

Review Article

## Human Papillomaviruses (HPVs)—A Review for Diagnosis and Vaccination

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### Article History

Received: 08.01.2024

Accepted: 13.02.2024

Published: 14.02.2024

**Abstract:** Human papillomaviruses (HPVs) are a group of more than 150 related viruses. They are called papillomaviruses because some of them cause papillomas, which are more commonly known as warts. Some types of HPV only grow in skin, while others grow in mucous membranes such as the mouth, throat, or vagina. All types of HPV are spread by contact (touch). More than 40 types of HPV can be passed on through sexual contact. Most sexually active people are infected with one or more of these HPV types at some point in their lives. At least a dozen of these HPV types are known to cause cancer. While HPV infections are very common, cancer caused by HPV is not. Most people infected with HPV will not develop cancer-related to the infection. However, some people with long-lasting infections of high-risk HPV types are at risk of developing cancer. HPV infections of the mucous membranes can cause genital warts, but they usually have no symptoms. There are no effective medicines or other treatments for HPV, other than removing or destroying cells that are known to be infected. But in most people, the body's immune system controls the HPV infection or gets rid of it over time. To learn more, see HPV and HPV Testing.

**Keywords:** 150 related viruses, HPV, genital warts, mouth, throat, sexual contact.

## BACKGROUND

Human papillomavirus (HPV) causes significant morbidity and mortality in women and men. Human papillomavirus infection is associated with anogenital cancer (including cervical, vaginal, vulvar, penile, and anal) and oropharyngeal cancer (back of tongue, tonsil) (Number of Human Papillomavirus–Associated and Estimated Number of Human Papillomavirus–Attributable Cancer Cases per Year). Human papillomavirus also is associated with genital warts. Of the more than 150 HPV genotypes, 13 genotypes have been shown to cause cervical cancer [1](#). Despite the success of cervical cancer screening in the United States, each year cervical cancer is diagnosed in more than 13,000 women and nearly 4,000 die from the disease. Most cases of cervical cancer occur in women who have had inadequate screening. Approximately 90% of cases of genital warts are caused by HPV genotypes 6 and 11. Human papillomavirus-associated cancer in men is increasing in the United States, as are HPV-associated anal and vulvar cancer in women.

Despite the benefits of HPV vaccines, only 54% of women and 49% of men in the recommended age groups have received all recommended doses. Compared with many other countries, HPV vaccination rates in the United States are unacceptably low. According to the Centers for Disease Control and Prevention, if healthcare professionals increase HPV vaccination rates in eligible recipients to 80% in the target age range, it is estimated that an additional 53,000 cases of cervical cancer could be prevented during the lifetimes of those younger than 12.

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**Citation:** Anil Batta (2024). Human Papillomaviruses (HPVs)—A Review for Diagnosis and Vaccination. *South Asian Res J App Med Sci*, 6(1), 25-29. 25

