Supply Should Exceed Demand

Meningitis *from page 1*

against meningococcal disease as part of any adolescent care visit speaks to the value of a medical home, where a teen's records would show whether he or she had received the MCV4 vaccine, Dr. Temte added in an interview. "The take-home message is to have a medical home and continuity."

Ideally, the expanded recommendations will increase the number of adolescents who are vaccinated against meningococcal disease, which although rare, is more prevalent in adolescents than in younger children or adults. The newly approved recommendations will be published in an upcoming issue of the CDC's Morbidity and Mortality Weekly Report. In addition, vaccination information can be found at the ACIP Web site: cdc.gov/vaccines/recs/acip.

Some members of the ACIP expressed concern over the increased risk of Guillain-Barré syndrome (GBS) that has been reported in adolescents who received the MCV4 vaccine, but they agreed that the opportunity to prevent meningococcal disease in more teens trumps the limited data that suggest an association between MCV4 and GBS. But individuals with a history of GBS may be at increased risk and should discuss their risk of meningococcal disease with their doctors, Dr. Cohn said in her presentation.

The revised recommendations continue to emphasize that 11- to 12-year-olds should receive the MCV4 vaccination at the 11- to 12-year-old preventive care visit, along with other routine adolescent vaccinations.

"The ACIP goal is routine vaccination of all adolescents beginning at age 11 years," said Dr. Cohn. She quoted from the draft of the recommendations to add that the ACIP and partner organizations, including the AAP, AAFP, and American Medical Association, recommend a health care visit for all 11- to 12-year-olds to receive recommended immunizations and other preventive medicine services.

Supply problems with the MCV4 vaccine in 2006 prompted ACIP to recommend a deferral of vaccinating 11- to 12-year-olds in favor of older adolescents (starting high school) who were deemed at greater risk for meningococcal disease. But representatives from Menactra manufacturer Sanofi Pasteur assured the committee that the company's total vaccine supply from January 2007 to September 2007 is on track to exceed 6 million doses resulting from surplus carried over from 2006 when the vaccine was deferred in the younger adolescents. In addition, the company representatives projected a supply of at least 9 million doses (including the previous year's surplus) to be available for the remainder of 2007 and into 2008 to meet and exceed demand.

Real demand for new vaccines is unpredictable, noted Dr. Gregory Wallace, chief of the CDC's vaccine supply and insurance branch. Adolescents in the public sector are difficult to reach after age 11-12 years, and demand for MCV4 has yet to pick up after the deferral for 11-to 12-year-olds was lifted, he said in a presentation at the meeting.

But the ACIP working group anticipates that the expanded recommendations will improve adolescent coverage by simplifying health care providers' decisions to vaccinate, said Dr. Cohn. Menactra was first licensed in January 2005, and it is indicated for use in persons aged 11-55 years to prevent invasive meningococcal disease caused by several *Neisseria meningitis* serogroups including A, C, and Y. ■

GlaxoSmithKline's HPV Vaccine Shows 90% Efficacy

BY ROBERT FINN
San Francisco Bureau

A bivalent vaccine for human papillomavirus manufactured by GlaxoSmithKline has shown greater than 90% efficacy against high-grade cervical intraepithelial neoplasia, according to interim results from a large, randomized controlled trial published online in the Lancet.

The study, led by Dr. Jorma Paavonen and colleagues, is called the Papilloma Trial to Prevent Cervical Cancer in Young Adults (PATRICIA), and involves 18,644 women, aged 15-25 years, from 14 countries in Europe, Asia, and North America. The participants were randomly assigned to receive three injections of the human papillomavirus (HPV) vaccine or a hepatitis A vaccine at months 0, 1, and 6 (Lancet 2007; DOI:10.1016/S0140-6736[07]60946-5).

The study was sponsored by GlaxoSmithKline. Several study investigators were employees of the company, and others, including Dr. Paavonen of the University of Helsinki received consulting and lecture fees from the pharmaceutical firm.

The vaccine, Cervarix, has not yet been approved by the Food and Drug Administration. Cervarix is a bivalent vaccine, active against HPV types 16 and 18, which account for 70% of all cases of cervical cancer.

In the current study, only 2 of the 9,319 women receiving Cervarix developed cervical intraepithelial neoplasia (CIN) of grade 2 or 3 and related to HPV 16 or 18, compared with 21 of the 9,325 women in the control group. This translates into an efficacy of 90%.

The vaccine showed 89% efficacy against grade 1 or higher CIN.

