



Understanding Anogenital HPV: Infections, Diseases, and Vaccines in Male and Female Patients

Learning Objectives

After completing this activity, participants should be better able to:

- Provide education and counseling to patients about human papillomavirus (HPV) infections, diseases, and vaccines
- Diagnose genital warts
- Treat patients with genital warts appropriately with the full range of both patient- and provider-administered therapeutic options
- Recognize that HPV is ubiquitous among sexually active people
- Offer vaccinations as appropriate to prevent this common sexually transmitted disease (STD) that can cause cancer and other genital tract diseases

Introduction

Human papillomaviruses (HPV) are a group of double-stranded DNA viruses, over 100 types of which have been identified. Approximately 40 HPV types are associated with anogenital infections that are primarily acquired through sexual contact, particularly through vaginal and anal intercourse.^{1,2} While uncommon, genital tract HPV is sometimes detected in persons with no reported history of sexual contact, although the exact route of transmission in such cases is not clear.³ Additionally, recent data suggest that performing oral sex is a risk factor for oropharyngeal HPV infection.⁴

Anogenital HPV infections are nearly ubiquitous among sexually active individuals: data indicate that up to 80% of sexually active persons experience 1 or more anogenital HPV infections.⁵ The incidence of anogenital HPV infection in the United States is estimated to exceed 6 million cases per year.²

Persistent infection of oncogenic HPV types is the cause of squamous cell cancers of the cervix, penis, vagina, vulva, and anus, as well as other squamous intraepithelial lesions (SILs) that often are precursors to cancer.⁶ Increasingly, data confirm a link between one oncogenic HPV type, HPV16, and a subset of squamous cell carcinomas of the pharynx.⁷ Non-oncogenic (“low-risk” types) rarely cause cancer, but 2 low-risk types—HPV6 and 11—cause approximately 90% of genital warts.⁸ Occasionally, the same types cause oral and laryngeal warts and, rarely, recurrent respiratory papillomatosis.

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The last 15 years have brought new screening technologies, vaccines, treatment options, and updated guidelines that have revolutionized the diagnosis and management of patients with sexually transmitted HPV and related diseases, especially within 2 prime areas of focus: cervical cancer and genital warts.

Cervical Cancer

The most clinically significant diseases associated with HPV are cervical precancers and cancers. Most cervical cancers originate in the cervical squamocolumnar junction (the transformation zone), and ~85% are squamous cell carcinomas, with the remainder being largely glandular cell adenocarcinomas.⁹

There are approximately 1.4 million cases of mild cervical abnormalities (usually classified as low-grade SIL, or LSIL) in the United States each year.¹⁰ The estimated incidences of moderate to severe precancerous lesions (high-grade SIL, or HSIL) and cervical cancers are 500,000 and 12,700, respectively.^{9,11} Mortality from cervical cancer exceeds 4000 annually.⁹ Cervical cancer tends to be diagnosed in women in the prime of life, with many cases among women in their 30s, and a median age of 48 years when diagnosed.¹²

Globally, cervical cancer is most often detected in impoverished women, with 85% of cases occurring in the developing world where cost and health infrastructures have not permitted routine Pap testing.¹³ As a result, cervical cancer—always the result of sexually acquired HPV infection—remains the fourth most common cause of cancer-related death in women worldwide.¹³ Wealthy nations are not immune to this, either: in the United States, racial and socioeconomic disparities in rates of cervical cancer are observed, with women of color far more likely to be diagnosed with cervical cancer and diagnosed at more advanced stages, when the prognosis is poorer.^{11,12}

The Role of HPV

Persistent infection with an oncogenic HPV type is the direct cause of cervical cancer and its precursors, and over 99% of cervical cancers contain the DNA of 1 or more high-risk HPV types.²

HPV infections become established in basal epithelium. Localized within these cells, the virus avoids immediate detection by the immune system and utilizes the life cycle of the cell to proliferate.¹⁴ Mild cervical lesions and often precancerous ones typically develop in the months subsequent to HPV infection, while overt cancer usually is delayed many years.^{15,16} According to the American Cancer Society, in the United States cervical cancer is most often detected in women who have either never had a Pap test, or in whom 5 or more years have lapsed since their last screening.⁹

HPV16 and HPV18, respectively, are the most oncogenic genotypes and are found in 50% of moderate or severe premalignant cervical lesions, and in about 70% of invasive cervical tumors.¹⁷