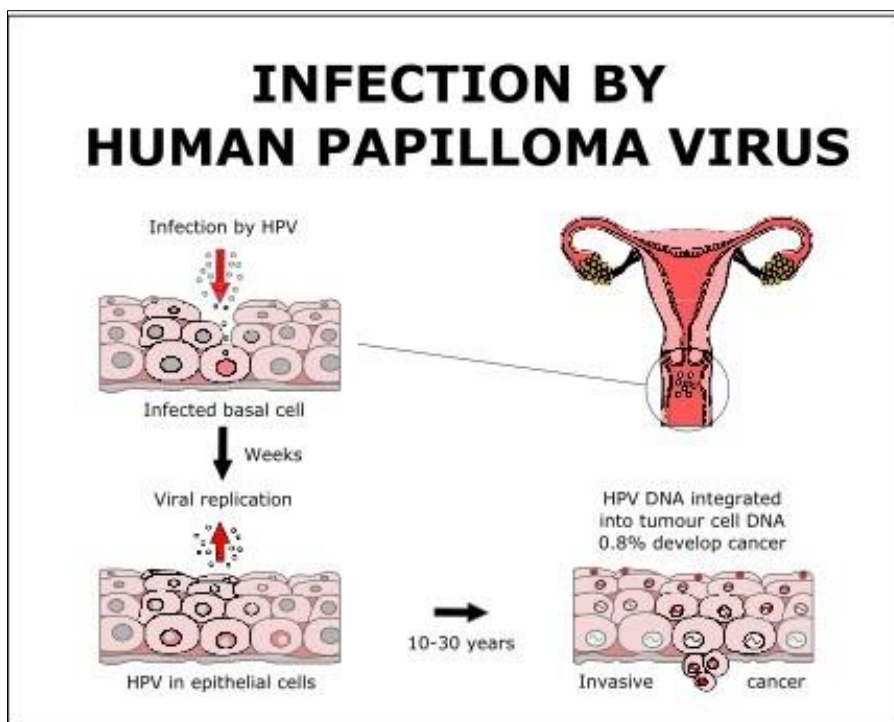


Fig. 1

### Human Papillomavirus Vaccination

The Advisory Committee on Immunization Practices and ACOG recommend routine HPV vaccination for girls and boys at the target age of 11–12 years (but it may be given from the age of 9 years) as part of the adolescent immunization platform to reduce the incidence of anogenital cancer and genital warts associated with HPV infection. Although obstetrician–gynecologists are not likely to care for many patients in the recommended HPV vaccination target population, they have the opportunity to provide catch-up vaccination for girls and women aged 13 and older and to discuss HPV vaccination with parents of children in the target age. Obstetrician–gynecologists should assess and vaccinate adolescent girls and young women with the HPV vaccine during the catch-up period (ages 13–26 years), regardless of sexual activity, prior exposure to HPV, or sexual orientation, if they were not vaccinated in the target age of 11–12 years. Further, obstetricians–gynecologists, and other healthcare professionals should educate parents in their decision-making regarding vaccinations for their daughters and sons. Finally, for some women aged 27–45 years who are previously unvaccinated, obstetrician–gynecologists and other health care professionals may use shared clinical decision-making regarding the HPV vaccination, considering the patient’s risk for acquisition of a new HPV infection and whether the HPV vaccine may provide benefit.

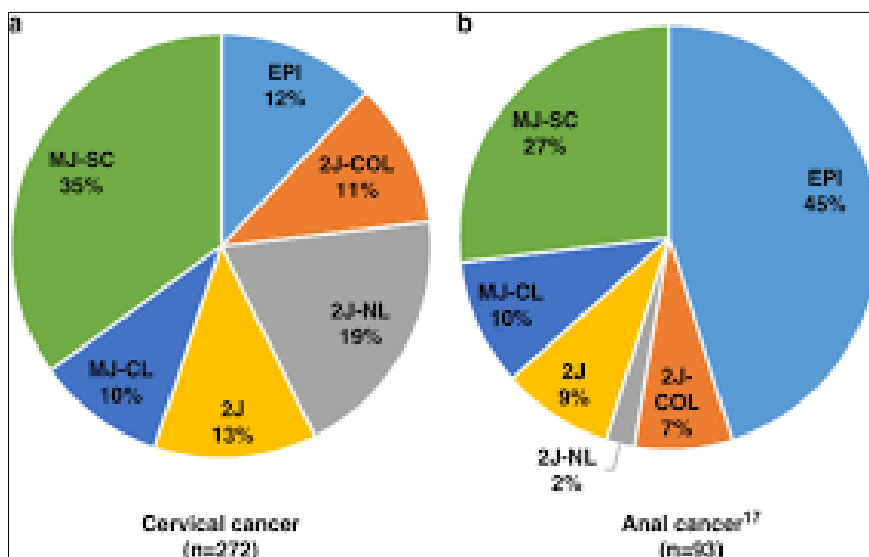


Fig. 2

## Human Papilloma Virus (HPV) Integration

### HPV Timing and Number of Doses

#### Children and Adolescents (9–14 years)

The target age for HPV vaccination is 11–12 years. For immunocompetent girls and boys who receive their first dose of HPV vaccine before 15 years of age, only two doses are needed because the immune response that develops at this age provides antibody levels equivalent to those in patients who receive three doses at the age of 15 years or older. The timing of the two doses is 0 (baseline) and 6–12 months. The 6-month interval between these two doses is critical for ensuring adequate immune titers and durability of protection. If the interval between the two doses is less than 5 months, a third dose is recommended. Studies show that two doses of HPV vaccine given 6 months apart in individuals aged 9–14 years resulted in antibody titers equal to those in individuals aged 15–26 years who were given three doses. Hence, only two doses, 6–12 months apart, are needed if HPV vaccination is initiated before 15 years of age in boys and girls.

