

## Human Papillomavirus (HPV) Vaccines: Questions and Answers

### Key Points

- Human papillomaviruses (HPVs) are a group of more than 100 viruses. Certain types of HPV are the major cause of cervical cancer (see Questions 1 and 2).
- The U.S. Food and Drug Administration (FDA) approved Gardasil®, a vaccine that is highly effective in preventing infection with some types of HPV (see Question 3).
- Studies involving another HPV vaccine called Cervarix™ are under way (see Question 4).
- Complete vaccination has the potential to reduce cervical cancer deaths around the world by as much as two-thirds (see Question 7).
- The vaccines are proven to be effective only if given before an individual is infected with HPV (see Question 11).
- It is important for both vaccinated and unvaccinated women to continue to undergo cervical cancer screening (see Questions 4 and 14).

### 1. What are human papillomaviruses?

Human papillomaviruses (HPVs) are a group of more than 100 viruses. They are called papillomaviruses because certain types may cause warts, or papillomas, which are benign (noncancerous) tumors. The HPVs that cause the common warts that grow on hands and feet are different from those that cause growths in the throat or genital area. Some types of HPV are associated with certain types of cancer. These are called “high-risk” oncogenic or carcinogenic HPVs.

Of the more than 100 types of HPV, over 30 types can be passed from one person to another through sexual contact. Although HPVs are usually transmitted sexually, doctors cannot say for certain when infection occurred. About 6 million new genital HPV infections occur each year in the United States. Most HPV infections occur without any symptoms and go away without any treatment over the course of a few years. However,



HPV infection sometimes persists for many years, with or without causing detectable cell abnormalities.

## **2. Do HPV infections cause cancer?**

Infection with certain types of HPV is the major cause of cervical cancer. Almost all women will have HPV infections at some point, but very few will develop cervical cancer. The immune system of most women will usually suppress or eliminate HPVs. Only HPV infections that are persistent (do not go away over many years) can lead to cervical cancer. In 2007, more than 11,000 women in the United States will be diagnosed with this type of cancer and nearly 4,000 will die from it. Cervical cancer strikes nearly half a million women each year worldwide, claiming more than a quarter of a million lives. Studies have found that HPV infection is also a strong risk factor for oropharyngeal cancer (cancer that forms in tissues of the oropharynx, which is the middle part of the throat and includes the soft palate, the base of the tongue, and the tonsils) (1, 2). Studies also suggest that HPVs may play a role in cancers of the anus, vulva, vagina, and penis.

## **3. Can HPV infection be prevented?**

The surest way to eliminate risk for genital HPV infection is to refrain from any genital contact with another individual.

For those who choose to be sexually active, a long-term, mutually monogamous relationship with an uninfected partner is the strategy most likely to prevent genital HPV infection. However, it is difficult to determine whether a partner who has been sexually active in the past is currently infected.

It is not known how much protection condoms provide against HPV infection, because areas not covered by a condom can be infected by the virus. Although the effect of condoms in preventing HPV infection is unknown, condom use has been associated with a lower rate of cervical cancer, an HPV-associated disease.

In 2006, the U.S. Food and Drug Administration (FDA) approved Gardasil®, a vaccine that is highly effective in preventing persistent infection with HPV types 16 and 18, two “high-risk” HPVs that cause most (70 percent) cervical cancers, and types 6 and 11, which cause virtually all (90 percent) genital warts (3).

## **4. What preventive HPV vaccines are available?**

The Gardasil vaccine, which is produced by Merck & Co., Inc. (Merck), is called a quadrivalent vaccine because it protects against four HPV types: 6, 11, 16, and 18. Gardasil is given through a series of three injections into muscle tissue over a 6-month period.

Another promising vaccine, Cervarix™, is produced and is being tested by GlaxoSmithKline (GSK), but is not yet approved by the FDA. This vaccine is called a bivalent vaccine because it targets two HPV types: 16 and 18. This vaccine is also given in three doses over a 6-month period. Early findings have shown that Cervarix also protects against persistent infection with HPV 16 and 18.