Cervical Cancer Screening

Widely available Pap testing in the United States has led to tremendous reductions in the incidence and mortality of cervical cancer. Once the leading cause of cancer death among women in the United States, annual mortality per 100,000 women decreased from 5.55 in 1975 to 2.42 in 2007.¹⁸ In the same interval, incidence dropped from 14.79 cases per 100,000 women to 6.58.¹⁹

A significant change to cervical cancer screening technology occurred in the 1990s with licensure of the first HPV DNA test to detect oncogenic types of the virus in clinical settings. Testing for high-risk HPV is useful as a tool to triage patients who are at greater risk for cervical precancers/cancer and are likely to benefit from colposcopy.²⁰ Several such tests are now on the market in the United States and, in conjunction with cervical cytology, are approved for use in specific screening situations:

- (1) As a follow-up test if the Pap result is unclear or borderline abnormal, as when atypical squamous cells of undetermined significance (ASC-US) are observed.²⁰
- (2) As a routine cervical cancer screening test in combination with a Pap test in women at or over 30 years of age (rather than just having the Pap test alone). Most anogenital HPV infections are acquired from the teen years through age 26; most infections resolve spontaneously, and most cancers result from long-persisting high-risk HPV infection.^{21,22} Therefore, HPV infections in women over 30 years of age are more likely to be a persistent infection and more likely to be associated with premalignant neoplasia or cancer, whereas most infections in younger women are transient and less likely to progress.²³ Thus, the combination test (Pap test plus HPV testing) can increase the effectiveness of detecting any problems early on, especially in women ≥ 30 years of age.²⁰

Additionally, HPV16/18 genotyping tests have been available since 2009. These tests check directly for HPV types 16 and 18, which together are responsible for approximately 70% of cervical cancers.¹⁷ The potential advantage to genotyping may be to allow women who are high-risk HPV-positive, but negative for the more aggressive HPV16/18 types, to avoid immediate referral to colposcopy in favor of repeating Pap and HPV tests in 12 months.²⁴

Onset of Cervical Cancer Screening and Intervals for Repeat Testing

Most HPV infections acquired in teens and young adults clear up spontaneously, including those caused by high-risk types.²¹ It is now recognized that screening young women soon after onset of sexual activity results in large numbers of HPV infections and Pap test abnormalities that can safely be ignored, but that historically have resulted in unnecessary treatment accompanied by preventable anxiety and stress. Accordingly, the American College of Obstetricians and Gynecologists (ACOG) recommends cervical cancer screening not be initiated until age 21, regardless of age of first intercourse.²³

Recommended screening intervals depend largely on a woman's age and health history. ACOG recommends that women aged 21 to 29 years be screened every 2 years. From age 30 years and older, women can be screened at 3-year intervals, providing they have at least 3 normal, consecutive Pap tests and are immunocompetent and have no past history of cervical cancer or precancerous lesions. The screening interval should also be 3 years when women 30 years and older are screened with a cytology/HPV test combination and both tests are normal.²³

Recent guidelines and recommendations call for more conservative approaches to screening adolescent women for cervical cancer and managing those under age 21 with abnormal cervical cancer screening tests.

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Figure 1. Cervical erosions due to CIN 1. Source: CDC Public Health Image Library.

Managing Women With Abnormal Screening Tests

The evolution of screening technology has led to more nuanced management of women with abnormal cervical cancer tests. Clinical management is influenced primarily by the severity of the abnormality detected, but is also influenced by the patient's oncogenic HPV status and age. Follow-up may involve simply monitoring the patient with repeat Pap and/or HPV tests at frequent intervals, colposcopy, or a diagnostic excisional procedure.²⁰

Two systems of terminology are used to describe cervical cellular abnormalities, sometimes confusing to patients and providers alike: one applies to cervical cytology (ie, Pap test results), and the other exclusively to biopsy results.

The Bethesda system for cytology results includes ASC-US, LSIL, HSIL, and cancer, as well as an intermediate stage between ASC-US and LSIL, called atypical squamous cells suspicious for high-grade changes (ASC-H). The terminology when biopsied tissue is examined microscopically is based on cervical intraepithelial neoplasia (CIN).²⁵ CIN 1, usually equivalent to LSIL, is mildly abnormal (Figure 1); most cases resolve without treatment and do not progress to cancer. CIN 2 and CIN 3, often difficult to distinguish from one another and hence combined as CIN 2/3, is more advanced and usually equivalent to HSIL. CIN 2/3 includes carcinoma *in situ*, the earliest stage of cancer. Table 1 summarizes both systems and corresponding management guidelines published by the American Society for Colposcopy and Cervical Pathology (ASCCP).



