Please note: Italics have been added to support the need of a timely update to the IDSA Lyme treatment guidelines. These quotes are pulled directly from studies authored or co-authored by individuals that participated in the initial creation of the IDSA Lyme treatment guidelines. Text not in italics is pulled directly from the Final Report of the Lyme Disease Review Panel unless otherwise noted.

Post Lyme Syndromes

2006 Recommendation

To date, there is no convincing biologic evidence for the existence of symptomatic chronic B. burgdorferi infection among patients after receipt of recommended treatment regimens for Lyme disease.

Panel Determination/Discussion - The Review Panel determined that this recommendation is medically/scientifically justified in light of all of the evidence and information provided (7-1).

When the 2006 Lyme Guidelines are next updated, the Review Panel suggests that consideration be given to changing the phrase "no convincing biologic evidence" to something more specific… It has been proposed by some that there are hardy, drug-tolerant reservoirs of B. burgdorferi, including intracellular cystic forms. To date, this has not been shown to correlate with symptom persistence, nor has eradication of these forms been shown to correlate with symptom improvement.

"We conclude that the presence of chronic Lyme disease cannot be excluded by the absence of antibodies against B. burgdorferi and that a specific T-cell blastogenic response to B. burgdorferi is evidence of infection in seronegative patients with clinical indications of chronic Lyme disease."[1]

-Dattwyler & Halperin

"Patients may develop chronic neuroborreliosis years after early manifestations of Lyme disease In the current study, B. burgdorferi DNA was detected in such patients a median of 7.3 years and as long as 27 years after disease onset. Although only 4 samples in this study were positive with more than one primer pair, this includes the sample obtained 27 years after disease onset, which was positive in both laboratories, and a sample obtained 7 years after disease onset. This provides the best evidence to date that the Lyme disease spirochete may persist actively or latently in the nervous system for years. This prolonged disease course, with long periods of active and latentinfection, is reminiscent of tertiary neurosyphilis."[2]

-Steere

"We have shown that treatment with high doses of amoxicillin or doxycycline for a 30-day period was not sufficient to eliminate the persistent infection."[3]

-Strle

[1] Dattwyler RJ, Volkman DJ, Luft BJ, Halperin JJ, Thomas J, and Golightly MG. Seronegative Lyme disease. Dissociation of specific T- and B-lymphocyte response to Borrelia burgdorferi. N Engl J Med 1988; 319(22): 1441-1446.

[2] Nocton JJ, Bloom BJ, Rutledge BJ, Persing DJ, Logigian EL, Schmid CH, and Steere AC. Detection of Borrelia burgdorferi DNA by polymerase chain reaction in cerebrospinal fluid in Lyme neuroborreliosis. J. Infect Dis 1996; 174: 623-627.

[3] Maraspin V, Ruzic-Sabljic E, Strle F, Cimperman J, Jereb M, Preac-Mursic V. Alpc Adria Microbiol J. Persistence of Borrelia burgdorferi after treatment with antibiotics.1995; 3: 211-216.

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"In the patient described herein, Borrelia apparently persisted for years without causing symptoms. After the surgical intervention, the spirochetes were detectable by PCR; however, their presence was assessed not only by PCR, but also by culture. This is clearly the best confirmation of present infection."[4]

-Stanek

"Results indicated that following antibiotic treatment, mice remained infected with nondividing but infectious spirochetes, particularly when antibiotic treatment was commenced during the chronic stage of infection."[5]

-Bockenstedt & Fish

"These findings demonstrate the capacity of viable B. burgdorferi sensu lato organisms to persist in clinically normal-appearing skin at the site of a resolved erythema migrans rash for periods ranging from 2 months to 3.5 years."[6]

-Strle

"…in Lyme arthritis, a small number of spirochetes are probably the antigenic stimulus for chronic synovial inflammation."[7]

-Steere

"Our study substantiates borrelial persistence in some EM patients at the site of the infectious lesion despite antibiotic treatment over a reasonable time period."[8]

