Prevents Precancerous Lesions

HPV Vaccine *from page 1*

a finding in the clinical trials that underlines "the importance of immunization before potential exposure to the virus."

In addition, because Gardasil does not include other less common HPV types, routine Pap screening remains "critically important to detect precancerous changes in the cervix to allow treatment before cervical cancer develops," the FDA said in the statement.

HPV 16 and 18 cause 70% of cervical cancers and other HPV-related cancers, 65% of high-grade precancerous lesions, and 25% of CIN 1 cases. HPV types 6 and 11 cause 90% of genital warts (in both men and women), 90% of recurrent respiratory papillomatosis lesions (in both men and women), and 10% of CIN 1 cases.

HPV is the most common sexually transmitted infection in the United States. More than 10,000 women in the United States every year are diagnosed with invasive cervical cancer, and about 3,700 women die from this disease, according to the Society of Gynecologic Oncologists.

In four Merck studies of 21,000 women aged 16-26, including one in the United States Gardasil was nearly 100% effective in protecting against disease caused by the four HPV types in females aged 16-26 years who had not been previously exposed. The women were not studied long enough to determine the impact on cervical cancer, but "the prevention of these cervical precancerous lesions is believed highly likely" to result in prevention of cervical cancer, according to the FDA.

Immunogenicity studies conducted in younger females, those aged 9-15, determined that the antibody responses to the vaccine in the younger females were similar to those in the older females, the basis of the approval in the younger group. Safety data in about 11,000 people indicate that the most common side effects are mild or moderate local reactions, such as pain or tenderness at the injection site.

Gardasil is considered the second vaccine approved that prevents a form of cancer. Hepatitis B vaccine was the first.

The vaccine is administered in three intramuscular injections in the upper arm, given over 6 months. Each dose will cost $120, according to Merck, the manufacturer.

In a statement, the company said that used with screening, the vaccine "can help significantly reduce the human and economic burden of cervical cancer and other HPV-related diseases in the United States."

Because of its price, whether women and younger females from all socioeconomic levels will have equal access to the vaccine has been raised as a concern. In the approval statement, Merck announced it had established a patient-assistance program for vaccines, which will make Gardasil and other Merck vaccines available in the third quarter of this year to adults who are not insured or can't otherwise afford the vaccines.

Among the postmarketing studies Merck has agreed to conduct are studies further evaluating the safety and long-term effectiveness and pregnancy outcomes in a registry of women who receive the vaccine while pregnant. In clinical trials, there were five congenital anomalies in babies born to women vaccinated within 30 days of conception, and none among the women who received placebo within that time frame, but the five cases were common anomalies and were diverse, according to Merck.

The vaccine is not recommended for use in pregnancy.

Other postmarketing studies planned by Merck include a study that will follow a Nordic population of vaccine recipients for life, and a study of 35,000 recipients to evaluate safety and pregnancy outcomes.

The women in the Nordic study will be about 3 years ahead of the general population of women who will receive the vaccine after approval, so if a booster vaccine is necessary, it will be known in advance, Dr. Eliav Barr of Merck Research Laboratory, Whitehouse Station, N.J., said at the panel meeting last month.

Data available up to 5 years after vaccination indicate the level of efficacy remains high, at about 96%, he told the panel.

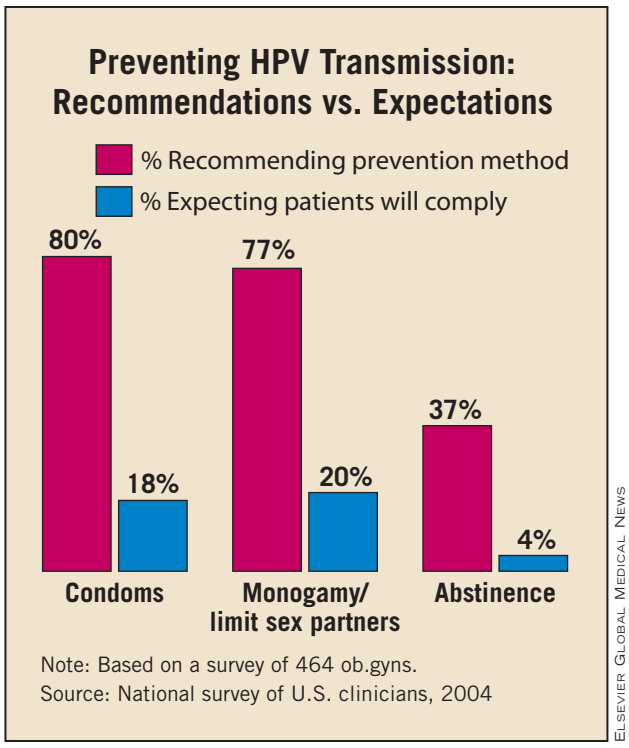
Among the concerns panel members raised at that meeting were that people might become complacent about screening for cervical cancer, and that people would remain at continued risk of infection with other HPV types not covered in the vaccine. Panelists stressed that the company should ensure that the vaccine's physician label and messages to consumers emphasize the continued need for regular screening and protection against STDs, including the other HPV types not covered by the vaccine.

