The Mayday Project: Response to the IDSA's Statement to FOX News

In response to our protest at the Infectious Diseases Society of America's headquarters in Arlington, Virginia, several points were aired on FOX news regarding the issues brought forth. In 2010, the IDSA held a special review of the Lyme disease treatment guidelines. They concluded that there is 'no convincing evidence of chronic Lyme infection.' One of the main goals in protesting the IDSA is to obtain acknowledgement that persistent infection is possible. An overwhelming abundance of evidence to support persistent infection already exists and further research must be done to update the clinical practice guidelines accordingly.

Symptoms in an affected person can persist weeks, months, and even years after treatment. These multi-systemic symptoms may include pain, impaired cognition, and fatigue (Jarefors, 2007). Repeated manifestations of similar symptoms during the course of infection prevent reliable classification of "early" versus "late" stage infection, making it extremely difficult to determine the longevity of the illness (Barbour, 2012).

In 2006, IDSA members Shapiro, Wormser, and Dattwyler confirmed that approximately 30% of people treated with 2-4 weeks of a single antibiotic for Lyme disease will have persistent or recurring symptoms (Green, 2009), which is contrary to their current stance. The research of Allen Steere, the man who initially produced the description and definition of Lyme disease, failed to show that all symptoms diminished after a short course of antibiotics. European research indicates success with extended use of antibiotic treatment (Ferguson, 2012).

A study by Logigian found that months to years after initial infection, chronic symptoms can occur and usually improve with antibiotic therapy (Logigian, 1990). It is notable that Steere co-authored this study focused on chronic presentation of the disease. A study by Hook et al. found

that over a three year time span, 42% of individuals diagnosed with Lyme disease remained ill for more than six months, 12% were ill for more than three years, and 36% of them were treated with antibiotics for more than eight weeks. Dr. Charles Ray Jones states that there has never been a study that demonstrates that a short course of antibiotic therapy results in eradication of the bacteria.

Diagnostic delays of two years often exist, possibly contributing to the fact that duration of illness can be between 4.7 to 9 years. In addition, patients that received delayed treatment were less likely to receive relief from initial antibiotic treatment (Cameron, 2010). With all of this research in mind, it is unfathomable to believe that there is no evidence for a persistent infection of Lyme disease.

The IDSA also referred FOX News to Paul Auwaerter, MD, the Clinical Director of the Division of Infectious Diseases at John Hopkins Medicine. He stated, “Four studies have concluded that antibiotics administered to patients complaining of long-term Lyme disease symptoms did no better than placebo pills.” Auwaerter was referring to the four federally-funded, randomized-controlled clinical trials (RCTs) of “post-treatment Lyme disease syndrome,” or PTLDS. He did not mention that both Brown University and Columbia University have found these studies to be flawed in design, statistical analysis, and result interpretation.

The first two RCTs in question were published in 2001 and authored by Klempner, *et al.* Both Brown and Columbia found major design flaws in this study as well as problems with the statistical methods used to analyze the results.

The third RCT referred to by Auwaerter was published in 2003 by Krupp, *et al.* DeLong found this study to be well-designed. The authors concluded that patients with reported severe fatigue

that were given an IV antibiotic, Ceftriaxone, showed improvement when compared to patients on a placebo (Krupp, 2003). However, four participants in this trial were hospitalized—3 receiving the placebo, and one receiving Ceftriaxone. In turn, the authors also concluded that treatment with repeated antibiotic therapy is too risky and recommended against it.

The fourth RCT was published in 2008 by Fallon, *et al*. The major short-coming of this study was the small sample size. Patients showed improvement in cognition, however this improvement declined once the IV antibiotics were stopped. This may have occurred because the antibiotics were working, but stopped prematurely (Fallon, 2008).

The trials referenced by Auwaerter do not provide any closure. In fact, it is horrifying that a physician in his position, specializing in tick-borne illness, is still referencing these four RCTs despite the research that has shown their methods to be faulty or the results to be nothing but inconclusive. To further reduce confidence in any conclusion coming from the RCTs, there is ongoing discussion in the *American Journal of Medicine* between Klempner and Fallon. Fallon argues that important findings within the RCTs are being dismissed, whereas Klempner argues that there is no need to do any further research on long-term antibiotics based on the results of the RCTs.

The Mayday Project would like to emphasize that the 2-4 weeks of antibiotic treatment recommended by the IDSA's Clinical Practice guidelines are severely limiting. The 4 RCTs, which have been reviewed by multiple entities, cannot disprove that long term treatment is beneficial to patients. Increased duration of initial treatment must be defined in the clinical practice guidelines and would, in many cases, eliminate the possibility of persistent infection. While long term antibiotics do help some afflicted with Lyme disease, alternative treatments work for others.