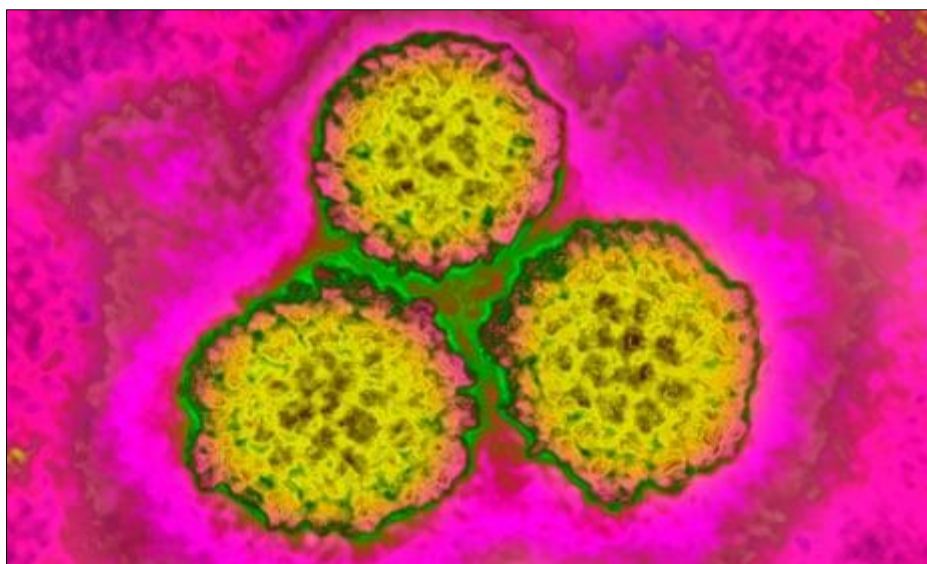


Fig. 3

#### It's Incredible': HPV Vaccine Saves Thousands of Women from Cervical Cancer

In addition to the ability to use two doses instead of three doses, earlier vaccination also is preferred because HPV vaccines are most effective when given before exposure and infection with HPV, which coincide with the onset of sexual activity. Statistics show that 20% of 9th graders and more than 55% of 12th graders have engaged in sexual intercourse. In Sweden, vaccine effectiveness in preventing genital warts was 93% among girls vaccinated between 10 years of age and 13 years of age compared with 48% and 21% if vaccinated at ages 20–22 years and 23–26 years, respectively. All of these findings underscore the importance of vaccination at the target age (11–12 years), which is before the onset of potential exposure in the vast majority of adolescents. Human papillomavirus vaccination is not associated with an earlier onset of sexual activity or increased incidence of sexually transmitted infections.

#### Teens and Adults (15–26 years)

If girls or boys receive their first dose at age 15 years or older, three doses are needed and given at 0 (baseline), 1–2 months after the first dose, and 6 months after the first dose. Unvaccinated women aged 26 years and younger should receive the HPV vaccine series regardless of sexual activity, prior exposure to HPV, or sexual orientation. Although the vaccine is less effective in previously infected individuals, it is expected that some benefit will be experienced because prior exposure to all nine vaccine types is highly unlikely. Vaccination is recommended for women through age 26 years even if the patient is tested for HPV DNA and the results are positive. Testing for HPV DNA is not recommended before vaccination.

#### Adults (27–45 years)

The HPV vaccine is now licensed in the United States for women and men through the age of 45 years. Although administration of the HPV vaccine is safe in patients aged 27–45 and can prevent new infections in women not previously exposed to the HPV-type protection generated by the vaccine, most women in this age range will have been exposed to HPV already. The overall public health benefit of HPV vaccination in women aged 27–45 years is markedly diminished compared with use in the target age range. Dally, the HPV vaccine should be given in early adolescence because vaccination is most effective before exposure to HPV through sexual activity. For some women aged 27–45 years who are previously unvaccinated, obstetrician–gynecologists and other health care professionals may use shared clinical decision-making regarding HPV vaccination, considering the patient's risk for acquisition of a new HPV infection and whether the HPV

vaccine may provide benefit. Those women aged 27–45 years who are most likely to benefit from vaccination are those at greater risk for HPV exposure or acquisition: younger women, women who are not in committed monogamous relationships, and women with recently diagnosed sexually transmitted infections. When counseling patients, clinicians should explain that women aged 27–45 years in long-term monogamous relationships are not likely at risk of acquiring a new HPV infection. It is not routinely recommended that these women receive the vaccine.

