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Prevention of human papillomavirus in women of childbearing age

FACULTY

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DISCLOSURES

Daron G. Ferris, MD, reports that he is a consultant to and is on the speakers bureau of Merck & Co., Inc., and that he has received grant/research support from Merck & Co., Inc., and from GlaxoSmithKline.

Lee P. Shulman, MD, reports that he is a consultant to and is on the speakers bureaus of GlaxoSmithKline and Merck & Co., Inc.

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States.¹ Nearly 76% of new infections occur in individuals aged 15 to 25 years,² usually soon after sexual debut.³ Another peak occurs between the ages of 30 and 40 years.⁴ By age 50, an estimated 80% of unvaccinated women are infected. The virus causes cervical and other cancers and diseases, as well as genital warts.¹ In 2005, 11,999 women in the United States were diagnosed with and 3924 women died from the cervical cancer.⁵

Burden of disease

Treatment of cervical cancer costs more than \$2 billion yearly.⁶ More than 1 million new cases of genital warts are reported each year, with 300,000 clinician office visits.⁷

Genital HPV is typically transmitted by penetrative genital contact (vaginal or anal) or by nonpenetrative contact, including genital-genital, oral-genital, and hand-genital contact. HPV is not spread via bodily fluids, including blood.¹ Most infections are asymptomatic; infected persons are often unaware of their status and may transmit the virus.⁸

Forty HPV types affect the lower genital tract.¹ HPV-types 16 and 18 are responsible for 70% of all cervical cancers; HPV types 6 and 11 are responsible for 90% of highly contagious genital warts.⁸ Approximately 90% of anal cancers; 40% of cancers of the vulva, vagina, and penis; and 10% to 20% of oropharyngeal cancers are also associated with HPV.¹ Rarely, infants born to mothers

infected with HPV types 6 and 11 develop recurrent respiratory papillomatosis.⁸

Disease prevention

HPV vaccination and Pap screening have made cervical cancer and genital warts mostly preventable. Quality clinical trials demonstrate that vaccinations significantly reduce the incidence of cervical precancer and non-invasive cervical cancer related to HPV types 16 and 18.⁹⁻¹¹

Two vaccines are currently available for protection against HPV: a quadrivalent vaccine (Gardasil®, Merck)¹² and a bivalent vaccine (Cervarix®, GlaxoSmithKline).¹³ The quadrivalent vaccine protects against HPV-types 6, 11, 16, and 18. The bivalent vaccine protects against HPV-types 16 and 18.

The quadrivalent vaccine is indicated in girls and women aged 9 through 26 years for prevention of cervical, vulvar, and vaginal cancer, and genital warts; cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma in situ (AIS); CIN grade 1; vulvar intraepithelial neoplasia grade 2 and grade 3; vaginal intraepithelial neoplasia grade 2 and grade 3; and in boys and men aged 9 through 26 years for prevention of genital warts. The bivalent vaccine is approved for use in females aged 10 through 25 years for prevention of cervical cancer, CIN grade 2 or worse, AIS, and CIN grade 1.

Both vaccines are administered by a series of 3 intramuscular injections over a 6-month period. If any injections are delayed, the series should be resumed, not restarted.

Because the bivalent vaccine was licensed only recently, ACIP recommendations are available only for the quadrivalent vaccine.

The vaccine is recommended universally to females without contraindications between ages 11 and 26 years, even with prior exposure to some HPV types in the vaccine.¹ Catch-up vaccination is recommended for females aged 13 to 26 years even if sexually active. Vaccination may be given in special circumstances (eg, equivocal or abnormal Pap test, positive HPV DNA test, genital warts, immunosuppression, breastfeeding).

Most adverse reactions to the quadrivalent HPV vaccine (redness, soreness, swelling at the injection site) usually resolve within 48 hours.¹⁴ More than 20 million doses of quadrivalent vaccine had been administered as of August 2008. Fewer than 6% of the 10,000 adverse events reported following vaccination were classified as “serious” (about half the average for other vaccines). The Centers for Disease Control and Prevention (CDC) considers the quadrivalent HPV vaccine to be as safe—or safer—than any other vaccine. However, an increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS), mostly among females aged 11 to 18 years, and some serious injuries have been reported. Thus, providers are advised to observe patients for 15 minutes postvaccination.

Use during pregnancy

Neither vaccine is licensed for use during pregnancy because of the lack of data in humans. The CDC’s Advisory Committee on Immunization Practices (ACIP) recommends postponement until after delivery. A registry has been established by the manufacturer of the quadrivalent vaccine for pregnant women who have started the series (800-986-8999). Pregnancy is not considered a cause for concern; the series may be resumed after pregnancy, regardless of delay duration.

Barriers to vaccination

Vaccine awareness differs by race, education, and income.¹⁵ Striking disparities in knowledge and awareness of HPV vaccines are reported among low-income minority groups. For example, 64% of respondents reported having heard of the HPV vaccine, but among Koreans the rate was only 42%. Only 28% of respondents overall said they had enough information to make an informed decision about HPV vaccination; Koreans (14%) and Chinese (17%) had the lowest rates compared with Latinas (31%) and blacks (56%). Mothers of unvaccinated girls cited barriers to HPV vaccination including concern about side effects, medical cost, and insufficient information to make an informed decision.

In another study conducted at 2 neighborhood-based safety net clinics operated by the Parkland Health & Hospital System in Dallas, results showed that only 39.7% of eligible patients received a recommendation by their healthcare provider to receive the HPV vaccine. Of those, 24.3% refused the vaccine.

Overall, 30% of patients received the first dose of the vaccine in the series but only 6.5% completed all 3 doses.

System changes

Based on these findings, the Parkland Health & Hospital System has adopted a new system to alert healthcare professionals if a patient is eligible for the HPV vaccine. An automatic telephone system reminds the patient to keep clinic appointments and to receive subsequent HPV vaccine doses.

As stated, barriers to vaccination also include patient concerns regarding cost and access to the vaccine, as well as fear that the vaccine will promote adolescent sexual behavior.¹⁶ However, teenage girls surveyed indicated no increased interest in risky sexual behaviors if they were vaccinated. Vaccination against HPV is now covered by many insurance plans; the vaccine is provided at no cost by various federal, state, and local government programs.

Education of healthcare professionals, interactive dialogue with patients specifically tailored to overcome misperceptions and barriers, and implementation of systems like those adopted by Parkland are important complementary components in reducing the incidence of cervical cancer, genital warts, and other HPV-related diseases in women of reproductive age. ■

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