
Course Objectives

The goal of this program is to provide nurses with information about the HPV vaccine for prevention of cervical cancer and related diseases. After studying the information presented here, you will be able to —

- Describe the criteria for which this vaccine has been approved for use in the United States.
 - Discuss the incidence of HPV and manifestations of infection.
 - Discuss education for the patient and parent/guardian about HPV and its sequelae.
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Vaccines eradicated smallpox worldwide and have significantly reduced several other deadly infectious diseases. Now a vaccine is available to reduce girls' and young women's risks of infection with the types of human papilloma virus (HPV) that cause most cervical cancers. This prophylactic vaccine presents an extraordinary opportunity for cervical cancer prevention.

Worldwide, cervical cancer is second only to breast cancer as the leading cause of death in women, with annual new cases exceeding 493,000 and 273,000 deaths every year.^{1,2,3} Cervical cancer was once one of the most common causes of cancer death for U.S. women but has declined in recent years. This is correlated to the use of the Pap smear, which changed the course of women's health.^{1,4} However, each day in the United States 10 women die of complications from cervical cancer. In 2007, the American Cancer Society (ACS) predicts there will be about 11,150 new cases of invasive cervical cancer in the U.S., with 3,670 deaths.¹ The new vaccine, Gardasil (quadrivalent human papillomavirus [types 6, 11, 16, 18] recombinant vaccine), is the first vaccine to prevent cervical cancer, precancerous genital lesions, and genital warts. It protects against the types of HPV that cause 70% of cervical cancers and 35% to 55% of vulvar and vaginal precancerous lesions (types 16 and 18) and the types that cause 90% of genital warts (6 and 11).^{5,6}

Who is eligible to receive Gardasil? What exactly does it prevent? How is it administered? Will insurance cover the costs? What counseling strategies should nurses offer patients?

Nurses have the unique opportunity to educate patients and parents about HPV and strategies for prevention, which now include a vaccine. The goal is to prevent the physical and psychological sequelae of future infections for both patients and their partners — and ultimately to prevent cervical cancer.

All-too-common HPV

HPV is the most common sexually transmitted infection in the United States and is easily transmitted through skin-to-skin contact.⁶ HPV-related anogenital diseases include cervical, penile, vulvar, vaginal, and anal precancerous lesions and cancers, as well as genital warts.⁶ More than 6.2 million new infections of HPV are estimated to occur annually, and 20 million people are infected at any given time.⁴ The estimated annual costs related to all aspects of HPV infection in the United States range from \$1.6 billion to \$6 billion, which does not include lost work time or wages — or account for emotional pain, anxiety, and disrupted relationships. HPV the second most costly sexually transmitted infection, after HIV infection.^{7,8}

About 75% of sexually active people aged 15 to 49 have been exposed to HPV or show evidence of previous exposure.^{9,10} The prevalence of HPV DNA in the immunocompetent female population ranges from 2.8% to 57%.^{9,11-13} Despite these numbers, many U.S. adults have never even heard of HPV.¹³

Teens at risk

Shortly after beginning sexual activity, about 50% of adolescents are exposed to HPV.¹⁴ Sexual intercourse is not necessary to acquire HPV infection; in one study, 7.8% of virginal females developed infection with nonpenetrative sexual practices, underscoring the importance of educating patients and parents or guardians of the risk.^{14,15} Condoms seem to provide some protection but do not cover the entire genital skin and cannot offer complete protection.¹⁵ HPV infections are generally asymptomatic, subclinical, and unrecognized. Many people do not know they are infected and can easily transmit this infection to others.^{6,15}