Both Gardasil and Cervarix are based on technology developed in part by National Cancer Institute (NCI) scientists. NCI, a part of the National Institutes of Health, licensed the technology to two pharmaceutical companies—Merck and GSK—to develop HPV vaccines for widespread distribution.

Neither of these HPV vaccines has been proven to provide complete protection against persistent infection with other HPV types, some of which cause cervical cancer. Therefore, about 30 percent of cervical cancers and 10 percent of genital warts will not be prevented by these vaccines. In addition, the vaccines do not prevent other sexually transmitted diseases, nor do they treat HPV infection or cervical cancer.

Because the vaccines will not protect against all infections that cause cervical cancer, it is important for vaccinated women to continue to undergo cervical cancer screening as is recommended for women who have not been vaccinated.

## **5. How do HPV vaccines work?**

The HPV vaccines work like other immunizations that guard against viral infection. The investigators hypothesized that the HPV's unique surface components might create an antibody response that is capable of protecting the body against infection, and these components could be used to form the basis of a vaccine. These surface components can interact with one another to form virus-like particles (VLP) that are noninfectious and stimulate the immune system to produce antibodies that can prevent the complete papillomavirus from infecting cells. They are thought to protect primarily by causing the production of antibodies that prevent infection and the development of those cervical cell changes seen on Pap tests that may lead to cancer (4). Although these vaccines can help prevent HPV infection, it is not known if they can help eliminate existing cervical cell changes due to HPV's.

## **6. How effective are the HPV vaccines?**

Gardasil and Cervarix are highly effective in preventing infection with the types of HPV that they target. FDA-approved Gardasil prevented nearly 100 percent of the precancerous cervical cell changes caused by the types of HPV targeted by the vaccine for up to 4 years after vaccination. Two follow-up studies of Gardasil confirmed these findings. The studies also found the vaccine to be less effective in women who had previously been exposed to HPV types 16 and 18 (5, 6).

**7. Why are these vaccines important?**

Widespread vaccination has the potential to reduce cervical cancer deaths around the world by as much as two-thirds, if all women were to take the vaccine and if protection turns out to be long-term. In addition, the vaccines can reduce the need for medical care, biopsies, and invasive procedures associated with the follow-up from abnormal Pap tests, thus helping to reduce health care costs and anxieties related to abnormal Pap tests and follow-up procedures (4).

**8. How safe are the HPV vaccines?**

Before any vaccine is licensed, the FDA must determine that it is both safe and effective. Both Gardasil and Cervarix have been tested in thousands of people in the United States and many other countries. Thus far, no serious side effects have been noted. The most common problem has been brief soreness at the site of injection and other local injection site symptoms commonly experienced with other vaccines.

**9. How long do the vaccines protect against infection?**

The duration of immunity is not yet known. Research is being conducted to find out how long protection will last. Studies thus far have shown that Gardasil can provide protection against HPV 16 for 4 years. Studies with Cervarix showed protection from infection with both HPV 16 and 18 for more than 4 years.

**10. Will booster vaccinations be needed?**

Studies are under way to determine whether booster vaccinations (supplementary doses of a vaccine, usually smaller than the first dose, that are given to maintain immunity) are necessary.

**11. Who should get the Gardasil vaccine?**

Gardasil is proven to be effective only if given before infection with HPVs, so it is recommended that it be given before an individual is sexually active. The FDA's licensing decision includes information about the age and sex for recipients of the vaccine. The FDA approved Gardasil for use in females 9 to 26 years of age.

After a vaccine is licensed by the FDA, the Advisory Committee on Immunization Practices (ACIP) makes additional recommendations to the Secretary of the U.S. Department of Health and Human Services (DHHS) and the Director of the Centers for Disease Control and Prevention (CDC) on who should receive the vaccine, at what age, how often, the appropriate dose, and situations in which it should not be administered. ACIP is made up of 15 experts in fields associated with immunization. ACIP provides advice on the most effective ways to use vaccines to prevent diseases. ACIP recommends that Gardasil be given routinely to girls ages 11 to 12. The recommendations also allow for the vaccination of girls beginning at 9 years of age and

the vaccination of girls and women ages 13 to 26. More information about the ACIP recommendations for vaccination against HPVs can be found on the CDC Web site at <http://www.cdc.gov/od/oc/media/pressrel/r060629.htm> and <http://www.cdc.gov/mmwr/pdf/rr/rr5602.pdf> on the Internet.

