, acrocyanosis, livedo reticularis, vasculitis, contact dermatitis and collagen diseases. Fibrotic nodules histologically are distinguished from gouty tophi, calcinosis cutis, rheumatoid nodules and xanthomas.

Article source: Journal of Spirochetal and Tick-borne Diseases; Vol2, No4: 97-100. For reprints of the article, address request to R.J. Scrimenti, MD, 3316 East Silver Spring Dr., Suite 302, Milwaukee, WI 53217 D.B.

LYMPHOCYTOMA OF EAR LOBE IS FOUND IN THE UNITED STATES:

- JOURNAL ARTICLE LA - Eng SO - J Wildl Dis 1996 Jul;32(3):560-2 UI - 97134735 AU - Picken RN AU - Strle F AU -Ruzic-Sabljić E AU - Maraspin V AU - Lotric-Furlan S AU - Cimperman J AU - Cheng Y AU - Picken MM TI - Molecular subtyping of *Borrelia burgdorferi* sensu lato isolates from five patients with solitary lymphocytoma. AD - Section of Infectious Disease, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois, USA. AB - Solitary lymphocytoma is a rare cutaneous manifestation of Lyme borreliosis that has been reported almost exclusively from Europe. This suggests that its etiologic agent may be absent or extremely rare on the North American continent. All three species of *B. burgdorferi* sensu lato known to be associated with human Lyme borreliosis (*B. burgdorferi* sensu stricto, *B. garinii*, and *B. afzelii*) have been isolated in Europe, whereas only *B. burgdorferi* sensu stricto has been found in North America. This suggests that either *B. garinii* or *B. afzelii* might be the etiologic agent of borrelial lymphocytoma. To investigate this hypothesis we characterized five strains of *B. burgdorferi* sensu lato isolated from lymphocytoma lesions of patients residing in Slovenia. The methods used included: large restriction fragment pattern analysis of restriction enzyme MluI-digested genomic DNA, plasmid profiling, protein

profiling, ribotyping using 5S, 16S, and 23S rDNA probes, and polymerase chain reaction amplification of the rrf (5S)-rrl (23S) intergenic spacer region. Molecular subtyping showed that four of the five isolates belonged to the species *B. afzelii*; however, this species is the predominant patient isolate in Slovenia and, therefore, may not represent a preferential association with lymphocytoma. The fifth isolate appeared to be most closely related to the DN127 genomic group of organisms. Further characterization of the isolate revealed that it possessed a unique molecular "fingerprint." The results not only show that borreliosis can be caused by *B. afzelii* but also demonstrate an association with another genomic group of *B. burgdorferi sensu lato* that is present in North America as well.

LYME DISEASE IS NOT UNCOMMON IN THE SOUTHERN UNITED STATES:

J Parasitol 1996 Dec;82(6):936-40 CONTINUE PRINTING? (YES/NO) USER: Y PROG: 19 UI - 97128861 AU - Oliver JH Jr TI - Lyme borreliosis in the southern United States: a review. RF - REVIEW ARTICLE: 134 REFS. AD - Institute of Arthropodology and Parasitology, Georgia Southern University, Statesboro 30460-8056, USA. AB - Lyme borreliosis (Lyme disease) is the most often reported arthropod transmitted disease in humans in the U.S.A. Although it has been reported from 43 states, cases are especially abundant in the mid-Atlantic and north-eastern regions. *Borrelia burgdorferi*, the etiologic agent, is transmitted primarily by the western blacklegged tick (*Ixodes pacificus*) in far western North America, and by the blacklegged tick (*Ixodes scapularis*) in eastern North America. Although Lyme disease cases have been reported from southern states, some researchers doubt the presence of *B. burgdorferi* or of human Lyme disease in the south. However, new data show that *B. burgdorferi* is widely distributed in the south and that strains are genetically more varied than in the north. Moreover, *B. burgdorferi* enzootic cycles appear to be more complex and more tick species are identified as vectors of the spirochete in the southern states.

A SPRING/AUTUMN CYCLIC PERIODICITY?

JOURNAL ARTICLE LA - Rus SO - Parazitologija 1996 Sep-Oct;30(5):458-60 33 UI - 97103641 AU - Grigor'eva LA TI - [Borreliosis in laboratory rabbits] AB - The borreliosis of laboratorian rabbits displays as a chronic infection with recurrences during a spring-autumn season. The clinical picture includes a skin-ulcerous lesion, arthritis accompanied by lymphocytosis and borreliemia.

