Letter to the Editor

Please find a response to the June 16, 2017 CDC MMWR publication entitled “Serious Bacterial Infections Acquired During Treatment of Patients Given a Diagnosis of Chronic Lyme Disease United States.” [1] In this report, Marzec, et al describe 5 cases regarding “...reports of serious bacterial infections resulting from treatment of persons who have received a diagnosis of chronic Lyme disease. Five of these cases are described to illustrate complications resulting from unproven treatments, including septic shock, Clostridium difficile colitis, abscess and death.” While this case series is troubling regarding poor outcomes for any individuals being treated by their clinicians, there are two major take home messages promoted by this paper that are disconcerting:

1. Characterization of chronic Lyme disease as a nebulous term for “various constitutional, musculoskeletal and neuropsychiatric symptoms.”
2. “Studies have not shown that such treatments lead to substantial long-term improvements for patients.”

We too are concerned about any individual whose outcomes represent complications to well-intentioned intervention. However, we truly feel that there is substantive support in the literature for the existence of

1. Chronic Lyme disease-the clinical manifestations of ongoing active infection by Borrelia burgdorferi (Bb) sensu latu complex in the setting of either chronic untreated or inadequately treated individuals.
In his 2013 review article, Stricker summarized “evidence from animal models, human studies and in vitro experiments that support persistent spirochetal infection as the cause of chronic Lyme disease.” [2]

The 2012 Embers study [3] on non-human primates involved 12 Rhesus monkeys that were infected with Bb and subsequently treated with the equivalent protocol used in the 2001 Klempner human trials. [4] Further, there was substantiation that adequate MICs and MBCs of ceftriaxone and doxycycline were employed. Four weeks after completion of this protocol, all of the animals were sacrificed. 12 of the 12 enrolled were positive by skin culture for Bb. In a 2014 murine report, Hodzic, et al [5] infected 48 mice with Bb and treated these animals with ceftriaxone for 25 days such that MBCs were clearly achieved. There was PCR evidence of Bb DNA at 2, 4 and 8 months after completion of treatment. Viability of infectivity was confirmed through xenodiagnostic methods, whereby Bb naive ticks feeding on the PCR positive mice, were then able to actively infect Bb naive mice. Hodzic went on to reference 7 other animal studies supporting persistence of this infection after standard courses of antibiotics. [6-12]

Additional human reports support this post treatment persistence of active Bb infection. [13-20]

A number of studies discount the second concern characterized in this MMWR report:

2. “Studies have not shown that such treatments lead to substantial long-term improvements for patients.”

In 2 of the 4 NIH supported prospective human trials by Fallon [21] and Krupp [22], sub-cohort analysis clearly showed statistically significant benefit to retreatment. In the former study 37 patients who were felt to have active neuroborreliosis, and were treated with 10 weeks of 2gms/day IV Ceftriaxone. Pain and physical functioning improved at 12 and was sustained at 24 weeks. The authors felt that “these benefits were felt to be independent of carefully assessed placebo effects.” In the latter study 55 patients who were felt to have active infection by Bb, with persistent severe fatigue of 6 or more months received 28 days of IV Ceftriaxone. A significant improvement in fatigue was sustained at 6 months.

Further, several other prospective trials of prolonged antimicrobial treatment were employed that also revealed statistically significant improved outcomes. [23-25] Cameron [25] reported improved outcomes using the SF36 quality of life metric, in 52 patients with persistent symptoms following treatment for acute Lyme disease. 52 received amoxicillin 3gms/day in divided doses compared to 32 who received placebo. Wahlberg [25] compared the treatment of patients with acute Lyme disease in three arms:
14days of IV Ceftriaxone only, 14days of IV Ceftriaxone followed by 100 days of amoxicillin and probenecid and 14days of IV Ceftriaxone followed by 100 days of cephadroxil. Using standard outcome measures, clinical improvement compared to baseline, was characterized by the author as 31%, 89% and 83% respectively. In 1998 Oksi [25] reported 30 patients with Lyme disease Threated for 100 days with “good or excellent” responses.

As unfortunate as these 5 cases are, we believe that they should not be used to discount a real entity, chronic Lyme disease. Nor should this series be used to entirely discount the judicious use of long term antibiotics for the carefully selected individual. In summary, in those individuals whose ongoing presentation is felt by their Clinician to be due to an active infection by Bb sensu latu complex, treatment according to clinical responses is more appropriate than use of an arbitrary “guideline.” Caveats are that a careful differential diagnosis will be generated, proactive management with probiotics and carefully monitoring will be undertaken. But that these often disabled individuals when felt to be appropriate by their Clinician at the point of care, warrant access to “prolonged antibiotics, with compassion and empathetic oversight.

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1. https://www.cdc.gov/mmwr/volumes/66/wr/mm6623a3.htm?s_cid=mm6623a3_e


CC: Honorable Thomas Price, MD
Secretary of Human Health Services