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Vaccine Is Developed Against Strep Infections

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GAZETTE STAFF

Climaxing 23 years of effort, Medical School researchers have produced a vaccine against group B streptococcus, the most common cause of potentially deadly infections in newborn infants. These bacteria infect about 5,000 babies a year and kill as many as 500 of them in the U.S. alone.

The microbes also cause brain and nervous system damage in infants and more than 60,000 less severe infections a year in adults, including new mothers, diabetics, and those with certain kinds of cancer.

"At least nine types of group B strep exist, but five of them cause 95 percent of the disease," says Dennis Kasper, William Ellery Channing Professor of

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Photo by Kris Snibbe

Dennis Kasper shows part of the equipment his team of researchers used to make the first vaccines against group B streptococcus. He holds an enlarged photograph of the bacteria.

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Medicine. "We have developed and are successfully testing vaccines for all five types."

The tests demonstrate that the vaccines elicit antibodies that protect both mother and baby against the bacteria. The pups of mother mice who received the human vaccine survived lethal doses of group B strep given in experiments. Trials to determine whether the five vaccines can be mixed and given in a single injection will begin shortly, according to Kasper, who also is director of the Channing Laboratory, a joint facility of the Medical School and Brigham and Women's Hospital. Other trials aimed at preventing growth of the bacteria in the vaginal tracts of healthy young women will be done this year, he says.

Eventually, the vaccine may be given to all pregnant women to prevent strep from infecting their infants.

An estimated 10 to 30 percent of women carry group B strep, a first cousin to the microbe responsible for strep throat. Kasper and his colleagues showed that women who have antibodies in their blood to protect against infection transfer this protection to their babies through the placenta. Without antibodies, however, infants are highly vulnerable to severe disease.

Kasper's team began by developing a vaccine that evokes antibodies to type III B strep, the type that commonly causes meningitis, a brain and spinal cord inflammation which can lead to mental retardation, seizures, deafness, and learning disabilities. Fifty percent of infected infants end up with some form of brain damage.

A type III vaccine made at Channing Lab stimulates production of the necessary antibodies by women. When taken from their blood, these antibodies kill the bacteria in test tubes and protect mice pups exposed to B strep.

The same type of experiments have been conducted successfully with separate vaccines against the four other disease-causing B strep types.

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WILLIAM ELLERY CHANNING PROFESSOR OF MEDICINE

A Sugar-Coated Vaccine

Kasper joined Channing Lab in the 1970s after working on a vaccine for meningitis at the Walter Reed Army Institute of Research. At the time, the disease was a major problem among Army recruits.

At Channing, Kasper met Carol Baker, a pediatrician who told him about the terrible toll that strep bacteria were taking. At the time, the microbes infected about 4 of every 1,000 newborns and killed almost half of them.

"I suggested that we work together and find a vaccine for the disease," Kasper recalled. "I didn't think it would take 23 years."

They started with the knowledge that the tiny, round B strep bacteria have at least nine different kinds of gel-like sugar coatings. Each coating defines a specific type of microbe capable of producing its own brand of misery — meningitis, pneumonia, bone and joint infections, and other severe illnesses.

"It occurred to me that we could use material from these surface coatings as a vaccine," Kasper said. The harmless coating, he reasoned, would be enough to raise the protective guard of the immune system without bringing on the disease, a common strategy used for many vaccines.

It took years of basic research to purify the sugar coatings and determine their structure. Once this was accomplished, Kasper and his colleagues made a type III vaccine and gave it to pregnant women during the late 1970s and early 1980s.

"The vaccine induced antibodies in these women, which crossed the placenta to their babies," Kasper says. "However, not enough women produced antibodies for us to make a significant impact on the disease. We needed to make a more potent vaccine."

Kasper's team decided to do that by linking molecules from the bacterium's sugar-coating with a protein known to boost immune activity. For the latter, the researchers chose a part of the tetanus vaccine, but putting the two together turned out to be tricky.

"The sugars are easily destroyed," Kasper explains. "Careful work was required to combine them with the tetanus protein."

Once made, Carol Baker, now at Baylor College of Medicine in Houston, tested the vaccine on women who were six months pregnant. Last year, 100 women received either the two-part vaccine, one made from the sugar coating alone, or an inactive saline solution.

Antibody levels in 90 percent of the women who got the combination vaccine increased four-fold. Only 60 percent of those who took the sugar-only compound experienced such a dramatic rise in protection.

"That was my 'Eureka!' moment," Kasper recalls. "Once we found that so many women responded to the vaccine, I more or less expected that the antibodies would protect their babies."

Similar experiments that combined coatings from other group B strep varieties with proteins from diphtheria vaccine, or from the strep bacterium itself, have produced the same results. All these vaccines protect mouse pups challenged with killer doses of the bacteria.

Preventive Measures

This year, the Food and Drug Administration is expected to approve studies to make sure the combination vaccines don't interfere with each other. Those studies will be followed by experiments to determine whether group B strep bacteria can be eliminated from the genital tract where they normally live.

Young non-pregnant women colonized by the bacteria will receive combination vaccines or dummy injections. The rates of bacterial colonization in the two groups will then be compared.

Kasper expects such experiments to finally produce a vaccine that will *prevent* group B strep infections in all women of child-bearing age.

Such shots would be given routinely, the way vaccinations are now used to prevent measles, mumps, tetanus, and polio.

In the meantime, the Centers for Disease Control and Prevention recommend that all women be screened for group B strep bacteria between the 35th and 37th weeks of pregnancy.

Those found to harbor the bacteria would receive high doses of penicillin. Adherence to this recommendation would result in about 1 million women receiving penicillin, or other antibiotics, during delivery of their babies.

"That will undoubtedly reduce the incidence of group B strep disease, but it is only an interim measure," Kasper cautions.

"We must be concerned about the emergence of bacteria resistant to penicillin, and about the fact that some women are allergic to this antibiotic."

Kasper doesn't know how long interim treatment with penicillin will be necessary because of the difficulty of getting approval in the United States to test vaccines on pregnant women.

Looking back over the past 23 years, Kasper notes that "it's been a tremendous opportunity to study the group B strep bacteria and to develop a vaccine. As a result of this prolonged effort, a great deal has been learned about immunity to infectious diseases. We have uncovered principles that can be applied in understanding and developing vaccines against other diseases."