Many types

Over 100 types of HPV exist, with 40 associated with infection of the genital tract.^{9,15-17} Clinical manifestations of infection are varied and may include condyloma acuminatum (genital warts) on the internal and external genitalia and around the anus; Pap smear abnormalities; cervical, vulvar, anal, and penile precancerous lesion and cancers; and, rarely, respiratory papillomatosis in infants and children.^{9,15} Infection with HPV is necessary for the development of cervical cancer, but most women infected with HPV have a self-limited, transient infection and do not develop genital warts or significant cervical involvement.^{15,18} Most young women are able to clear the infection in one to two years (i.e., HPV DNA undetectable).^{10,15-18}

Although almost any type of HPV can cause an abnormal Pap smear, types 16, 18, 31, 33, 35, 39, 45, 51, and 52 are considered high risk, and persistent infection with these types is associated with most cervical and anal cancers.^{15,18} Low-risk types, 6, 11, 42, 43, and 44, are usually associated with benign lesions and rarely linked with squamous cell carcinoma.^{9,11,15}

The new vaccine

The FDA approved Gardasil in June 2006 for use in girls and young women between 9 and 26 years old.¹⁹ Ideally, girls or women will receive the vaccine before becoming sexually active since the vaccine is most effective in females who have not yet acquired HPV infection.

Gardasil is a noninfectious recombinant (contains no live virus) quadrivalent HPV vaccine approved for the prevention of diseases caused by genital HPV types 6, 11, 16, and 18. Types 16 and 18 cause most cervical cancer and precursors, cervical intraepithelial neoplasia grades 1,2, and 3; cervical adenocarcinoma in situ; vulvar intraepithelial neoplasia 2 and 3; and vaginal intraepithelial neoplasia 2 and 3. Types 6 and 11 cause most genital warts.^{5,7} The vaccine is prepared from highly purified virus-like particles that are noninfectious and nononcogenic. It allows the immune system to mount an antibody response to the HPV types in the vaccine if prior infection has not been established. The vaccine does not protect against HPV types it does not include.^{5,17}

Gardasil has been studied in the United States and other countries. Four clinical trials were conducted in over 21,000 girls and women, with a focus on young women ages 16 to 26 who had not been exposed to HPV types 6, 11, 16, and 18. Study participants received vaccine or placebo.^{5,7,17,18,20} The vaccine was shown to have 100% efficacy in preventing precancerous cervical lesions and nearly 100% efficacy in preventing precancerous vaginal and vulvar lesions and genital warts targeted by the vaccine's HPV types. Ninety-nine percent the participants developed antibodies after vaccination, with higher titers in younger participants.^{5,17,19,21} Studies of the vaccine's effectiveness in girls 9 to 15 showed an immune response similar to that found in the older study participants, indicating similar effectiveness in the younger group.^{5,17,21}

Women with ongoing or prior infection with one or several of the HPV types in the vaccine (those "partially exposed") still derived some benefit. Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types. The vaccine was of little benefit for women already infected with all the HPV types targeted by the vaccine (those "fully exposed," fewer than 1% of participants). The most benefit was achieved when the vaccine was given before infection. Although the study was not long enough to evaluate the development of cervical cancers, the prevention of precursors and antibody production are believed to be highly predictive of prevention of these cancers.¹⁷

On schedule

The vaccine should be delivered over six months in a series of three intramuscular injections. Patients receive the second injection two months after the first and the final injection six months after the first. The vaccine can be administered at the same visit as other vaccinations, such as tetanus, diphtheria, and pertussis (Tdap); tetanus and diphtheria (Td); meningococcal conjugate vaccine (MCV4); and hepatitis B vaccination.^{5,17}

Each 0.5 mL injection can be given IM in the deltoid or anterolateral thigh. No dilution or reconstitution is needed, and the vial should be well shaken before administration. A white cloudy appearance is normal after agitation. The vaccine should be stored in the refrigerator (36 F to 46 F) and protected from light. It should not be frozen.⁵ If the vaccine schedule is interrupted, the patient does not need to be "restarted." If the interruption occurs after the first dose, the second should be administered as soon as possible, and the second and third doses should be at least 12 weeks apart. If only the third dose is delayed, it should be administered as soon as possible.^{5,7}

