Rationale for Prolonged Antibiotic Therapy in Treating Lyme Disease

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In my opinion and in my experience in treating over ten thousand young people with Lyme disease, decisions on duration of treatment in many cases where there is central nervous system involvement and chronic persistent infection, are best determined by clinical response, as would be the case with any other illness or infectious disease and not by any arbitrary limit of days given. There is very ample documentation in the peer reviewed medical literature of the ability of the Lyme organism to survive intensive and prolonged antibiotic treatment, including intravenous antibiotics. A recent report in *Infection* by Steven Phillips, et al. (1998 Nov-Dec 26 (6): 364-367) indicates that *Borrelia burgdorferi* spirochetes can be reliably cultured from the blood of patients with Lyme disease, even from those previously aggressively treated with antibiotics. In my experience, patients with chronic central nervous system infection can benefit from many months of intravenous antibiotic treatment. Although such durations of treatment are controversial within the medical community, at the 1991 NIH State-of-the-Art Conference on Lyme disease, there was general agreement that optimal regimens of antibiotic therapy for central nervous system Lyme disease remained to be defined. Thus, it is not sustainable to adopt a doctrinaire position about what constitutes “sufficient” therapy in individual cases.

Much has been made of the risks and expenses of prolonged oral, intramuscular and intravenous antibiotic therapy. Without such treatment, however, patients are likely to remain very compromised, may become unable to finish their education, earn a living, and run the risk of pursuing a course of progressive deterioration. The following evidence, supporting the rationale for prolonged antibiotic therapy for Lyme disease, can be used to evaluate and determine the therapy for anyone with this infection.

Lyme disease is a chronic, persisting, difficult disease to treat, which is caused by *Borrelia burgdorferi* spirochetes. There has never been a study in the history of Lyme disease that, even in the simplest way, proves that a short course, 2-6 weeks, therapy results in bacteriologic cure. There is no double blind study to determine the optimal duration of antibiotic treatment for Lyme disease. There is evidence, however, that if antibiotic treatment therapy is stopped before symptoms resolve, then the patient will relapse and Lyme disease will progress. 1,2,3,4,5 Lyme disease can respond favorably to antibiotic treatment in all stages, but it is far from clear whether currently available methods of treatment achieve genuine bacteriologic cure. Many other patients with Lyme disease remain well following oral, IM, or IV antibiotic therapy. Many other patients with Lyme disease, however, improve while on antibiotic therapy but deteriorate or relapse when the antibiotic therapy is stopped. The relief of symptoms when taking another round of antibiotics is consistent with persistent infection. Patients with Lyme disease on antibiotic therapy experience a worsening of symptoms during the first days of antibiotic therapy and periodically as the therapy continues. This worsening of symptoms is consistent with a Jarisch-Herxheimer reaction which is an immune response to the destruction of *Borrelia burgdorferi* spirochetes, the bacteria that cause Lyme disease. A Jarisch-Herxheimer reaction indicates an active *Borrelia burgdorferi* infection. Despite the fact that *Borrelia burgdorferi* spirochetes are almost impossible to culture from any infected host, 6,7,8 there are well-documented culture confirmations of persisting *Borrelia burgdorferi* infection in antibiotic-treated patients. 1,9 *Borrelia burgdorferi* spirochetes have been cultured from patients who have been given intensive (21 days to one year) antibiotic therapy with IV third generation cephalosporins. 3,9,10,11,12
There are many ways by which *Borrelia burgdorferi* spirochetes resist antibiotic and immune destruction. The Lyme spirochetes can attain in vivo antibiotic resistance by their ability to live intracellularly in fibroblasts, endothelial and glial cells, as well as other cells. Another way in which *Borrelia burgdorferi* can escape destruction by antibiotics is by virtue of its slow rate of division. Since many antibiotics, such as beta-lactams, only kill actively dividing organisms, the fact that some cultures of *Borrelia burgdorferi* have taken up to 10.5 months to grow, suggests that certain treatment length guidelines are too short.

L-forms of many bacteria have long been shown to be pivotal in setting up chronic infection. The discovery of L-forms of *Borrelia burgdorferi* implies that antibiotics would likely result in treatment failures. These mutant forms of *Borrelia burgdorferi* develop resistance to antibiotics in several ways. One is by loss of their cell wall, thereby circumventing cell wall-acting antibiotics such as beta-lactams, and taking this step even further, many L-forms actually lose their ability to replicate, easily sidestepping replication-dependent antibiotics. *Borrelia burgdorferi* spirochetes can evade immune surveillance by releasing blebs which bind free antibodies, forming immune complexes. These immune complexes are not detected by Lyme ELISA and Lyme western blot assays, which only detect free antibodies. *Borrelia burgdorferi* spirochetes can also escape immune detection by altering surface protein antigens.

Considering the difficulty in eradicating the organism that causes Lyme disease, it is realistic to use two antibiotics simultaneously, one antibiotic that acts on the surface of the organism and the other internally.

Antibiotic therapy should be continued for at least two months after any Jarisch-Herxheimer reaction has occurred, at least two months after there is no recurrence of Lyme symptoms in response to other infections or menstruation, and after all Lyme symptoms are resolved or stabilized. If antibiotic therapy is stopped prematurely, the patient’s Lyme disease will relapse and result in more *Borrelia burgdorferi* brain and body injury by a more resilient and difficult-to-treat Lyme organism.

References:


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