SCIENCE NEWS of the week

Meningitis Vaccine Stirs Controversy

A quiet storm is brewing in medical circles over the effectiveness and, possibly, the safety of the only childhood meningitis vaccine currently approved in the United States. The vaccine, approved by the Food and Drug Administration (FDA) in 1985, is aimed at the bacterium *Haemophilus influenza* type b (Hib). Each year in the United States, the spinal-fluid-invading bacterium takes the lives of about 1,000 children under 5 years of age (SN: 9/26/87, p.198).

The unusual controversy has increasingly dominated discussions among pediatricians and epidemiologists, and is likely to culminate in the speedy approval of a new vaccine, a number of physicians told SCIENCE NEWS. Meanwhile, the American Academy of Pediatrics Committee on Infectious Diseases last week tentatively approved an unprecedented statement suggesting that physicians, under certain circumstances, may choose not to use the currently approved vaccine.

"For most of the United States, the data suggest that the vaccine is working and that we should continue using it," says Dan Granoff, a pediatrician at Washington University's Children's Hospital in St. Louis. However, he notes, recent studies of the vaccine's efficacy in different parts of the country show an "unprecedented regionality." In Minnesota, for example, immunized children were *more* likely to become infected with Hib than were children who hadn't been vaccinated. Such findings, Granoff says, suggest that the vaccine might best be discontinued in Minnesota.

The Minnesota study, along with others in four states and one conducted by the federal Centers for Disease Control (CDC), was initiated last year after a surprising number of meningitis cases were reported in children who had received the Hib vaccine. The results of all five retrospective studies were presented at an FDA workshop last April, and a lively debate has ensued ever since.

Never has a vaccine shown such regional variation in efficacy, according to researchers in the field. The original trials that led to the vaccine's approval were performed not in the United States but in Finland, where it was found to be 90 percent effective. Follow-up U.S. trials have ranged from a high of 89 percent in some states to a negative correlation in Minnesota, where those who got the disease were 86 percent more likely than controls to have been vaccinated. The new results lead some physicians to question the applicability of vaccine trials performed on certain foreign populations.

"There's some trouble extrapolating data derived from other countries with a more homogeneous population to a country as diverse genetically as the United States," says Robert Daum, associate professor of pediatrics and head of the section on pediatric diseases at Tulane University in New Orleans. "All told, the vaccine probably has a positive effect in the United States, but it is almost certainly less than that . . . in Finland."

Researchers don't know how to account for the geographic variation of vaccine-induced Hib immunity in the United States. It has been known for years that certain unvaccinated populations — blacks, American Indians and Eskimos, for example — are more susceptible to Hib infection than unvaccinated Caucasians. Separate studies have shown that certain individuals, even after being vaccinated, seem altogether incapable of mounting immune responses against Hib. But while such studies suggest a genetic connection to the Hib puzzle, the pieces are not easily integrated into a single theory.

While the immuno-demographics of Hib are being studied, many physicians agree that a new and better vaccine is needed. The topic was a popular one at last month's meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy, an organization devoted to research on infectious diseases. According to Granoff, "The consensus. . .was that FDA should move rapidly to license a conjugate vaccine."

Unlike the currently approved Hib vaccine, which is made from a polysaccharide fragment of the virus, conjugate vaccines link such fragments to immune system stimulants capable of amplifying antibody production. At least three such Hib vaccines are under development, including one that has undergone extensive human trials. Unfortunately, notes Daum, those trials were also performed in Finland and not in the United States. Nevertheless, he says, several individuals at last week's American Academy of Pediatrics committee meeting felt that "licensure of a conjugate vaccine may not be too distant."

Even if a new vaccine is approved, problems may remain. Ongoing studies suggest, for example, that even among those who respond to the current vaccine, there may be a "window" of increased susceptibility to Hib infection during the first seven days after immunization. The reasons for this aren't clear, Granoff says, but he and others theorize that the vaccine temporarily binds up the body's naturally occurring Hib antibodies. Thus, until the body is able to respond to the vaccine with a full-scale immune response, one may be especially susceptible to Hib for a few days.

This problem may soon be resolved, however, given recently published research in the Oct. 8 NEW ENGLAND JOURNAL OF MEDICINE. In that research, Mathuram Santosham of the Johns Hopkins School of Public Health in Baltimore — in collaboration with colleagues at Harvard Medical School, the CDC and the American Red Cross — reports the first successful demonstration of meningitis protection in children by direct injection of Hib-specific immune proteins. The proteins, or immune globulins, were taken from the plasma of adults who had previously been immunized against Hib. Unlike the current (and the pending conjugate) vaccine, which stimulates the body to make its own antibodies, "passive" immunization such as Santosham's provides rapid protection against bacterial infection.

Passive immunization does have its disadvantages, Santosham says. It is expensive and its protection is only temporary, requiring repeated doses. Others point out that since it is made from human blood products, it carries some small risk of being contaminated with hepatitis or AIDS.

Nevertheless, Santosham says, it may be useful in individuals incapable of mounting their own immune response — either because of an immune defect or because they are too young to do so. The currently approved Hib vaccine is only effective in children 2 years old or older, even though most cases of meningitis occur in the first 24 months of life. Conjugate vaccines may prove effective in children 6 months old or younger, but may also leave a window of susceptibility immediately after injection.

Indeed, says Daum, it may be that passive, immune globulin vaccines will be useful as an adjunct to the current or conjugate vaccine — to provide protection during the susceptibility window.

For now, however, only one type of vaccine is available in the United States, and its efficacy is less certain than was previously believed. If the full board of the American Academy of Pediatrics approves the infectious disease committee's statement, physicians will have to choose between the Academy's view and that of the CDC as they decide whether to administer Hib vaccinations. The CDC continues to recommend essentially universal immunization for children at 24 months of age, while the committee's statement, Daum says, allows that in areas where efficacy is demonstrably absent, physicians may choose to follow local rather than federal health-authority guidelines. — *R. Weiss*