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Human Papilloma Virus (HPV)

Human papillomaviruses (HPVs) are a group of more than 100 types of 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, which grow on hands and feet, are different from those that cause growths in the mouth and genital area. Some types of HPVs are associated with certain types of cancer.
Of the more than 100 types of HPVs, more than 30 types can be passed from one person to another through sexual contact. HPV infection is one of the most common sexually transmitted diseases (STDs). Some types of HPVs may cause warts to appear on or around the genitals or anus. Genital warts (technically known as condylomata acuminatum) are most commonly associated with two HPV types, numbers 6 and 11. Warts may appear within several weeks after sexual contact with a person who has HPV, or they may take months or years to appear; or they may never appear. HPVs also may cause flat, abnormal growths in the genital area and on the cervix (the lower part of the uterus that extends into the vagina). HPV infections often do not cause any symptoms.

HPVs and Cancer Risk
HPVs are now recognized as the major cause of cervical cancer. Studies also suggest that HPVs may play a role in cancers of the anus, vulva, vagina and penis, and some cancers of the oropharynx (the middle part of the throat that includes the soft palate, the base of the tongue, and the tonsils).
Some types of HPVs are referred to as "low-risk" viruses because they rarely develop into cancer; these include HPV-6 and HPV-11. HPV viruses that can lead to the development of cancer are referred to as "high-risk." Both high-risk and low-risk types of HPVs can cause the growth of abnormal cells, but generally only the high-risk types of HPVs may lead to cancer. Sexually transmitted, high-risk HPVs have been linked with cancer in both men and women; they include HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 and 69. These high-risk types of HPVs cause growths that are usually flat and nearly invisible, as compared with the warts caused by HPV-6 and HPV-11. It is important to note, however, that the majority of HPV infections go away on their own and do not cause any abnormal growths.

Precancerous Cervical Conditions
Abnormal cervical cells can be detected when a Pap test is done during a gynecologic exam. Various terms have been used to describe the abnormal cells that may be seen in Pap tests. In the Bethesda system (the major system used to report the results of Pap tests in the United States), precancerous conditions are divided into low-grade and high-grade squamous intraepithelial lesions (SILs). Squamous cells are thin, flat cells that cover internal and external surfaces of the body, including the tissue that forms the surface of the skin, the lining of the hollow organs of the body, and the passages of the genital, respiratory, and digestive tracts. Other terms sometimes used to describe these abnormal cells are cervical intraepithelial neoplasia (CIN) and dysplasia. Low-grade SILs (mild dysplasias) are a common condition, especially in young women. The majority of low-grade SILs return to normal over months to a few years. Sometimes, low-grade SILs can progress to high-grade SILs. High-grade SILs are not cancer, but they may eventually lead to cancer and should be treated by a doctor.

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Risk Factors for HPV and Cervical Cancer

Behaviors, such as beginning sexual intercourse at an early age (especially age 16 or younger) and having many sexual partners, increase the chance that a woman will develop an HPV infection in the cervix. Most HPV infections go away on their own without causing any type of abnormality. It is important to note that infection with high-risk HPV types may increase the chance that mild abnormalities will progress to more severe abnormalities or cervical cancer. Still, of the women who do develop abnormal cell changes with high-risk types of HPV, only a small percentage will develop cervical cancer if the abnormal cells are not removed. Studies suggest that whether a woman develops cervical cancer depends on a variety of factors acting together with high-risk HPVs. The factors that may increase the risk of cancer in women with HPV infection include smoking, having many children, and human immunodeficiency virus (HIV) infection.

Screening and Follow-up for Precancerous Cervical Conditions

Screening for cervical cancer consists of regular Pap tests for women who are sexually active or who have reached 18 years of age. If high-grade abnormal cell changes are found on a Pap test, colposcopy and biopsy of any abnormal areas are recommended. (Colposcopy is a procedure in which a lighted magnifying instrument called a colposcope is used to examine the vagina and cervix. Biopsy is the removal of a small piece of tissue for diagnosis.) If low-grade changes are found, repeat Pap tests or colposcopy may be recommended.

Treatment of HPV Infection

Although there is currently no medical cure to eliminate a papillomavirus infection, the SILs and warts these viruses cause can be treated. Methods used to treat SILs include cryosurgery (freezing that destroys tissue), laser treatment (surgery using a high-intensity light), LEEP (loop electrosurgical excision procedure, the removal of tissue using a hot wire loop), as well as conventional surgery. Similar treatments may be used for external genital warts. In addition, three powerful chemicals (podophyllin, bichloroacetic acid, and trichloroacetic acid) will destroy external genital warts when applied directly to them. Podofilox (podophyllotoxin) can be applied topically either as a liquid or a gel to external genital warts. Imiquimod cream has also been approved to treat external warts. Also, fluorouracil cream (sometimes called 5-FU) may be used to treat the warts. Some doctors use interferon alpha to treat warts that have recurred after being removed by traditional means. Imiquimod and interferon alpha work by stimulating the immune (defense) system to fight the virus.

Current Research

The ASCUS/LSIL Triage Study (ALTS), a major study organized and funded by the National Cancer Institute (NCI), is currently evaluating different management approaches for women with mildly abnormal Pap test results. (ASCUS and LSIL are acronyms for the two mild abnormalities detected by Pap tests. ASCUS stands for atypical squamous cells of undetermined significance and LSIL for low-grade squamous intraepithelial lesions.) Preliminary findings from the ALTS study suggest that testing cervical samples for HPV is an excellent option to help direct follow-up for women with an ASCUS Pap test result. Repeat Pap tests or direct referral to colposcopy remain options for the follow-up of ASCUS results. The final study results, which are expected to be published in about three years, will help women and their doctors decide what course of action to take when mild abnormalities show up on Pap tests.

Researchers at NCI and elsewhere are studying how HPVs cause precancerous changes in normal cells and how these changes can be prevented. They are using HPVs grown in the laboratory to find ways to prevent the infection

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and its associated disease and to create vaccines against the viruses. Vaccines for certain papillomaviruses, such as HPV-16 and HPV-18, are being studied in clinical trials (research studies with people) for cervical cancer; similar trials for other types of cancer are planned.

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. p53 is present 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 growth of abnormal cells and, eventually, cancer.

(Adapted from the American College of Obstetricians and Gynecologists handout)