Aiming at Adolescent Vaccination

Pertussis *from page 1*

showing that reported pertussis cases dropped from a peak of more than 250,000 in the 1930s to 100,000 in the 1940s after introduction of the diphtheria-tetanus-pertussis vaccine, and then further declined through the 1950s, to an all-time low of 1,006 cases in 1976.

Rates stayed low into the 1980s but began to rise in the mid-1980s. There were a little more than 10,000 cases in 2003, Dr. Murphy said.

In the United States, the incidence is highest for children under 1 year and for adolescents aged 10-19 years, she said. Pertussis still affects adults, as well, which may explain why infants are being infected.

An analysis of pertussis in children under 4 months in four states found that of the known sources of the illness, 16% came from adults aged 20-39; 7% of the cases came from adolescents. Thus, it appears that adolescents and adults are infecting unvaccinated infants, she said.

And yet physicians often aren't on the lookout for pertussis in older age groups. "It's hard to find an internist who will tell you pertussis exists in adults," she said.

There has been an increase in pertussis cases in Canadian adults, adolescents, and very young infants, said Scott Halperin, M.D., a pediatrics professor at Dalhousie University in Halifax, N.S.

Canada has begun a program to vaccinate adolescents. The first groups were vaccinated in Newfoundland 5 years ago; since then, there have been no cases in teens there. Immunizations, which are recommended but not mandatory, have continued across the provinces, Dr. Halperin said.

Canada is using Aventis Pasteur's vaccine, Adacel, which is approved in that country and Germany. Aventis applied for Food and Drug Administration approval of Adacel in August 2004. (See story, below right.)

GlaxoSmithKline also submitted a DTP formulation, Boostrix, to the FDA this summer. Boostrix is already approved in Australia, Asia, Europe, and South America, according to company press releases. (See story, below left.)

The United States and Canada aren't alone in terms of rising pertussis rates. In a poster at the ICAAC meeting, Alberto Tozzi, M.D., of Bambino Gesu Hospital in Rome reported data from the Surveillance Community Network for Vaccine Preventable Infectious Diseases (EUVAC-NET), a project funded by the European Parliament and Council.

It appears that adolescents and adults are infecting unvaccinated infants, according to a study of children under 4 months in four states.

Sixteen western European countries participate in the project, and from 1998 to 2002, they reported 80,000 pertussis cases. There were 32 deaths, primarily in children less than 6 months old. Infants under 1 year had the highest frequency of disease; rates were stable in 10- to 14-year-olds, but increased 115% in those over 14 years.

France, Malta, Germany, and Australia have begun vaccinating adolescents to protect them and to prevent spread to unvaccinated infants.

There's still no definitive explanation as to why adults and adolescents are getting pertussis. It could be due to greater recognition of the illness, waning immunity from vaccination, or changes in the circulating pathogen.

Carl-Heinz Wirsing von Koenig, M.D., director of the laboratory at Klinikum Krefeld (Germany) observed that pertussis reporting has increased and that diagnosis in children has improved thanks to the use of polymerase chain reaction (PCR) testing, which is reliable in that group. Children are also easily diagnosed by the "whoop" that they make when coughing.

But PCR and serology testing is less reliable in adults, and there is very little agreement on testing standards, which makes diagnosis more difficult, he said. ■

Safety, Efficacy of Pertussis Booster For Teens Similar to Current Vaccines

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — GlaxoSmithKline's candidate reduced-antigen content tetanus-diphtheria–acellular pertussis booster vaccine for adolescents compares favorably with other currently licensed vaccines, Leonard Friedland, M.D., reported during the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

In a pivotal clinical study of 4,114 healthy 10-18 year olds, Boostrix (tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed [Tdap]) was comparable in both immunogenicity and safety with a currently licensed tetanus-diphtheria toxoid(Td) vaccine and produced antibody responses at least as high as those seen in infants who receive the current higher-antigen DTaP vaccine, said Dr. Friedland, director of clinical research and development and medical affairs for GlaxoSmithKline's Vaccines North America division.

Of all the diseases against which children are routinely immunized in the United States, pertussis is the only one still increasing. That's because immunity from the childhood vaccine wanes after about 10 years, and there is currently no pertussis vaccine licensed for persons over the age of 7 years. In 2003, adolescents aged 10-19 made up 39% of all pertussis cases in the United States.

Boostrix is currently under review by the U.S. Food and Drug Adminstration for use as a single-dose booster in adolescents. If approved, it could replace the current Td booster, thereby protecting adolescents against pertussis without adding an extra injection, he noted at the conference, sponsored by the American Society for Microbiology.