DIRECT DETECTION METHODS SHOWN SUPERIOR:

JOURNAL ARTICLE PT - REVIEW PT - REVIEW, ACADEMIC LA - Eng SO - Curr Probl Pediatr 1996 Jul;26(6):189-207 52 UI - 96412884 AU - Strle F AU - Nelson JA AU - Ruzic-abljic E AU - Cimperman J AU - Maraspin V AU - Lotric-Furlan S AU - Cheng Y AU - Picken MM AU - Trenholme GM AU - Picken RN TI - European Lyme borreliosis: 231 culture-confirmed cases involving patients with erythema migrans. AD - Department of Infectious Diseases, University Medical Centre, Ljubljana, Slovenia. AB - In 1994, we isolated *Borrelia burgdorferi sensu lato* from 231 patients with erythema migrans who presented to the University Medical Center in Ljubljana, Slovenia. Samples of erythema migrans-affected skin were placed in

media to support the growth of *Borrelia* species and evaluated in Ljubljana and Chicago. Patients whose cultures were positive included 132 women and 99 men; 136 of these 231 patients recalled a tick bite. Patients noted a rash an average of 24 days after a bite and presented a mean of 34 days after the bite with erythema migrans (mean diameter. 16 cm). Itching (44%) burning (18%), and pain (11%) were the most common local symptoms. Systemic complaints (40%) included headache, fatigue, malaise, and arthralgia. Other than erythema migrans, findings on physical examination were minimal (< 5% had fever, and in < 10% local lymph nodes were affected). Serial serological studies using indirect immunofluorescence assay, ELISA, and Western blot methods were performed, and antibodies to *B. burgdorferi sensu lato* were detected in < 50% of samples from patients. **This is the largest series reported to date of patients with culture-confirmed Lyme borreliosis. It highlights the deficiencies of serological tests in early disease, demonstrates the sensitivity of direct detection methods for evaluation of patients with erythema migrans, and suggests that patients with early Lyme borreliosis in Slovenia may suffer a milder illness than those in the United States.**

LYME ARTHRITIS - FROM RUSSIA WITH LOVE

In an article in *Ter Arkh* 1995;67(11):43-5, written in the Russian Language, with English title "Lyme Arthritis: the joint lesions in Lyme borreliosis in the USA" written by Allen C. Steere, the following excerpts are quoted for information; from the abstract:

“Lyme's arthritis arises due to invasion of *Borrelia burgdorferi* into articular tissues.”

“The study of different cytokine concentrations in the synovial fluid in 83 patients with Lyme's arthritis showed that chronicity of arthritis depends on IL-1b and IL-1ra balance. As indicated by examination of 80 patients with Lyme's arthritis chronic persistence of articular syndrome in 57% was associated with HLA-DR4, in 43% with HLA-DR2.”

“Lyme's arthritis requires long-term treatment. In it's failure arthroscopic synovectomy is indicated.”

Note: This is the first publication I am aware of in which A.C.Steere indicates the requirement for long-term treatment. Previous articles, such as that in *Infectious Arthritis “Lyme Disease”* by Robert Kalish, MD, Vol.19, No.2, May 1993, indicated that “Treatment with appropriate antibiotics is successful in the majority of cases of Lyme disease. However, some patients may not respond, and in these cases multiple repeated courses are usually ineffective and unwarranted.” The finding that long-term treatment is REQUIRED suggests the answer for the ineffectiveness of repeated short term (10 days to 28 days) treatments that have proven ineffective in the past. My review and analysis of some of world medical literature furnished to me in 1994 and 1995 by the CDC indicated a more likely effectiveness of duration would be six weeks minimum. This is contrary to published guidelines by the ACP and the European Union Concerted Action on Lyme Borreliosis (EUCAIR) which recommend shorter durations. D.B.

Editor's comments and Disclaimer.

Certainly it is the treating physician alone who must bear the choices he or she makes concerning a patient's health. In the busy world of medical care, the time to keep up with the latest information concerning all conditions or diseases is not available. Knowledge is one foundation of clinical judgment, and it is hoped that the information provided in this brief bulletin may be found useful in some ways. The other foundation of clinical judgment is, of course, experience. The pathogenicity of Lyme disease is beginning to become known slowly. Bad experiences due to lack of, or misunderstanding of the disease in question is to be avoided. This is difficult to do given the context of controversy currently surrounding all issues concerning Lyme disease. Opinions vary, and "expertness" can quickly obsolesce.

LymeSig, which publishes this bulletin "PAL", is a Special Interest Group of American Mensa, Inc. Special Interest Groups (SIGs) are formed by individual members of Mensa as they so choose. Mensa itself is not responsible for the opinions of their members, who only have one thing in common: a recognized "genius" IQ. Basically, LymeSig is a group of people who have voluntarily decided to talk to one another about Lyme disease. Some of us have Lyme disease. The quote "a function of intelligence in any species is survival," applies not just to ourselves as victims, but to our unwelcome guest *Borrelia burgdorferi*. As genius begins to understand its relationship as host to the pathogen, and explores the scientific and medical literature extant about the relationship, it is hoped that our group dialectic may help, in some ways, not just ourselves, but others. Therefore, PAL is distributed world-wide.

Comments and criticism, as always, are invited. Send any, good or bad, to LymeSig, 323 Chapel Avenue, Allentown, PA , United States of America, 18103-3457. E-mail to JRQR18A@prodigy.com. Responses to ideas and opinions offered are made as often as possible. If you have anything you would like to publish in this, or the regular newsletter of LymeSig, forward that article, memo, whatever to the same address.

There are two distributions of this publication. One is through our Lyme E-Sig via the internet. Depending on communications and printing capabilities, the internet version may have various appearances. Another distribution is through hard copy. Hard copy originals have a red bulls-eye on the top right front page.

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**David P. Bartholomew
Coordinator**