In addition, states can decide whether or not to require vaccinations prior to enrollment in schools or child care. Each state makes this decision individually. Information about specific state vaccine decisions is available from the National Network for Immunization Information (NNii) Web site at <http://www.immunizationinfo.org/vaccineInfo/index.cfm#state> on the Internet.

**12. Should the vaccines be given to people who are already infected with HPV?**

Although the preventive vaccines currently under study have been found to be generally safe when given to women who are already infected with HPV, it is important for women to know that the vaccines protect against infection and provide maximum benefit for a woman who is vaccinated before she is sexually active. This is because these vaccines do not treat infections. For example, one recent study found that Cervarix was not effective in helping women who are already infected to clear the infection (7). However, women who have already been infected with one or more HPV types might still get protection from the vaccine types they have not acquired. Few young women are infected with all four HPV types in the vaccines. This possibility has not yet been formally studied.

It is not feasible to prescreen all women to see who has been exposed to the HPV types in the vaccines. At present, there is no generally available test to tell whether an individual has been exposed to HPV. The currently approved test only shows whether a woman has a current HPV infection and identifies the HPV type. It does not provide information on past infections. The decision to vaccinate or not, based on likelihood of prior exposure to these HPV types, is being discussed by ACIP and other advisory groups.

**13. Should women who already have cervical cell changes get the vaccine?**

Gardasil appears to be safe in women who have cervical abnormalities, but it is not known if the vaccine would help clear the abnormality. Women should talk with their health care providers about treatment for abnormal cervical cell changes.

**14. Do women who have been vaccinated still need to have Pap tests?**

Because Gardasil does not protect against all HPV types, Pap tests to screen for cervical cancer continue to be essential to detect cervical cancers and precancerous changes. In addition, Pap tests are critically important for women who have not been vaccinated or are already infected with HPV.

**15. How much will Gardasil cost, and will insurance pay for it?**

The retail price of the vaccine is \$120 per dose and \$360 for the full series. Individual or group insurance plans are subject to state laws. These laws generally establish coverage based on recommendations from the ACIP. Medicaid coverage is in accordance with the ACIP standard, and immunizations are a mandatory service under Medicaid for eligible individuals under age 21. Medicaid also includes the Vaccines for Children Program (VFC). This program provides immunization services for children 18 and under who are Medicaid eligible, uninsured, underinsured, and receiving immunizations through a Federally Qualified Health Center or Rural Health Clinic, or are Native American or Alaska Native.

**16. What research is being done with HPV?**

Researchers at NCI and elsewhere are studying how HPVs cause precancerous changes in normal cells and how these changes can be prevented. For example, a study is under way to determine if a vaccine can prevent infection with HPV types other than those targeted by Gardasil and Cervarix and to better understand the way the vaccines work (see Question 5) and factors that predict duration of protection. NCI is conducting a large clinical trial of the HPV vaccine manufactured by GSK in Costa Rica, where cervical cancer rates are high. This study is designed to obtain information about the vaccine's long-term safety and the extent and duration of protection. NCI is also collaborating with other researchers on therapeutic HPV vaccines that would prevent the development of cancer among women previously exposed to HPV. For use in the general population, the ideal vaccine strategy would combine a preventive and therapeutic vaccine.

Laboratory research has indicated that HPVs produce proteins known as E5, E6, and E7. These proteins interfere with the cell functions that normally prevent excessive growth. For example, HPV E6 interferes with the human protein p53, which is expressed by the p53 gene in all people and acts to keep tumors from growing. This research is being used to develop ways to interrupt the process by which HPV infection can lead to the growth of abnormal cells.