The vaccine costs about \$120 per dose, or \$360 for the full series. Most large insurance groups are expected to cover the vaccine although there may be a lag time. Some states provide free or low-cost vaccines at health department clinics to people without insurance. The federal Vaccine for Children program (www.cdc.gov/nip/vfc) provides vaccines free to children and teens under 19, including the HPV vaccine. The program covers the uninsured, the Medicaid-eligible, American Indians, and Alaskan natives. Children and adolescents with private insurance that does not cover vaccination may also qualify.²¹

Federal law doesn't require girls or young women to receive the vaccine, and each state has its own school and daycare entry laws regarding vaccinations.¹⁹ Some state lawmakers have tried to mandate the vaccine, but such a move has proved controversial. Some parents and groups oppose making the vaccine a requirement.^{22,23}

The best candidates

Several groups have issued recommendations on Gardasil, including the Centers for Disease Control and Prevention (guided by the Advisory Committee on Immunization Practices [ACIP]; the American College of Obstetricians and Gynecologists (ACOG); and the ACS.

The ACIP recommends routine vaccination for 11- and 12-year-old girls. At the discretion of clinicians, high-risk girls as young as 9 can be considered candidates for vaccination.^{6,17,19,24}

Girls and women who may be sexually active could also benefit; therefore, the ACIP and ACOG recommend a "catch-up" vaccine for girls and women 13 to 26 years of age. Patients who have not been infected with any of the HPV types in the vaccine would get the full benefit. Those who have already been infected with one or more HPV types would still get protection from the vaccine types they have not yet acquired. Few young women are infected with all four vaccine HPV types.^{5,17,19}

No commercially available serology test exists to determine which of the four types of HPV, if any, a female has been infected with. No screening tests are recommended before vaccination, i.e., HPV DNA testing. Testing for HPV DNA reveals current, not past, infections.^{5,17}

ACOG's recommendations on the vaccine largely conform to the ACIP recommendations. In addition, ACOG recommends that girls have their first reproductive health visit between the ages of 13 and 15 and that all young women between 16 and 26 talk to their healthcare provider about HPV and the vaccine. Providers should review patients' vaccination status and offer the vaccine (or completion of the series) if necessary.²⁰

In January, the ACS released its recommendations, which are similar to the other groups', with one exception: It did not issue a recommendation on universal vaccination for women 19 to 26, citing "insufficient evidence" for its effectiveness in this group. The ACS does recommend vaccination of at-risk girls as young as 9, routine vaccination of 11- and 12-year-old girls, and "catch-up" vaccination for ages 13 to 18.⁴ The ACS also recommends women and their healthcare providers discuss the risk of previous exposure to HPV because the benefit of the vaccine is likely to diminish with an increased number of sex partners.⁴

Special populations

Special recommendations on Gardasil apply to certain populations:

Sexually active women: The ACIP recommends the vaccination of sexually active girls and women between the ages of 9 and 26. These patients should be counseled that the vaccine may be less effective for girls and women who have already been exposed to HPV.^{5,6,17,19}

Women with previous abnormal Pap tests: A woman with previously abnormal Pap tests, positive HPV DNA tests, or genital warts can receive the vaccine because rarely is she exposed to all four types of HPV in the vaccine. Women should understand that the vaccine will not treat current or ongoing infection, existing Pap smear abnormalities, HPV infection, or genital warts. Patients need continued management of these conditions.^{5,6,17,19}

Cervical cancer screening recommendations (see table) have not changed for girls and women receiving the vaccine because the vaccine does not cover all types of HPV that can cause cervical disease.

Women over 26: Research is under way on vaccination of women over 26; data are insufficient to recommend Gardasil for this age group.

Boys and men: Gardasil is not licensed for use among boys and men, and it is not known whether they would benefit. Boys aged 9 to 15 were included in the clinical trials, but no efficacy data are available. Studies are ongoing to determine whether the vaccine works in males.^{5,6,17,19} For information on a clinical trial, visit www.hpvvaccinetrials.com/secure/index.html.