-Strle

"These findings, however, do not rule out phenotypic resistance mechanisms similar to those assumed to cause relapse in syphilis and leptospirosis."[8]

-Strle

"In contrast, among six patients with prolonged illness, the IgM response to the 41-kD protein sometimes persisted for months to years…The appearance of a new IgM response and the expansion of the IgG response late in the illness, and the lack of such responses in patients with early disease alone, suggest that B. burgdorferi remains alive throughout the illness." [9]

-Steere

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[4] Marlovits S, Khanah G, Striessniq G, Vécsei V, and Stanek G. Emergence of Lyme arthritis after autologous chondrocyte transplantation. Arthritis Rheum. 2004; 50: 259-264.

[5] Bockenstedt LK, J Mao, E Hodzic, SW Barthold, and D Fish. Detection of attenuated, non-infectious spirochetes in Borrelia burgdorferi-infected mice after antibiotic treatment. J Infect Dis 2002; 186: 1430-1437.

[6] Strle F, Cheng Y, Cimperman J, Maraspin V, Lotric-Furlan S, Nelson JA, Picken MM, Ruzic-Sabljic E, and Picken R. Persistence of Borrelia burgdorferi sensu lato in resolved erythema migrans lesions. Clin Inf Dis 1995; 23: 380-389.

[7] Steere AC, Duray PH,, and Butcher EC. Spirochetal antigens and lymphoid cell surface markers in Lyme synovitis. Comparison with rheumatoid synovium and tonsillar lymphoid tissue. Arthritis Rheum 1988; 31: 487-495

[8] Hunfeld KP, Ruzic-Sabljic E, Norris DE, Kraiczy P, and Strle F. In vitro susceptibility testing of Borrelia burgdorferi sensu lato isolates cultured from patients with erythema migrans before and after antimicrobial chemotherapy. Antimicro Agents Chemother 2005; 49: 1294-1301.

[9] Craft J, Fischer DK, Shimamoto GT, Steere AC. Antigens of Borrelia burgdorferi recognized during Lyme disease appearance of a new immunoglobulin M response and expansion of the immunoglobulin G response late in the illness. J. Clin. Invest. 1986; 1978: 934-939.

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"Erythema migrans recurred in a patient 6 months after a course of treatment with minocycline for Lyme disease. Polymerase chain reaction on heparinized peripheral blood at that time demonstrated the presence of Borrelia burgdorferi-specific DNA. The patient was seronegative by Lyme enzyme-linked immunosorbent assay but showed suspicious bands on Western blot" [10]

-Shapiro & Halperin

"Despite antibiotic therapy, there was progression to a chronic stage, with multisystem manifestations... Viable spirochetes were identified."[11]

-Krause

"All of these histologic derangements suggest immunologic damage in response to persistence of the spirochete, however few in number."[12]

-Steere

"Fibroblasts protected B. burgdorferi for at least 14 days of exposure to ceftriaxone. Mouse keratinocytes, HEp-2 cells, and Vero cells but not Caco-2 cells showed the same protective effect. Thus, several eukaryotic cell types provide the Lyme disease spirochete with a protective environment contributing to its long-term survival." [13]

-Klempner

"These observations suggest that B. burgdorferi can adhere to, penetrate, and invade human fibroblasts in organisms that remain viable." [14]

-Klempner

"These novel findings suggest that reactive alterations of the phagocytes may contribute to the pathogenesis of Lyme borreliosis, which could help to focus future histopathological studies. Moreover, these results may provide new insights into the pathogenesis of other infectious diseases characterized similarly by microbial persistence."[15]

-Krause

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[10] Liegner KB, Shapiro JR, Ramsay D, Halperin AJ, Hogrefe W, and Kong L. Recurrent erythema migrans despite extended antibiotic treatment with minocycline in a patient with persisting Borrelia burgdorferi infection. J Am Acad Dermatol 1993; 28: 312-314.

[11] Häupl T, Hahn G, Rittig M, Krause A, Schoerner C, Schonherr U, et al. (1993) Persistence of Borrelia burgdorferi in ligamentous tissue from a patient with chronic Lyme borreliosis. Arthritis Rheum; 36(11): 1621-1626.

