CUBAN BIOTECHNOLOGY

A NEW MENINGITIS VACCINE ENTERS MASS TRIALS

HAVANA—In an unimposing suburban dwelling, scientists at the Meningococcal Research Center here have quietly developed an extremely promising candidate vaccine against Group B meningococci—a variety of meningitis-causing bacteria that had previously defied all attempts at prophylaxis.

The team, a section of the Cuban National Center for Biologicals led by Concepcion Campa Huerga, is nearing the completion of clinical trials involving over 200,000 individuals in high-risk populations. Group B meningococci are the most important cause of menigococcal disease in Cuba (97.3 percent), and epidemiologically considered to be the single most serious health problem of the country. But Group B disease is not confined to the Caribbean. It is widespread in Scandinavia, Canada, and the United Kingdom, and continues to cause local outbreaks in the United States.

The disease, which is caused by *Neisseria meningitidis*, can be fatal in as few as five hours after the onset of symptoms. It annually strikes about 1,000 Cubans between the ages of six months and 20 years, and leads to about 200 deaths. Although vaccines against Groups A and C meningococci have been available for some time, until now no promising candidate for a Group B vaccine had appeared. Groups A and C vaccines are based on polysaccharide derived from the bacterial capsule. Unfortunately, Group B polysaccharide, for reasons that are still unclear, is not immunogenic.

Campa and her team therefore decided to investigate the possibility of developing a subunit vaccine based on the outer membrane protein (OMP) of the predominant circulating serotype of *N. meningitidis* Group B. Researchers at the Center purified enough OMP (about 15 mg) for preliminary clinical trials in 500 volunteers, and formulated an intramuscular preparation with alum and Group C polysaccharide—to solubilize the OMP and at the same time give a bivalent vaccine. The results of these trials, presented at the Fifth International Conference on Pathogenic Neisseria, held last summer in Amsterdam, were so encouraging that large-scale protection studies were inaugurated.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

An electron micrograph of purified outer membrane protein from *Neisseria meningitidis* Group B Type 4P1:15. The membranous vesicles are formulated as a vaccine (inset) by solubilization with Group C polysaccharide and the addition of alum.

The vaccine is remarkably free of even minor reactogenic responses, and gives antibody and bacteriocidal titers far in excess of what are generally considered to be good indications of protection—in some cases, 30 times higher than unvaccinated controls. In addition, it remains stable upon storage for one year at 4°C.

After consultations with colleagues at the conference, two sorts of trials were designed. In one (initially the only kind the Cubans wanted to undertake), which began on May 11, the entire susceptible population (about 123,000 persons) of the Province of Ciego de Avilla is to be vaccinated. The incidence in this province (30/100,000) is the highest in the country, and has been constantly so for many years. Evaluation of protection will be based on the recorded prevalence after one year.

A second, double-blind placebo trial is also underway. Eighty-five thousand boarding school children have already received their first dose, and by the end of June all will have gotten their six-week booster. Because of the close contact in school dormitories, the incidence in this population is also very high. And these studies, which are free of any possible ambiguities the Ciego de Avilla trials may contain, will provide a solid basis on which to evaluate the efficacy of the new vaccine.

It is perhaps more than coincidental that as the first phase of these trials neared completion, the Carlos J. Finlay Medal—named for the scientist who eradicated yellow fever from Cuba, and the country's highest scientific award—was presented to another public health pioneer, Albert Sabin.

—Harvey Bialy