Clinicians should keep in mind that catch-up HPV vaccination is not recommended for all adults older than 26 years and that HPV vaccination does not need to be discussed with most adults older than 26 years. The American College of Obstetricians and Gynecologists does not recommend that an individual who received the quadrivalent HPV vaccine be revaccinated with 9-valent HPV vaccine, including those aged 27–45 years who previously completed some, but not all, of the vaccine series when they were younger. Further, having a new partner increases the risk of a new HPV infection at any age; however, with increasing age and more past exposure to HPV, it is less likely that vaccination provides benefit [7](#). Typically, routine vaccine recommendations are made for specific at-risk populations (identified either by age group or underlying health-related conditions) after considering vaccination cost, availability, and public health impact. The 9-valent HPV vaccine is costly and in short supply globally. In addition, routine HPV vaccination of all women aged 27–45 would be expected to have a very limited effect on the global fight to prevent cervical cancer. Thus, in this case, the shared clinical decision-making approach is recommended by the Centers for Disease Control and Human papillomavirus vaccination is not recommended during pregnancy; however, routine pregnancy testing is not recommended before vaccination. When the vaccine has been inadvertently administered to a pregnant woman, safety data are reassuring, although the data are somewhat limited because the vaccine is not used routinely in pregnancy. Patients and obstetrician–gynecologists or other health care professionals are encouraged to register women exposed to the 9-valent HPV vaccine around the time the pregnancy began or during pregnancy.

### Considerations for Special Populations

The presence of immunosuppression, like that experienced in patients with human immunodeficiency virus infection or organ transplantation, is not a contraindication to HPV vaccination. However, the immune response may be less robust in an immunocompromised patient. Thus, the three-dose schedule is recommended for immunocompromised women and men, adults and adolescents, even if younger than 15 years. In children with a history of sexual abuse or assault, the HPV vaccine should be given as early as possible, starting at age 9 years.

### Boosters, Revaccination, and Series Completion

The durability of the immune response (ie, how long protection lasts) of the HPV vaccine is being monitored in long-term studies, and currently, there is no indication for a booster vaccine. The vaccine series does not need to be restarted in the case of a delay in administration of the second or third dose, regardless of the amount of time of the delay. Further, revaccination with the 9-valent HPV vaccine in individuals who previously completed the three-dose series with the quadrivalent HPV vaccine or the bivalent HPV vaccine is not a routine recommendation. The bivalent and quadrivalent vaccines are extremely effective at preventing HPV-related disease.

If obstetrician–gynecologists or other health care professionals do not know or do not have the same HPV vaccine product previously administered, or are in settings that are transitioning to the 9-valent HPV vaccine, any available HPV vaccine product may be used to continue or complete the series for women for protection against HPV genotypes 16 and 18; the 9-valent HPV vaccine or the quadrivalent HPV vaccine may be used to continue or complete the series for men.

### Vaccine Safety

The 9-valent and quadrivalent vaccines had similar safety profiles, except that the 9-valent HPV vaccine had a higher rate of injection site swelling and erythema than the quadrivalent HPV vaccine, and the rate increased after each successive dose of the 9-valent HPV vaccine. The Vaccine Adverse Events Reporting System reports from December 2014 to December 2017 demonstrated no additional or unexpected safety concerns related to the 9-valent HPV vaccine. Available data demonstrate no safety concerns in individuals who were vaccinated with the 9-valent HPV vaccine after having been vaccinated with the quadrivalent HPV vaccine.

Anyone who has had a life-threatening allergic reaction to any component of the HPV vaccine, or a previous dose of the HPV vaccine, should not get the vaccine. Obstetricians–gynecologists and other health care professionals should assess patients for severe allergies, including but not limited to an allergy to yeast or prior HPV vaccine dose. An individual with a moderate or severe febrile illness should wait until the illness improves before receiving a vaccine. Obstetricians–gynecologists and other healthcare professionals should counsel patients to expect mild local discomfort after the vaccination and that such discomfort is not a cause for concern. Syncope and site reactions are common after this vaccine, but serious adverse events are rare. Adolescents should be observed for at least 15 minutes after vaccination because of the risk of fainting.

## Vaccine Efficacy

Human papillomavirus vaccines are among the most effective vaccines available worldwide, with unequivocal data demonstrating greater than 99% efficacy when administered to women who have not been exposed to that particular type of HPV. The HPV vaccine significantly reduces the incidence of anogenital cancer and genital warts in women and in men. Additionally, HPV vaccination may decrease the incidence of oropharyngeal cancer. In the United States, the prevalence of vaccine-type HPV infection decreased 71% among women aged 14–19 years between 2006 (when the quadrivalent HPV vaccine was introduced) and 2014. Additionally, a marked reduction in genital warts has occurred in countries with high HPV vaccine coverage.

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