Lingering bacteria don't indicate chronic Lyme disease

1 April 2008

The bacteria that cause Lyme disease, the most common tick-borne illness in the United States, can linger in mouse tissues long after a full round of antibiotic treatment is completed, report researchers from the University of California, Davis.

The scientists caution that the discovery does not suggest the presence of chronic disease, nor does it support extended use of antibiotics to treat Lyme disease in humans. Their findings are reported in the March issue of the journal *Antimicrobial Agents and Chemotherapy*.

However, they say, the results of this study do set the stage for controlled laboratory research investigating potential therapies for persistent Lyme disease infections.

"Lyme disease is a tough nut to crack. The bacterium Borrelia burgdorferi has evolved to evade the body's immune system so it's not surprising that it can also evade antibiotics," said Stephen Barthold, lead researcher on the study. Barthold is director of the UC Davis Center for Comparative Medicine, a cooperative research center in the schools of Medicine and Veterinary Medicine that investigates animal models of human disease.

"It's important to note that the numbers of residual bacteria identified in this study were very low and there was no evidence that they were causing inflammation," Barthold said. "Their presence shouldn't be misconstrued as a sign of chronic disease."

Borrelia burgdorferi, the corkscrew-shaped bacterium that causes Lyme disease, is transmitted to humans and animals through bites from infected deer ticks. In the United States, Lyme disease is most prevalent in the Northeastern and Great Lakes states, and is present to a lesser extent in Northern California. Other high-risk Lyme disease areas are scattered throughout the nation, usually in shady, moist deciduous forests where the carrier ticks and their wildlife hosts flourish.

Symptoms of Lyme disease are highly variable and may include fever, headache, fatigue and a skin rash. If the infection is not treated, it can spread to the joints, heart and nervous system.

Usually, Lyme disease can be successfully treated with about four weeks of antibiotics. Treatment is most successful during the early stages of infection. A few patients, particularly those treated during late infection, may experience persistent or recurring symptoms after the antibiotic treatment is finished, in which case a second round of antibiotics may be prescribed.

According to the U.S. Centers for Disease Control and Prevention, antibiotic treatment above and beyond one repeat round has not been shown to be beneficial and has been linked to serious complications, including death.

Many of those involved with Lyme disease -- including patients, doctors, researchers and health insurance companies -- are divided over how to treat the ailment when it persists beyond a second round of antibiotics. Some patients with persistent or recurrent Lyme disease symptoms report experiencing fatigue, joint pain, extreme headaches, facial paralysis and memory loss. Much of the controversy revolves around debate over whether symptoms reflect continued infection after treatment.

There has been minimal scientific evidence to support the claim that infection with the Lyme disease bacterium can persist in a chronic state following antibiotic treatment. As a result, treatment guidelines recommend against prescribing long-term antibiotics for persistent Lyme disease symptoms. Many physicians and health insurance companies refuse to prescribe or pay for extended

antibiotic treatments.

Barthold and colleagues studied antibiotic treatments for Borrelia burgdorferi infection in laboratory mice.

One group of mice was treated for one month with the antibiotic ceftriaxone, beginning during the first three weeks of infection. A second group received the same antibiotic for one month, but beginning at four months after infection, representing a chronic infection. A third group, serving as the control, received only saline for one month, rather than the antibiotic.

When the antibiotic treatments were completed, DNA analysis showed that small numbers of the Lyme disease-causing bacteria remained in the tissues of the antibiotic-treated mice. Ticks allowed to feed on these infected mice were also able to acquire and transmit the infectious bacteria. Curiously, despite the apparent viability of the bacteria, they could not be detected by standard laboratory cultures.

The findings support the theory that the bacteria remain viable and that some bacteria evade antibiotic treatment by taking refuge in collagen-rich tissues, skin, ligaments and tendons.

"Our theory is that these remaining bacteria are in a metabolically dormant, non-dividing state," Barthold said. "This would explain why we were unable to culture them.

"In future studies we need to look at the long-term fate of these bacteria," he said. "They seem to be non-dividing. If so, are they permanently crippled by the antibiotics and eventually would die out, or would they grow back over the long term and cause a recurrence of the disease?"

While the residual bacteria do not appear to cause disease, they may contribute to the persistence of Lyme disease symptoms, the researchers suggested.

"This may explain why some Lyme disease patients recover slowly following antibiotic treatment, exhibiting what has been termed "post-Lyme disease syndrome," Barthold said.

The existence of a small number of sequestered bacteria should not come as a surprise, he added, noting that with disease-causing agents like herpes virus and the bacteria that cause tuberculosis and syphilis, it is not unusual for the infectious organisms to persist at levels that do not actually cause symptoms.

"This is just part of our world of microbes," Barthold said. "Antibiotics are designed to kill large numbers of bacteria -- to knock them down to the point that the body's immune system can get control of the infection."

Bacteria have evolved the means to survive antibiotics in the natural world, he noted. Furthermore, if disease-causing organisms such as Borrelia have evolved the means to escape clearance by the immune system, it is not surprising that the bacteria that survive antibiotic treatment would not be eliminated.

In the case of Lyme disease, the research findings do not suggest that continued use of antibiotics would succeed in getting rid of the lingering bacteria.

"I suspect that if the initial round of antibiotics hasn't eliminated them, it's not likely that a longer regimen of antibiotics would be any more successful," Barthold said. "It's more likely that a completely different class of antibiotics would be needed to accomplish that. This laboratory mouse model will allow us to address those possibilities."

Source: University of California - Davis