Virtually all women receiving the HPV vaccine (99.5%) had developed antibodies against HPV 16 and 18 after the second of the three injections.

In an editorial, Dr. Jessica A. Kahn of the University of Cincinnati and Dr. Robert D. Burk of the Albert Einstein College of Medicine, New York, called the results "encouraging" (Lancet 2007; DOI:10.1016/S0140-6736[07]60947-7).

However, they noted that the follow-up time was only about 15 months, which is short compared with the several decades over which cervical cancer often evolves. The enrollment criteria in the trial were relatively narrow, so it's unknown whether seroconversion rates, antibody titers, and efficacy rates will be as high when the vaccine is distributed to a wider population.

Dr. Kahn and Dr. Burk also emphasized that the vaccine was not without side effects. Although generally well tolerated and safe, the HPV vaccine caused significantly more local adverse events such as pain, redness, and swelling, than did the hepatitis A vaccine. Risks of general adverse events, including arthralgia, fatigue, and myalgia, also were significantly higher in the HPV group.

Dr. Kahn and Dr. Burk stressed the need for the vaccine to be made available in less-developed regions of the world, where cervical cancer makes the largest contribution to years of life lost to cancer. "Poverty is strongly associated with high-risk HPV infection and cervical cancer," they wrote. "If those who live in poverty cannot access highly effective interventions such as HPV vaccines, disparities could worsen dramatically." ■

Largest Study to Date Supports Gardasil's Safety After 1 Year of Use

BY HEIDI SPLETE
Senior Writer

ATLANTA — Postlicensure safety data from the first year of widespread use of Gardasil show that serious adverse events from the quadrivalent human papillomavirus vaccine are rare.

Dr. John Iskander presented the postlicensure data at the June 2007 meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

The safety data, which encompass the first 11 months of the U.S. experience with Gardasil, were from the United States Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD), two vaccine surveillance mechanisms supported by the CDC.

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The data are likely to increase the comfort level of doctors, said Dr. John Iskander.

The postlicensure data are likely to increase comfort levels for doctors when they talk to patients about the HPV4 vaccine, said Dr. Iskander of the CDC's Immunization Safety Office.

More than 5 million doses of Gardasil have been distributed as of the end of March 2007, according to the vaccine's manufacturer (Merck), although the exact number of doses that have been administered is uncertain at this time.

So far, the HPV4 overall vaccine adverse event reporting rate is 33 per 100,000 doses, and the serious adverse event reporting rate is 1.8 per 100,000 doses, based on VAERS data.

A total of 1,763 adverse events related to use of the HPV4 vaccine had been reported to the VAERS as of May 8, 2007. Of these, 87% involved the use of HPV4 alone. Nearly 70% of the reports involved girls and women aged 9-26 years (the age range used in prelicensure clinical trials).

"A substantial proportion of vaccine events began on the day of vaccination (39%), or in the days [immediately] following vaccination," Dr. Iskander noted. Similarly, 42% of serious adverse events occurred on the day of vaccination, with an average onset time of 1 day afterward. A total of 857 vaccine events (49%) were reported after a single dose of HPV4.

The most common symptoms in reports of serious adverse events were vomiting (14%), syncope (12%), fever (11%), nausea (11%), and headache (11%). Similarly, the most commonly reported symptoms associated with vaccine use were dizziness (13%), injection site pain (10%), syncope (10%), and nausea (9%).

Although data on associations between HPV4 use and reports of Guillain-Barré syndrome are limited, the VAERS data included 13 reports of GBS in patients who received HPV4. Of these, 11 cases occurred in girls aged 13-16 years; one case occurred in a 50-year-old woman, and the age of the other patient is unknown. More than half of these cases involved coadministration of Menactra and Gardasil.

The VAERS data also included two nonfatal cases of thromboembolism in patients who received the HPV4 vaccine. In addition, 11 serious event reports from VAERS involved syncope, all of which occurred within 10 minutes of vaccination. "Current recommendations suggest a 15-minute waiting period after vaccination … to avoid syncope," Dr. Iskander noted. Many of the frequently reported adverse events, such as syncope, are common in the general population and do not have a specific relationship to this vaccine or to vaccinations in general, he said.

Dr. Iskander presented details on four cases of death in patients who had been vaccinated with HPV4. None of the deaths appear to be causally related to vaccination, Dr. Iskander said. But the CDC will continue to collaborate with the Food and Drug Administration, the World Health Organization, and other organizations to monitor postlicensure surveillance and other communication related to HPV4. ■