HPV Vaccine Not Linked To Serious Adverse Events

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ATLANTA — Postlicensure safety monitoring by three national vaccine safety systems indicates that, in the more than 2 years since the human papillomavirus vaccine Gardasil was licensed, serious adverse events have been rare and have not been specifically linked with the product.

More than 20 million doses of Gardasil, manufactured by Merck & Co., had been distributed and are under passive surveillance, and more than 375,000 doses are under active surveillance as of Aug. 31, the Centers for Disease Control and Prevention officials reported at the fall meeting of the CDC's Advisory Committee on Immunization Practices.

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Dr. Angela Calugar said serious adverse events occurred mostly in those with contributing factors.

Of the more than 10,300 adverse events reported thus far to the Vaccine Adverse Event Reporting System (VAERS), 94% have been nonserious. Most of the adverse event reports to VAERS were consistent with prelicensure trial data. Among the adverse events reported are syncope, dizziness, nausea, Guillain Barré syndrome, venous thromboembolism, and death, said Dr. Angela Calugar of the CDC.

About 51 reports, 3 of which were serious, have been made per 100,000 doses given. About half of all reports are in those aged 11-18 years, and 25% are in those aged 19-26 years, Dr. Calugar said, noting that this likely reflects the proportion of patients in these age groups who are receiving HPV vaccine.

Serious adverse events—including syncope, venous thromboembolism (VTE), and Guillain Barré syndrome—occurred mostly in individuals with other contributing factors. For example, of 18 reports of VTE, 14 were in patients who also used hormonal contraceptives, which are known to increase VTE risk, she noted.

As for the 17 deaths reported in association with HPV vaccination, no clusters based on patient age, timing of vaccination, or other factors were identified that might hint at a causal relationship, she said.

Furthermore, the Clinical Immunization Safety Assessment (CISA) Network—a collaboration of six U.S. academic centers that conduct research on adverse events associated with immunizations—has found insufficient evidence to support a causal relationship between HPV vaccination and the reported serious adverse events, reported Dr. Barbara Slade, also of the CDC.

Likewise, findings of the Vaccine Safety Datalink project—which was established in 1990 to improve the evaluation of vaccine safety through active surveillance and epidemiologic studies—showed that among more than 375,000 doses administered and monitored, no statistically significant risk for any prespecified adverse event (Guillain Barré syndrome, seizures, syncope, anaphylaxis, other allergic reactions, appendicitis, stroke, and VTE) occurred after vaccination in either youth (ages 9-18 years) or adults (ages 19-26 years), Julianne Gee of the CDC reported. ■

Survey Cites Some Gaps in Doctors' HPV Vaccine Knowledge

ATLANTA — Family physicians and pediatricians are knowledgeable about key aspects of human papillomavirus epidemiology and have largely adopted use of the HPV vaccine in their practices, but some important knowledge gaps about the disease and vaccine remain, results of a survey suggest.

Findings from a national HPV vaccination practices survey of 331 family physicians and 349 pediatricians, which was conducted 18 months after licensure of the HPV vaccine Gardasil, indicate that both groups understand that most genital HPV infections are asymptomatic (86% and 85%, respectively, responded correctly on a related survey item), and that almost all cervical cancers are caused by HPV (95% and 85%, respectively, responded correctly).

However, only 58% of family physicians and 43% of pediatricians correctly answered "false" to an item stating that genital warts are caused by the same HPV types as cervical cancer.

The findings, reported at the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices fall meeting by Dr. Matthew F. Daley, also show that 88% of family physicians and 98% of pediatricians who responded are administering HPV vaccine to female patients.

When surveyed about whether parents feel vaccination might encourage earlier or riskier sexual behavior, 49% of family physicians and 42% of pediatricians said they strongly agree or somewhat agree that parents have such concerns, but only 6% and 4%, respectively, said they had such concerns themselves.

