Strain-specific Lyme disease immunity lasts for years, research finds

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Borrelia burgdorferi is the bacterial culprit behind Lyme disease. A new study by University of Pennsylvania researchers shows that humans can develop immunity to particular strains of the bacteria that protect against reinfection for several years. Credit: CDC

Lyme disease, if not treated promptly with antibiotics, can become a lingering problem for those infected. But a new study led by researchers from the University of Pennsylvania has some brighter news: Once infected with a particular strain of the disease-causing bacteria, humans

appear to develop immunity against that strain that can last six to nine years.

The finding doesn't give people who have already had the disease license to wander outside DEET-less, however. At least 16 different strains of the Lyme disease bacterium have been shown to infect humans in the United States, so being bit by a tick carrying a different strain of the disease is entirely possible. But the discovery does shed light on how the immune system recognizes and builds a defense against the pathogen and could inform future attempts to design a vaccine that would protect against multiple strains of the disease.

The study, published in the April issue of *Infection and Immunity*, was led by Dustin Brisson, an assistant professor in the Department of Biology in Penn's School of Arts and Sciences, and Camilo E. Khatchikian, a postdoctoral associate in Brisson's lab. They collaborated with Robert B. Nadelman, John Nowakowski, Ira Schwartz and Gary P. Wormser of New York Medical College.

When someone notices the telltale bull's-eye rash that can signal Lyme disease, the infected person may receive antibiotics from a physician but generally will not know what strain of *Borrelia burgdorferi* caused the infection. But a 2012 study by Wormser's group, published in the *New England Journal of Medicine*, reported on 17 patients who had been infected multiple times with Lyme disease and had the strain of each infection cultured and identified.

"The point of the paper published in the *New England Journal of Medicine* was to see if there is evidence that these recurrent infections were in fact caused by subsequent tick bites and not by a relapse of the original infection," Brisson said. "That study overwhelmingly confirmed that they were new infections; only one patient was infected by the same strain multiple times."

The only patient infected by the same strain twice actually had Lyme disease four times in six years, contracting strain K twice, five years apart, with an infection by a different strain in between.

"In the present study, we wanted to see if so few patients were infected by the same strain multiple times because they were protected against subsequent infections with the same strain."

Deer ticks are the primary vector of Lyme disease in North America. Credit: University of Pennsylvania

The Penn-led team used two statistical approaches to answer this question.

The first involved calculating the probability of arriving at the data

obtained from the 17 patients who had multiple Lyme disease infections by chance alone.

"If there was no strain-specific immunity, then there should be a random distribution of strains in patients, and you would expect several of the patients to be affected by the same strain twice," Brisson said. "But only one patient was."

Using multinomial probabilities, similar to rolling a die many times, the team found it would be nearly impossible to arrive at the data presented by the 17 patients if no strain-specific immunity were present. The same held true no matter if the calculations assumed it was equally likely that a patient would be infected with any strain of *B. burgdorferi*, or if the "die" was weighted based on the prevalence of each strain in New York state.

In a second statistical test, the researchers used the data from the 17 patients in what is known as a stochastic model to determine the expected number of total infections during a set period of time as well as the expected number of infections of the same strain during that time period.

The model allowed the researchers to vary assumptions such as the presence or absence of type-specific immunity, the duration of immunity and the length of time a patient was "available" to having been bitten by a tick—in other words, the time from the first visit to the clinic to the last visit, or from the first visit to the completion of the study.

The results of all of their simulations indicated that strain-specific immunity would need to last a minimum of four years in order to result in the suite of infections that the 17 patients acquired. And parameterizing the model with actual data from 200 patients who had been infected at least once with a known strain of *B. burgdorferi*, the

simulation indicated that immunity lasts in the range of six to nine years.

While studies in mice had suggested that strain-specific immunity might exist, this is the first time it's been investigated in humans who have acquired infections naturally.

"If you infect a mouse with one strain and then clear it with antibiotics, it can't be infected again with the same strain but can be with a different strain," Brisson said "But mice only live for a year or so. No one had explored if immunity persists over the course of many years."

The fact that the strain-specific immunity is lasting has implications for vaccine design.

"If you could make a vaccine that covers several of these strains," Brisson said, "you could substantially reduce the probability of infection in vaccinated people. The vaccine could last several years, perhaps requiring a booster once every several years."

Brisson noted that there is likely to be variation in the strength and duration of immunity among people and perhaps even among strains of the Lyme bacterium. His group is also investigating whether becoming infected and generating an immune reaction against one strain could offer protective cross-immunity against other strains.

Provided by University of Pennsylvania