



BY STEPHEN I. PELTON, M.D.

ID CONSULT

Check Gardasil Adverse-Event Data

Since July 22nd, you have no doubt received phone calls from anxious parents who heard the news report about

adverse events associated with the human papillomavirus vaccine, Gardasil. As usual, the media did a good job of creating anxiety both among parents and prescribing physicians. I've heard how much time clinicians now are spending discussing vaccine safety with their patients, and that some have begun administering the HPV vaccine separately from other recommended adolescent vaccines and others have just stopped giving it altogether.

I'd like to review what we know so that you can be prepared to answer questions and, I hope, alleviate fears about Gardasil and other recommended childhood and adolescent vaccines. A statement, issued jointly by the Centers for Disease Control and Prevention and the Food and Drug Administration, summarized all reports concerning Gardasil that were filed with the Vaccine Adverse Events Reporting System (VAERS) from the time the vaccine was licensed on June 8, 2006, through June 30, 2008.

A total of 9,749 adverse events were reported to VAERS in association with administration of Gardasil, of which 94% were classified as nonserious events, and 6% as serious events. It's important to keep in mind the denominator: At the

time the statement was issued, Merck & Co. had distributed over 16 million doses of Gardasil in the United States.

Also remember that VAERS is a passive reporting system that receives unconfirmed reports of possible side effects following the use of all vaccines licensed in the United States.

Data from the system are reviewed on an ongoing basis to look for possible signals that require further investigation. Data from VAERS cannot and should not be viewed as implying causation.

The 9,164 nonserious reports included syncope, injection site pain, headache, nausea, and fever. Indeed, fainting after receipt of any vaccine is common among teenagers. Providers are reminded to keep patients seated for at least 15 minutes after vaccination to avoid injury from a possible fall.

The 585 serious adverse events included 20 deaths. There was no common pattern to these deaths that would suggest they were caused by the vaccine. Where autopsy results were available, the cause of death was unrelated to vaccine.

Other serious adverse event reports following receipt of Gardasil were attributable to Guillain-Barre Syndrome, a rare neurologic disorder for which the typical attack rate is highest during adolescence. Further investigation by FDA and CDC found no increase in GBS cases beyond the expected number among Gardasil recipients.

Thromboembolic disorders also were reported following vaccination with Gardasil, most of which occurred in individ-

uals with risk factors for clotting, such as oral contraceptive use.

In addition to VAERS, there also is a safety monitoring system called the Vaccine Safety Datalink Project, a collaboration between CDC and eight managed care organizations that is set up to investigate any possible safety signals arising from VAERS. Gardasil and all other vaccines are monitored with these systems on an ongoing basis. In the meantime, the CDC has not made any changes to its recommendations for the use of Gardasil based on the available information, nor has the FDA revised its prescribing information.

Gardasil, the first HPV vaccine to be licensed, was approved for use in girls and women aged 9-26 years. It was recommended by the CDC's Advisory Committee on Immunization Practices (ACIP) as a three-dose series for routine vaccination of girls aged 11-12 years, and for catch-up in girls and women aged 13-26 years.

The vaccine is made from noninfectious particles, not live or attenuated virus. It contains no thimerosal. It protects against HPV strains 16 and 18, which cause 70% of all cervical cancers, and strains 6 and 11, responsible for 90% of all genital warts in the United States. Data show that the vaccine is most effective when given prior to onset of sexual activity.

When speaking with a worried parent, I think it's critical to explain that association does not imply causation. I also would review the rationale behind giving the HPV vaccine and reiterate that maximum benefit is achieved by immunization before sexual debut.

Every year, about 12,000 women in the United States are diagnosed with cervical cancer and almost 4,000 die from it. Worldwide, cervical cancer is the second most common cancer in women, causing an estimated 470,000 new cases and 233,000 deaths per year. I don't think you can put a price on the value of saving lives by administering a vaccine, although of course plenty of health economists have tried to do just that.