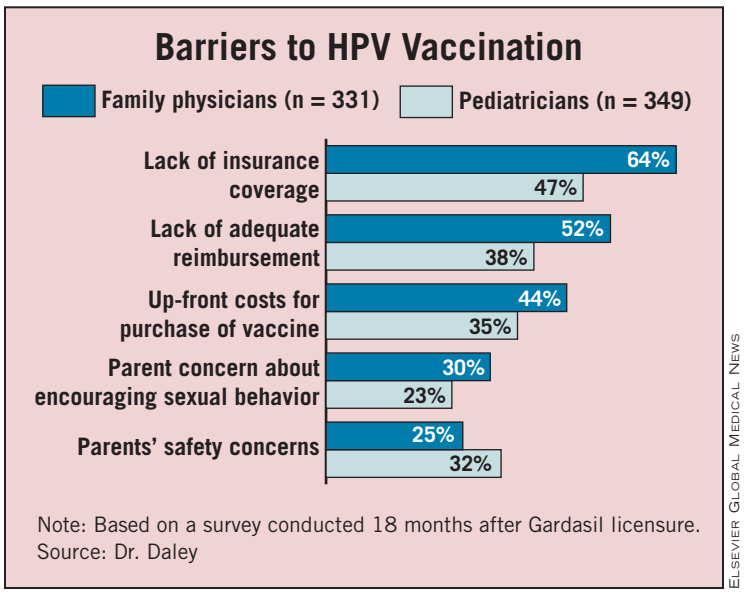
As for which patient populations the respondents target for vaccination, physicians (82% of family physicians and 89% of pediatricians) said they more strongly recommend vaccination for 13- to 15-year-olds than for 11- to 12-year-olds (49% and 56%, respectively), said Dr. Daley of the department of pediatrics at the University of Colorado at Denver.

After adjustment for respondents' specialty and region of the country, factors found to be associated with not strongly recommending vaccination in 11- to 12-year-olds were considering it necessary to discuss sexuality before recommending vaccination (odds ratio, 1.6); reporting that parents of 11- to 12-year-olds have been more likely to refuse vaccination than parents of 16- to 18-year-olds (OR, 4.0); and believing that the time it takes to discuss HPV vaccination is definitely or somewhat of a barrier (OR, 1.9).

Parents' refusal to have a child vaccinated and deferral of vaccination were also addressed in the survey. Parents are more likely to defer than to refuse vaccination, the results suggested. Also, refusal is most common for 11- to 12-year-olds, with about 25% of parents reportedly refusing vaccination in that age group, he noted.

The most common reported reasons for refusal or deferral were the "newness" of the vaccine, patient age, lack of sexual activity on the patient's part, and lack of insurance coverage/inability to pay.

Factors that were reported as definitely or somewhat of a barrier to vaccination included lack of insurance coverage, lack of adequate reimbursement, and up-front costs for purchase of vaccine. (See box.) ■



ELSEVIER GLOBAL MEDICAL NEWS

Hib Shortage Persists; Defer Booster Dose in All but At-Risk Kids

ATLANTA — The *Haemophilus influenzae* type B vaccine shortage that began last December following a voluntary recall of 1.2 million lots of vaccine continues, so booster doses in most children still should be deferred.

Dr. Jeanne Santoli announced this recommendation at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

Interim recommendations made following the recall last year by Merck & Co., the maker of PedvaxHIB, called for deferral of the booster dose recommended for children aged 12-15 months, except in children at risk for Hib disease. Those at risk include children with asplenia, sickle cell disease, or leukemia or other malignant neoplastic diseases, and American Indian and Alaska Native children living in American Indian and Alaska Native communities, said Dr. Santoli of the CDC.

Since the interim plan was put in place, vaccine supply has been adequate to cover the more limited dosing schedule, thanks to vaccine supplies from Sanofi Pasteur, which manufactures two Hib vaccines (TriHIBit, a combination vaccine against diphtheria and tetanus toxoids and acellular pertussis/Hib, and ActHIB, a monovalent Hib vaccine).

The Sanofi Pasteur vaccines are being used for all children but American Indian and Alaska Native children living in American Indian and Alaska Native communities; these children are receiving vaccine from the CDC stockpile of Merck vaccines that were not recalled.

Merck had planned a return of PedvaxHIB to the U.S. market in the fourth quarter of this year, but the company announced on Oct. 17 that a return wouldn't be possible at this time.

"The reason for this delayed return is an additional manufacturing process change that requires a regulatory filing with the [U.S. Food and Drug Administration] that needs to be approved prior to a return to the market," Dr. Santoli said.

As a result, the CDC will not change the interim Hib recommendations at this point. Providers should continue to register and track children in whom the booster dose is deferred to facilitate recall and reinstatement of the booster dose when the product becomes available, she said, adding that the CDC is working with Sanofi Pasteur as the company reviews capacity to serve the U.S. market. "They are confident they have sufficient doses … to cover the three-dose series through mid-2009, and the CDC stockpile has sufficient PedvaxHIB for American Indian and Alaska Native children living in those communities for this new, unexpected duration of the Hib shortage." ■