VACCINE RESEARCH

Biting Back at Lyme Disease

As the summer heat rolls across the country, enticing people into the fields and forests, it brings with it the seasonal concern about Lyme disease. And although there isn't yet any surefire way to prevent the disease, researchers are making progress toward a vaccine to combat this tick-borne illness. Among the promising candidates is one based on a protein from the surface of the bacterium that causes Lyme disease: *Borrelia burgdorferi*, a spirochete that is transmitted to humans from its natural hosts—mice and deer—by tick bites.

In the 15 June *Proceedings of the National Academy of Sciences*, a team of researchers from Harvard and Yale reports that mice vaccinated with this protein successfully fight off infection from tick bites. Moreover, to the group's amazement, the antibodies that were triggered by the vaccine in the mice also managed to kill off the spirochetes in the ticks that bit them, according to lead authors of the study Erol Fikrig and Sam Telford III of the Harvard University School of Public Health. This active immunization "is the most interesting part of the paper," says Lyme researcher Alan Barbour of the University of Texas Health Science Center in San Antonio, who suggests that it might be possible to curtail the spirochete's population severely and limit the spread of Lyme disease by vaccinating mice and deer.

Fikrig and his colleagues at Yale had already shown, almost 2 years ago, that the same protein protects mice from illness caused by direct injections of the spirochetes (*Science*, 26 October 1990, p. 553). But would it enable mice to fight off the more realistic challenge of infection by a tick bite? For a number of reasons, researchers thought there might be a difference. One theory held that the tick's saliva might have immunosuppressive properties that aid the infectious bacteria. But the latest round of experiments seems to put such concerns to rest. "Protection was still complete," says Fikrig, who specializes in infectious diseases.

"Will [a vaccine based on surface protein] work in humans? We don't know."
–Erol Fikrig

As for the offensive action of the antibodies to the protein, he and his co-workers think they have an explanation. As the tick feeds on deer or mice, it engorges itself on blood, which pools in the insect's gut. In the gut, the theory goes, the concentration of antibodies becomes high enough to kill all the spirochetes living in the tick.

The next step in the research, says Fikrig, is to come even closer to the natural conditions in which Lyme disease is transmitted. He explains that their work so far has used a single strain of spirochetes that live in laboratory-bred ticks. Asks Fikrig, "How variable are spirochetes in nature? Can we protect against wild ticks from a wide variety of locations?" To answer these questions, they plan to repeat their vaccination experiments with ticks collected from around the country.

The ultimate goal of this research, of course, is to develop a human vaccine for Lyme disease. But while Fikrig calls the surface protein "the most likely candidate" for a vaccine, others working with it have not had the same success when vaccinating hamsters. And at a Lyme conference held earlier this month in Arlington, Virginia (*Science*, 5 June, p. 1384), one researcher presented data suggesting that the antibodies to the protein could trigger arthritis in some people. Moreover, notes Barbour, the surface protein is considerably different in European spirochetes, which means that a single vaccine may not be effective worldwide.

"Will it work in humans? We don't know," admits Fikrig. No one has yet started clinical trials in humans, he says, although a number of companies did express interest at the Lyme conference. And even if human trials prove fruitless, there is the tantalizing possibility of immunizing wildlife by lacing food or water with a suitable vaccine, a method now being tried to combat rabies. And while researchers must overcome numerous technical hurdles in this effort, says Barbour, "If a people vaccine is not possible, this may be the next best thing."

–John Travis

THE GALLO PROBE

Popovic Defended by Technician

Elizabeth Read-Connole, a technician who works in Robert Gallo's lab, has come to the defense of beleaguered virologist Mikulas Popovic, the pipetting wizard who helped Gallo in his controversial isolation of the AIDS virus. A proposed final report from the National Institutes of Health's (NIH) Office of Scientific Integrity (OSI) concluded that Popovic had commited four counts of scientific misconduct. Now Read-Connnole claims that OSI investigators did not question her about lab notes she wrote that were central to one of the four counts.

In the OSI report, delivered last month to Assistant Secretary of Health and Human Services James Mason, Popovic was found, among other things, to have arbitrarily substituted his own reading of 10% of cells positive for HIV in an immunofluorescence assay for Read-Connole's reading. (The 10% figure appeared in a table in a key paper from the Gallo lab published in *Science* in May 1984.) The OSI staff interpreted an entry in Read-Connole's lab notebook as: "very few cells positive for rabbit antibody." Since 10% isn't equal to "very few," the report says, Popovic was potentially biasing the results by substituting his own reading.

Now Read-Connole has come forward to say that what the OSI team interpreted as one statement was actually two and that she never made an estimate of the number of positive cells. In a 13 May letter to NIH Director Bernadine Healy, she wrote: "My statement 'very few cells' was a comment on the number of the cells on the slide." The second statement, "positive for rabbit antibody," she says, meant only that some cells on the slide were positive. In an interview with *Science*, Read-Connole added that because there were so few cells in the total, she felt unable to estimate the fraction of positive cells. She expected Popovic to make an estimate, she said, and he did.

If Read-Connole's account is true, the problem for Popovic is that he didn't remember this when he was initially questioned by OSI investigators in December 1990. At that time, he apparently accepted the notion that Read's entry meant "very few cells positive" and suggested that he had somehow averaged his reading and hers. In March 1991, however, Popovic argued "more definitely," according to the report, that he had used his reading in place of Read's original notation.

The decision by OSI not to question Read-Connole about the entry has led to a protest by Popovic's attorney, Barbara Mishkin. In a letter to Health and Human Services (HHS) staff, she wrote: "This failure to ask obvious questions has been a continuing problem with OSI, and underscores the importance of permitting counsel for the accused to cross-examine witnesses."

OSI director Jules Hallum isn't impressed. Asked whether OSI had interviewed Read-Connole about her notes, Hallum replied: "It's totally irrelevant whether we did or not. We discussed it with Popovic, and we have his response. His response is the only one that has significance—he was the senior author of the paper." Whether HHS staff will support this position remains to be seen.

–Jon Cohen

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