Going forward, I think it behooves physicians who administer vaccines to stay abreast of the news. When you see a headline about any vaccine, check out the Web sites of the CDC (www.cdc.gov), the American Academy of Pediatrics (www.aap.org), or your local health department for the latest reliable information and refer your patients to those sites as well.

As we're seeing from the recent measles outbreaks across the country, the majority of cases are not the result of vaccine failure but of failure to vaccinate. Our role is to help parents make the right decision. We must be armed with data to prevent associations between daily events from being interpreted as causation.

I am a member of global advisory boards on vaccine for Novartis, Wyeth, and GlaxoSmithKline, for which I receive honoraria. ■

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Safety, Not Sex, Tops Parents' Concerns About HPV Vaccine

BY HEIDI SPLETE
Senior Writer

Safety, not sexuality, was a key factor in the reluctance of mothers to have their teenage daughters vaccinated against human papillomavirus, according to results from a study published in the *Journal of Adolescent Health*.

The Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices currently recommends a three-dose vaccine against the human papillomavirus (HPV) for all girls aged 11-12 years and young women aged 13-26 years. HPV has been identified as a leading cause of cervical cancer.

Previous studies have shown that parents were in favor of vaccination for adolescents but hesitant to vaccinate younger girls. But data from these studies have shown that in most cases, this resistance was not brought on by concerns that the vaccination might make teenage girls more likely to engage in risky sexual activities.

To examine the factors that influence parents' acceptance of the HPV vaccine, Susan L. Rosenthal, Ph.D., of the University of Texas Medical Branch in Galveston and her colleagues interviewed mothers with daughters aged 11-17 years who were visitors to a university-based primary care clinic.

The study included complete results from 153 mothers of various ethnicities (average age 41 years) who completed a questionnaire. The questionnaire included ratings of seven health beliefs including perceptions of HPV disease severity and barriers to vaccination, such as cost. The questionnaire also addressed aspects of the par-

ent/child relationship, including how closely the girls' activities were monitored by parents and whether the parents had discussed topics such as birth control, dating, and making decisions about sex (*J. Adolesc. Health* 2008; 43:239-45).

Overall, 18% (27) of the mothers had been offered the HPV vaccination for their daughters but had not chosen it, and did not plan to vaccinate their daughters within the next year, while 34% (52) had not been offered the vaccination and did not plan to vaccinate their daughters within the next year.

Another 22% (34) had not been offered the vaccine but were aware of it and planned to vaccinate their daughters within the next year, and 26% (40) of the mothers reported that their daughters had started or completed the HPV vaccination series.

None of the mothers whose daughters had been vaccinated said they viewed the vaccine as unsafe, but objections to the vaccine were focused mostly on the lack of safety data because of the newness of the vaccine.

Mothers who were offered the vaccine but did not plan to vaccinate their daughters within the year often cited a lack of information about the vaccine, and some cited a lack of urgency based on their perceptions of their daughters' likely exposure to HPV.

Significant predictors of HPV vaccination after a multivariate analysis were mothers who had less than a high school education, had a history of sexually transmitted

infections, had monitored their daughters' activities with peers, and had thought their daughters would not mind getting the shots.

There was no significant association between HPV vaccine acceptance and the ages and ethnicities of the mothers and daughters, the daughters' dating status, mothers' history of HPV, mother/daughter discussion of sex topics, or the general family environment.

"Although the study was not designed to examine the process of and impact of physician counseling, it appeared that those who had been counseled had more positive attitudes toward the vaccine and understood better the reasons for vaccinating their daughters prior to initiation of sexual activity," the researchers noted.

The study was limited by the relatively small sample and by the university setting, which might have provided more education to parents and daughters than would other settings.

But the results suggest that even those parents and daughters who were counseled about the HPV vaccine wanted more information, and further studies are needed to determine the most effective ways to provide more education, the researchers wrote.

Many mothers who were not planning to vaccinate their daughters within the next year planned to vaccinate them eventually, they added.

The study was funded by grants from Merck & Co. and the National Institutes of Health. ■

It appeared that mothers who had been counseled by a physician had more positive attitudes toward the vaccine and better understood the reasons for it.