Pregnant and lactating women: Although the HPV vaccine is classified as Category B (the lower-risk classification for drug safety during pregnancy), the vaccination of pregnant women is not recommended. Pregnancy outcomes of women who become pregnant during the vaccination schedule will be monitored. Exposure to Gardasil during pregnancy should be reported to the pregnancy vaccine registry ([800] 986-8999) maintained by the vaccine's manufacturer, and completion of the series should be delayed until after delivery.^{5,6,17} Lactating women can receive the vaccine although it's not known whether the quadrivalent

vaccine antigens or antibodies are excreted in breast milk; caution should be exercised.^{11,18,26}

The immunocompromised: The vaccine's efficacy may be diminished in females who are immunocompromised from illness or medications. But patients in this group may still receive the vaccine.^{5,6,17,19}

Is it safe?

In a study of about 11,000 participants ages 9 to 26, the vaccine was found to be safe and caused no serious adverse effects. Adverse effects included mild to moderate local reactions, such as pain, erythema, swelling, and tenderness at the site of injection. Fever and pruritus were also reported. Few participants (0.1%) discontinued the vaccine series because of adverse experiences.^{5,6,17,19}

The vaccine is not contraindicated with mild acute illness, such as diarrhea or mild upper respiratory infection with or without low-grade fever. Girls and women with moderate or severe acute illness should postpone getting the vaccine until the conditions improve.⁵

The CDC and manufacturer are monitoring the vaccine's safety. Adverse events may be reported to the CDC through the Vaccine Adverse Event Reporting System.⁵ For information, call (800) 822-7967 or visit www.vaers.hhs.gov. The manufacturer will monitor long-term safety as part of cancer registries in several countries.⁵

Contraindications to vaccination include acute illness or a history of hypersensitivity to yeast or any other vaccine component. Gardasil contains no thimerosal or mercury.^{6,5,17}

Studies indicate Gardasil is effective for at least five years, with no waning immunity. Beyond that, the duration of effectiveness is not clear, but the manufacturer will monitor the long-term effectiveness.¹⁹ Long-term data on duration of antibody response and clinical protection will be obtained via studies in the U.S. and other countries. Participants aged 9 to 15 will continue for up to 10 years, including evaluation of antibody titers and, as participants . Follow-up of vaccine trial reach age effectiveness.^{5,19 16}, evaluation of vaccine

It will take years to measure the impact of vaccination, but decreases in cervical cancer precursors and genital warts should be realized sooner. Studies will monitor these lesions and other HPV-related outcomes.¹⁴ The full effects of vaccination will probably not be seen until study participants reach the median age of cervical cancer diagnosis, which is 48.

What to tell patients

Regardless of whether girls and women receive the vaccine, they need to continue recommended cytology screenings.²⁴ Other patient education points include:^{5,6,15,24}

- The new vaccine does not prevent all types of HPV infection.
- Patients ideally should receive the vaccine before they begin sexual activity.
- Patients must complete the three-dose series to obtain the full benefits.
- The vaccine does not take the place of safer sex practices. Skin-to-skin contact is a risk; penile penetration need not take place to transmit HPV infection.
- The vaccine will not protect from other sexually transmitted infections nor prevent all cases of genital warts or Pap smear changes.
- No screening tests are recommended before vaccination.
- Most insurance companies will cover vaccination although there may be a lag time before coverage is approved.

This vaccine is a promising new approach for the prevention of HPV and the morbidity and mortality associated with HPV-related anogenital conditions. Another vaccine, one to prevent HPV types 16 and 18, called Cervarix, may receive FDA approval later this year.⁴ Clinicians need to identify girls and women at highest risk for cervical cancer and help make vaccines available for members of all socioeconomic, racial, and ethnic groups.

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