There was some concern about the suggestion in one study that vaccination might increase progression of disease caused by one of the HPV types in the vaccine in females already infected with that type. However, when the data from all studies were combined, there was no indication that this occurred.

During the FDA's review of the data concerns were raised that the very high level of efficacy was observed in unexposed subjects. Some vaccine recipients who had already been infected with one or more HPV types in the vaccine developed HPV disease related to that type. In addition, it was observed that subjects who had not been exposed to the vaccine subtypes could still develop disease caused by one of the HPV types not covered by Gardasil.

The results of an efficacy study of Gardasil in 16- to 26-year-old men is underway; results will be available in late 2008. Merck plans to study the vaccine in boys and also in women aged 26-45 years. GlaxoSmithKline is testing another cervical cancer vaccine, Cervarix, which targets HPV 16 and 18. ■

A consumer fact sheet about the vaccine is available on the FDA's Web site at www.fda.gov/womens/getthefacts/hpv.html.



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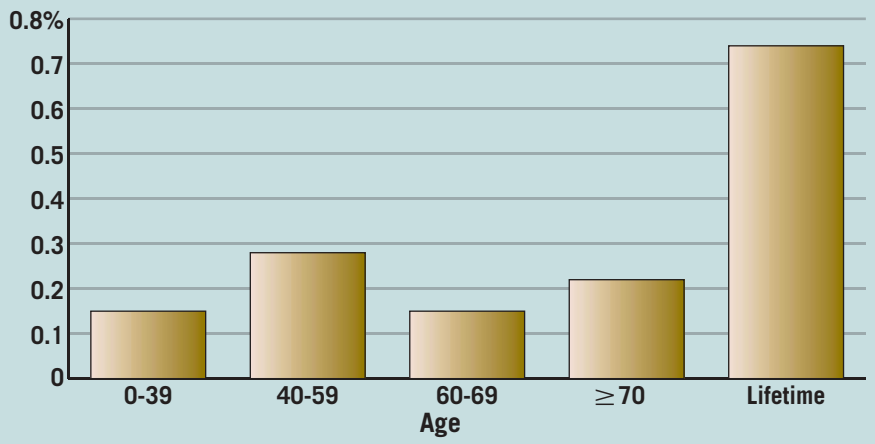

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Pap Tests to Spot Endometrial Cancer Recurrence Questioned

BY DOUG BRUNK
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PALM SPRINGS, CALIF. — Routine vaginal cytology as a surveillance test for endometrial cancer recurrence is costly, inefficient, and benefits less than 1% of patients, Dr. Robert E. Bristow and his associates reported in a poster session at the annual meeting of the Society of Gynecologic Oncologists.

"The rationale for intensive surveillance of endometrial cancer patients in clinical remission is based on the premise that early detection of an asymptomatic recurrence will translate into improved survival outcomes," the researchers, who are affiliated with the Kelly Gynecologic Oncology Service at Johns Hopkins Medical Institutions, Baltimore, wrote in their poster.

Although this premise is widely held, studies have not demonstrated a significant survival advantage for patients whose recurrences are detected during routine follow-up, compared with symptomatic patients presenting for interval evaluation, they noted.

The researchers reviewed the medical records of 377 endometrial cancer patients who were treated at the Kelly Gynecologic Oncology Service between July of 1997 and June of 2005.

They calculated the total number of Pap tests performed during surveillance or until the time of recurrence. Costs were assigned based on 2005 Pap test costs adjusted retroactively using the consumer price index.

Of the 337 patients, the majority (63.7%) had stage I cancer; 10.1% had stage II; 18.8% had stage III; and 7.4% had stage IV. The median follow-up was 30 months. A median of five Pap samples per patient were collected during the study period, for a total of 2,134 Pap tests.

The researchers found that endometrial cancer recurred in 61 patients (16.2%), while 11 (2.9%) had an isolated vaginal recurrence.

Of the isolated vaginal recurrences, seven were detected by physical examination alone, two were detected by interval computed tomography, and two asymptomatic vaginal recurrences were detected by routine vaginal cytology, for a rate of 0.5%.

"Detection of each asymptomatic vaginal recurrence required 1,067 Pap tests, generating $44,049 in cumulative charges," the researchers noted in their poster.

They concluded that "elimination or reduction in the use of vaginal cytology for this purpose offers an opportunity for significant cost savings in gynecologic oncology health care."

Dr. Bristow directs the Kelly Gynecologic Oncology Service. ■