[12] Duray PH and Steere AC. Clinical pathologic correlations of Lyme disease by stage. Ann N Y Acad Sci 1988; 539: 65-79.

[13] Georgilis K, Peacocke M, and Klempner MS. Fibroblasts protect the Lyme disease spirochete, Borrelia burgdorferi, from ceftriaxone in vitro. J Infect Dis 1992; 166: 440-444.

[14] Klempner MS, Noring R, and Rogers RA. Invasion of human skin fibroblasts by the Lyme disease spirochetes, Borrelia burgdorferi. J Infect Dis 1993; 167: 1074-81.

[15] Rittig MG, Häupl T, Krause A, Kressel M, Groscurth P, Burmester GR. Borrelia burgdorferi-induced ultrastructural alterations in human phagocytes: a clue to pathogenicity? J Pathol 1994; 173: 269-282.

Excerpt from The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America

In many patients, post treatment symptoms appear to be more related to the aches and pains of daily living rather than to either Lyme disease or a tick-borne coinfection. Put simply, there is a relatively high frequency of the same kinds of symptoms in "healthy" people. For example, 20%–30% of adults complain of chronic fatigue [261–263], and in the 2003 National Health Interview Survey, the frequency of doctor-diagnosed arthritis cases among adults was 21.5% [264]. A study in England found a point prevalence of 11.2% for the presence of self-reported chronic widespread pain among adults that was frequently associated with feelings of depression and anxiety, fatigue, and somatic symptoms [265]. A recent study of the general adult United States population estimated a point prevalence of self-reported serious pain (level 3) to be 3.75%– 12.10%, depending on the assessment tool used; for level 3 emotional or cognitive dysfunction, it was 2.17%–3.42% [266]. Population-based surveillance in the United States indicates a mean of 6.1 self-reported unhealthy days during the preceding month [267]. Thus, the presence of arthralgia, myalgia, fatigue, and other subjective symptoms after treatment for Lyme disease must be evaluated in the context of "background" complaints in a significant proportion of individuals.

*"Compared with the control group (*n *= 43), the Lyme group (*n *= 38; mean duration from disease onset to study evaluation, 6.2 years) had more arthralgias (61% compared with 16%;* P *< 0.0001); distal paresthesias (16% compared with 2%;* P *= 0.03); concentration difficulties (16% compared with 2%;* P *= 0.03); and fatigue (26% compared with 9%;* P *= 0.04), and they had poorer global health status scores (*P *= 0.04). The Lyme group also had more abnormal joints (*P *= 0.02) and more verbal memory deficits (*P *= 0.01) than did the control group. Overall, 13 patients (34%; 95% CI, 19% to 49%) had long-term sequelae from Lyme disease (arthritis or recurrent arthralgias [*n *= 6], neurocognitive impairment (*n *= 4), and neuropathy or myelopathy [*n *= 3]). Compared with controls, patients who had long-term sequelae had higher IgG antibody titers to the spirochete (*P *= 0.03) and received treatment later (34.5 months compared with 2.7 months;* P *< 0.0001)."*[16]

-Steere

"In adults a subtle encephalopathy characterized primarily by memory impairment, irritability and somnolence may occur months to years after classic manifestations of Lyme disease."[17]

-Steere

"Children may develop neurocognitive symptoms along with or after classic manifestations of Lyme disease. This may represent an infectious or post infectious encephalopathy related to B. burgdorferi infection." [17]

-Steere

"It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances."

[16] Shadick NA, Phillips CB, Logigian EL, Steere AC, Kaplan RF, Berardi VP, et al. The long-term clinical outcomes of Lyme disease. A population-based retrospective cohort study. Ann Int Med 1994; 121: 560-567.

[17] Bloom BJ, Wyckoff PM, Meissner HC, and Steere AC. Neurocognitive abnormalities in children after classic manifestations of Lyme disease. Pediatric Infect. Dis. J. 1998; 17(3): 189-196.