

## Lyme bacteria survive 28-day course of antibiotics months after infection

December 13 2017





Adult deer tick, Ixodes scapularis. Credit: Scott Bauer/public domain

Bay Area Lyme Foundation, a leading sponsor of Lyme disease research



in the US, today announced results of two papers published in the peerreviewed journals *PLOS ONE* and *American Journal of Pathology*, that seem to support claims of lingering symptoms reported by many patients who have already received antibiotic treatment for the disease.

Based on a single, extensive study of Lyme disease designed by Tulane University researchers, the study employed multiple methods to evaluate the presence of Borrelia burgdorferi spirochetes, the <u>bacteria</u> that cause Lyme disease, before and after antibiotic <u>treatment</u> in primates. The study also measured the antibody <u>immune response</u> to the bacteria both pre- and post- treatment, as this is how current diagnostics typically evaluate Lyme disease in humans.

The data show that living *B. burgdorferi* spirochetes were found in ticks that fed upon the primates and in multiple organs after treatment with 28 days of oral doxycycline. The results also indicated that the immune response to the bacteria varied widely in both treated and untreated subjects.

"It is apparent from these data that *B. burgdorferi* bacteria, which have had time to adapt to their host, have the ability to escape immune recognition,tolerate the antibiotic doxycycline and invade vital organs such as the brain and heart," said lead author Monica Embers, PhD, assistant professor of microbiology and immunology at Tulane University School of Medicine.

"In this study, we were able to observe the existence of microscopic disease and low numbers of bacteria, which would be difficult to 'see' in humans but could possibly be the cause of the variable and nonspecific symptoms that are characteristic of post-treatment Lyme disease syndrome. Although current antibiotic regimens may cure most patients who are treated early, if the infection is allowed to progress, the 28-day treatment may be insufficient, based on these findings," Embers said.



The findings also demonstrated:

- All subjects treated with antibiotics were found to have some level of infection 7 12 months post treatment.
- Despite testing negative by antibody tests for Lyme disease, two of 10 subjects were still infected with Lyme bacteria in heart and bladder.
- Lyme bacteria which persist are still viable.

To better elucidate previous animal studies demonstrating that some *B*. *burgdorferi* bacteria survive antibiotics, the study explored Lyme disease infection in rhesus macaque primates treated with antibiotics and a control group who were also infected but not treated. This species has been shown to demonstrate a progression of Lyme disease most similar to humans, particularly related to erythema migrans, carditis, arthritis, and neuropathy of the peripheral and central nervous systems.

"Clearly, some medical practices governing diagnosis and treatment of Lyme disease should be reconsidered in light of this study. This study shows that we must reevaluate the current paradigm of antibody response tests for diagnosis and move away from the one size fits all approach to Lyme treatment," said <u>Wendy Adams</u>, Research Grant Director, Bay Area Lyme Foundation. "Every day, patients with Lyme disease are told their symptoms cannot be caused by Lyme, because they test negative on antibody tests or because they have received a single course of antibiotics. More research and funding are imperative."

In the study, ticks carrying *B. burgdorferi* spirochetes fed on ten primates. Four months post infection, half of the primates (five) received the antibiotic doxycycline orally for 28 days at a proportional dose to that used in human treatment. Five subjects were treated with placebo and all ten were evaluated by more than five different diagnostic methods to characterize any remaining infection. The researchers used



several important techniques, including xenodiagnoses, to determine if the spirochete bacteria persisted.

The results show:

- Few subjects displayed a rash. Although all subjects were infected, only one of the 10 displayed a rash with central clearing, the classical "bulls-eye" rash. The subject that developed this rash, interestingly, never mounted an immune response to five borrelia antigens throughout the study period, prior to and following treatment.
- Organs may be infected even if antibody tests are negative. One subject which tested negative for *B. burgdorferi* by skin biopsy cultures, PCR and in vivo cultures, was found to have *B. burgdorferi* infecting the heart. Another untreated subject, who was ultimately shown to have residual Lyme bacteria inthe bladder, showed a decrease in immune response over the course of infection, with a negative xenodiagnosis test in the late stage, which would signal that the animal self-cured.
- Intact spirochetes were found in three of five treated and four of five untreated subjects based on xenodiagnosis results 12 months after the tick bite.
- Immune responses to *B. burgdorferi* varied greatly posttreatment, with one subject's antibody levels dropping to pre-bite levels for three antigens while another subject experienced elevated antibodies for the same antigens throughout the study period. This is significant because it demonstrates that subjects infected with the same strain of *B. burgdorferi* may have different immune responses to the same antigen. And, because humans, like primates, are genetically diverse, it underscores that testing antibody responses may be inherently unreliable as a singular diagnostic modality for Lyme disease.
- Widespread and variable microscopic disease was observed in all



infected subjects, despite <u>antibiotic treatment</u>. Compared to uninfected subjects of the same age, infected subjects in this study (treated and untreated) demonstrated Inflammation in and around the heart, in skeletal muscles, joints, and the protective sheath that covers the brain, and near peripheral nerves.

• Rare, but intact *B. burgdorferi* spirochetes were found in the tissues of both the treated and untreated subjects. In two subjects treated with doxycycline, multiple Lyme bacteria were observed in the brain tissue. Others organs in which the spirochetes were observed included the heart, joints, bladder, skeletal muscle and adjacent to peripheral nerves.

**More information:** Monica E. Embers et al. Variable manifestations, diverse seroreactivity and post-treatment persistence in non-human primates exposed to Borrelia burgdorferi by tick feeding, *PLOS ONE* (2017). DOI: 10.1371/journal.pone.0189071

Nicholas A. Crossland et al. Late Disseminated Lyme Disease: Associated Pathology and Spirochete Persistence Post-Treatment in Rhesus Macaques, *The American Journal of Pathology* (2017). DOI: <u>10.1016/j.ajpath.2017.11.005</u>

Provided by Tulane University

Citation: Lyme bacteria survive 28-day course of antibiotics months after infection (2017, December 13) retrieved 5 May 2024 from <u>https://medicalxpress.com/news/2017-12-lyme-bacteria-survive-day-antibiotics.html</u>

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