At the Mayday Project, we would like to stress that we are not necessarily fighting for the right to use long-term antibiotics. It seems that long term antibiotics do help some afflicted with Lyme disease to improve greatly, but alternative treatment methods work for others. We are asking the IDSA to allow clinicians to work independently with each individual Lyme disease patient to decide what form and length of treatment is appropriate. The guidelines published in 2006 state, "*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*." However, doctors are still prosecuted for choosing to treat outside the treatment guidelines in the patient's best interest, and several members of the IDSA have served on these medical malpractice suits as expert witnesses, undermining the cautionary statement within the guidelines. We are asking the IDSA to revise their guidelines for those of us who do see improvement with long-term antibiotics. We are asking the IDSA to acknowledge that the bacterium which causes Lyme disease can persist despite the standard treatment. We need researchers to develop tests to determine if an infection is active and ongoing after treatment. We need researchers to improve on testing methods to make an accurate diagnosis. We are asking for increased research of this extremely complex disease.

In summary, Brown University's Allison DeLong, a biostatistician, performed a biostatistical review of the four studies. Her findings: antibiotic retreatment can be beneficial (DeLong, 2012). When properly analyzed, two of the RCTs, showed clinically significant improvement in their respective areas of measurement, which totally contradicts the point that the IDSA was

attempting to make: that repeated antibiotics are ineffective. The only conclusion that can be reached by referencing these RCTs is that more research is needed in this area. Thousands upon thousands of lives are at stake, and some will continue to be lost until change is made.

References

Barbour, A. (2012). Remains of infection. *Journal of Clinical Investigation, 122*(7), 2344-2346.

Cameron, D. J. (2010). Proof That Chronic Lyme Disease Exists. *Interdisciplinary Perspectives on Infectious Diseases, 2010* (8), 1-4.

DeLong, A.K., *et al.* Potential Benefits of Retreatment Highlight the Need for Additional Lyme Disease Research. *Am J Med.127*(2), e9 - e10.

Delong, A.K., Blossom, B., Maloney, E.L., Phillips, S.E. (2012). Antibiotic retreatment of Lyme disease in patients with persistent symptoms: a biostatistical review of randomized, placebo-controlled, clinical trials. *Contemp Clin Trials*. *33*(6), 1132-42.

Fallon, B.A., et al. (2008). A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy. *Neurology. 70*(13), 992-1003.

Fallon, B.A., Petkova, E., Keilp, J.G., Britton, C.B. (2014). Ongoing discussion about the US clinical Lyme trials. *Am J Med. 127*(2), e7.

Ferguson, J. (2012). Cure unwanted? Exploring the chronic Lyme disease controversy and why conflicts of interest in practice guidelines may be guiding us down the wrong path. *American Journal of Law & Medicine, 38*(1), 196-224.

Green, C. (2009). Challenge to the clinical definition of late Lyme disease and post-Lyme disease syndrome. Unpublished paper. Los Altos, CA: Green Oaks Medical Center.

Infectious Diseases Society of America. (2010, April 22) *Special Review Panel Unanimously Upholds Lyme Disease Treatment Guidelines.* http://www.idsociety.org/Lyme_Review_Panel_News_Release/

Jarefors, S., Janefjord, C. K., Forsberg, P., Jenmalm, M. C., & Ekerfelt, C. (2007). Decreased up-regulation of the interleukin-12Rβ2-chain and interferon-γ secretion and increased number of forkhead box P3-expressing cells in patients with a history of chronic Lyme borreliosis compared with asymptomatic Borrelia-exposed individuals. *Clinical & Experimental Immunology, 147*(1) 18-27.

Jones, C.R. (2005). Rationale for prolonged antibiotic therapy in treating Lyme disease.

Klempner, M.S., *et al.* (2014). The Reply. *Am J Med. 127*(2), e11 - e12.

Klempner, M.S. *et al*. (2014). Treatment Trials for Post-Lyme Disease Symptoms Revisited. *Am J Med. 126*(8), 665 – 669.

Klempner, M.S., *et al.* (2001). Two Controlled Trials of Antibiotic Treatment in Patients with Persistent Symptoms and a History of Lyme Disease. *N Engl J Med.* 345, 85-9

Krupp, L.B., Hyman, L.G., Grimson, R., Coyle, P.K., Melville, P., Ahnn, S., Dattwyler, R., Chandler, B. (2003). Study and treatment of post Lyme disease (STOP-LD): a randomized double masked clinical trial. *Neurology*. *60*(12), 1923-30.

Logigian, E. L., Kaplan, R. F., & Steere, A. C. (1990). Chronic neurologic manifestations of Lyme disease. *The New England Journal of Medicine*, *323*(21) 1438-44.

Wormser, G.P., *et al*. (2006). The clinical assessment, treatment, and prevention of Lyme disease, human Granulocytic Anaplasmosis, and Babesiosis: Clinical practice guidelines by the Infectious Diseases Society of America. *Clinical Infections Diseases*, 43:1089-134.