Researchers at the NCI and elsewhere are also studying what people know and understand about HPVs and cervical cancer, the best way to communicate to the public about the latest research results, and how doctors are talking with their patients about HPVs. This research will help to ensure that the public receives accurate information about HPVs that is easily understood and will facilitate access to appropriate tests for those who need them.

**17. How can people learn more about HPV infection?**

The following Federal Government agencies can provide more information about HPV infection:

The NCI's Digest Page on Human Papillomavirus (HPV) Vaccines for Cervical Cancer provides links to NCI materials about HPV vaccines as well as general information about HPVs, cancer vaccines, and cervical cancer. This Web site can be found at <http://www.cancer.gov/cancertopics/hpv-vaccines> on the Internet.

The National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health, supports research on HPV infection and offers printed materials. NIAID can be contacted at:

**Organization:** National Institute of Allergy and Infectious Diseases  
**Address:** Office of Communications and Public Liaison  
6610 Rockledge Drive, MSC 6612  
Bethesda, MD 20892-6612  
**Telephone:** 301-496-5717  
**TTY:** 1-800-877-8339  
**Internet Web site:** <http://www3.niaid.nih.gov>

The CDC-INFO Contact Center provides information on sexually transmitted infections, including HPVs, and how to prevent them. The center can be reached by calling toll-free 1-800-CDC-INFO (1-800-232-4636). Both English- and Spanish-speaking specialists are available 24 hours a day, 7 days a week, 365 days a year. Staff provide information about sexually transmitted diseases (STDs) and referrals to free or low-cost clinics nationwide. Free educational literature about sexually transmitted infections and prevention methods is also available. More information from the CDC about sexually transmitted infections is available at <http://www.cdc.gov/std> on the Internet.

The CDC's Division of STD Prevention Web site also has information about HPVs, including treatment guidelines and surveillance statistics. This Web site can be found at <http://www.cdc.gov/std/hpv/> on the Internet.

## Selected References

1. Division of STD Prevention. *Prevention of genital HPV infection and sequelae: Report of an external consultants' meeting*. Centers for Disease Control and Prevention, 1999.
2. D'Souza G, Kreimer A.R., Viscidi R., et al. Case-control study of human papillomavirus and oropharyngeal cancer. *New England Journal of Medicine* 2007; 356:1944-1956.
3. Koutsky LA, Ault KA, Wheeler CM, et al. A controlled trial of a human papillomavirus type 16 vaccine. *New England Journal of Medicine* 2002; 347(21):1645-1651.
4. Steinbrook R. The potential of human papillomavirus vaccines. *New England Journal of Medicine* 2006; 354(11):1109-1112.

5. Garland SM, Hernandez-Avila M, Wheeler CM, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *New England Journal of Medicine* 2007; 356(19):1928–1943.
6. The Future II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *New England Journal of Medicine* 2007; 356(19):1915–1927.
7. Hildesheim A, Herrero R, Wacholder S, et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: A randomized trial. *Journal of the American Medical Association* 2007; 298(7):743–753.

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**Related NCI materials and Web pages:**

- National Cancer Institute Fact Sheet 3.20, *Human Papillomaviruses and Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Risk/HPV>)
- National Cancer Institute Fact Sheet 5.16, *The Pap Test: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Detection/Pap-test>)
- Cervical Cancer Home Page (<http://www.cancer.gov/cancertopics/types/cervical/>)
- Digest Page on Human Papillomavirus (HPV) Vaccines for Cervical Cancer (<http://www.cancer.gov/cancertopics/hpv-vaccines>)
- *Understanding Cervical Changes: A Health Guide for Women* (<http://www.cancer.gov/cancertopics/understandingcervicalchanges>)
- *What You Need To Know About™ Cancer of the Cervix* (<http://www.cancer.gov/cancertopics/wyntk/cervix>)

**For more help, contact:**

**NCI's Cancer Information Service**

Telephone (toll-free): 1-800-4-CANCER (1-800-422-6237)

TTY (toll-free): 1-800-332-8615

*LiveHelp*® online chat: <https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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