All study subjects had previously received the routine childhood vaccinations against diphtheria, tetanus, and pertussis according to the recommended schedule. Most had received their first three doses as whole-cell pertussis vaccine. Some had received their fourth and/or fifth doses as acellular pertussis vaccine.

The proportion achieving a four-fold rise in titers of antidiphtheria antibody at 1 month post vaccination was 90.6% among the subjects who received Tdap, compared with 95.9% of those given Td. For antitetanus antibody, the proportions were 89.7% and 92.5%, respectively. Moreover, seroprotective levels of both antibodies were achieved in more than 99.9% of the subjects in both groups. These results met the pre-defined criteria for "noninferiority" of Tdap vs. Td, Dr. Friedland said.

Since there is no established serologic correlate of protection for pertussis, the antibody responses to each of the three pertussis antigens (PT, FHA, and PRN) of the subjects in this study were compared with those seen in infants following receipt of GlaxoSmithKline's DTaP vaccine (Infanrix). For each antigen, the geometric mean titers (enzyme-linked immunoabsorbent assay units/ml) were considerably higher in the adolescents following Tdap than among the infants who received DTaP (85.9 vs. 48.6 for PT, 617.3 vs. 89.1 for FHA, and 469.3 vs. 124.2 for PRN).

It is therefore "reasonable to assume that Tdap will be at least as effective as Infanrix for preventing pertussis in adolescents," Dr. Friedland said.

Overall pain at the injection site did not differ between Tdap (75.3%) and Td (71.7%). The proportion reporting grade 2 or 3 pain was slightly greater in the Tdap group (51.2% vs. 42.5%), but the percentage with grade 3 pain—preventing normal activity—was less than 5% in both groups and not significantly different between them, he said.

Study subjects were instructed to immediately contact investigators if they developed large areas of swelling at the injection site, an adverse effect that has been observed in children receiving the DTaP booster. Only two subjects—one from each vaccine group—reported diffuse swelling. The swelling did not involve adjacent joints and resolved completely in both subjects, Dr. Friedland said.

Headaches preventing normal activity were slightly more frequent in the Tdap subjects (15.7% vs. 12.7%), but there were no differences in fever, fatigue, or GI symptoms. No serious events occurred in either group in the 31 days after vaccination, Dr. Friedland reported. ■

Aventis Pasteur's Tetanus-Diphtheria–Acellular Pertussis Booster Appears Safe in Teens

BY MIRIAM E. TUCKER
Senior Writer

WASHINGTON — The safety profile of Aventis Pasteur's reduced-antigen tetanus-diphtheria–acellular pertussis vaccine in adolescents is similar to that of the currently-licensed tetanus-diphtheria vaccine, Michael E. Pichichero, M.D., reported in a poster presentation at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

Aventis Pasteur's reduced-antigen tetanus-diphtheria–acellular pertussis (Tdap) vaccine, called Adacel, has been licensed in Canada for booster immunization of adolescents and adults. It is under review by the Food and Drug Administration for use in individuals aged 11-64 years.

Two randomized multicenter U.S. trials included 2,990 adolescents aged 11-17 given Tdap and 792 given tetanus-diphtheria toxoid (Td), said Dr. Pichichero, a specialist in pediatric infectious diseases who practices in Rochester, N.Y.

Immediate reactions (within 30 minutes) were reported at comparably low frequencies in both the Tdap and Td groups (0.5%-0.6%). Most reactions were mild and resolved within a day. Also comparable were the frequency, intensity, and mean duration of fever of 38° C or greater (seen in 5.0%-5.2% with Tdap, 2.7% with Td) and injection site erythema and/or swelling (20.8%-24.3% with Tdap, 18.3%-19.7% with Td).

Pain at the injection site was slightly but significantly more frequent in the Tdap group (79.2% vs. 71.0%), but this pain was usually of mild intensity and its mean duration did not differ significantly between the two groups, Dr. Pichichero said at the conference, sponsored by the American Society for Microbiology.

Postvaccination limb circumference measurements within 2 weeks of vaccination were very similar between the two groups (increases of more than 3 cm occurred in roughly 5% of each group), and no study subjects had whole arm swelling. Headache, generalized body ache, and tiredness (mostly mild) were the three most commonly reported solicited systemic events, all in less than 30% of each group.

Unsolicited events such as pharyngitis, nasopharyngitis, and cough within 28 days of vaccination were reported with equal frequency, intensity, and type between the two groups. Most were mild or moderate and not related to vaccination. Serious events were rare (1% or less in both groups), comparable in frequency, and unrelated to vaccination, he said. ■