Figure 2. Penile warts. Source: CDC Public Health Image Library.

Genital Warts

At any point in time, around 1% of the US population is estimated to have anogenital warts.²⁶ Overall, it has been estimated that 6% of US residents report a history of genital warts.⁵ Warts vary in appearance: most lesions are external and can be raised (ie, “cauliflower” formation) or flat, single or multiple, small or large. Typically, warts are asymptomatic but sometimes itch, bleed, or cause irritation.⁵ Warts can be found in multiple anogenital sites including the vulva, vagina, cervix (less common), penis (including under the foreskin in uncircumcised males)(Figure 2), scrotum, urethra, anus, and perineum.²⁷ The groin and lower abdomen can be involved, but this is uncommon.

Visual inspection by an experienced clinician usually is sufficient for accurate diagnosis. However, biopsy sometimes is required if the visual diagnosis is uncertain or for lesions that are uncharacteristic in appearance (eg, pigmented or ulcerated).²⁷ The currently available HPV tests are not approved or recommended for diagnosis of warts. Application of acetic acid, which has been promoted as a diagnostic aid by highlighting the wart-involved tissues, is neither sensitive nor specific, and is not recommended.²⁶

Table 1.

Reporting Terminology and Management Guidelines for Cervical Abnormalities^{20,25}

Bethesda System ²⁵	CIN System ²⁵	What the Report Means	ASCCP Guidelines ²⁰
Within normal limits		No abnormal cells, negative.	Continue with normal screening.
ASC-US		Cells that do not look entirely normal, but are not definitely abnormal. Most women with this Pap are normal, but a few will have HSIL.	Several options are available: 1) Repeat Pap every 6 to 12 months until 2 Paps are normal. Any abnormal repeat Pap requires colposcopy. 2) Refer immediately for colposcopy (recommended with ASC-H). 3) Perform an HPV test. Women positive for HPV should have colposcopy. Women negative for HPV are likely normal and may safely be followed by Pap tests at 12 months.
ASC-H		ASC-H: similar to ASC-US reading, except the cells are abnormal in a way that means HSIL (see below) cannot be excluded.	<i>Women age 20 and under with a Pap reading of ASC-US should be managed with repeat Pap tests at 12 months.</i>
LSIL	CIN 1	Mildly abnormal cells. Changes are most often due to HPV. Most women with this reading have mild cervical dysplasia, but some (10%-30%) may have more abnormal changes (HSIL, moderate or severe dysplasia, CIN 2/3).	Colposcopy (and possibly biopsy) is the preferred follow-up option rather than repeat Pap testing or HPV testing. Most women with LSIL are positive for HPV and would not benefit as much from this test as women with ASC-US. <i>Women age 20 and under with a Pap reading of ASC-US should be managed with repeat Pap tests at 12 months.</i>
HSIL	CIN 2/3	Moderately to severely abnormal cells. Changes are almost always due to HPV. Most women with this Pap reading will have more abnormal findings on the cervix (HSIL, moderate or severe dysplasia, CIN 2/3).	Colposcopy and biopsy with treatment determined by biopsy results OR immediate diagnostic excisional procedure, such as loop electrosurgical excision procedure (LEEP) (this option is NOT acceptable for women age 20 and under).
Cancer	Invasive squamous cell carcinoma; invasive glandular cell (adeno-) carcinoma	The Pap will be read as suspicious for cancer if the cells are so abnormal as to indicate cancer. The possibility of cancer is high enough to require immediate evaluation.	Colposcopy and biopsy. Refer for a specialized evaluation and treatment as needed.

HPV

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Treatment of Genital Warts

The goal of treatment is to eliminate warts. While it is possible that doing so helps prevent transmission by reducing the HPV viral load, this is speculative. No available therapy has been shown to cure HPV infection or reduce the risk of transmission, in part because the virus typically is also present in skin or mucosa that appears normal, without visible warts.

There are numerous therapeutic options for genital warts, including both provider- and patient-directed treatments. No single approach to treating warts is universally superior. The selection of a treatment option is influenced by factors that include size of warts, anatomic site, number and distribution of lesions, as well as provider and patient preferences.²⁷ Warts eventually regress naturally, sometimes within a few months, so a “watchful waiting” approach occasionally is appropriate. Recurrences are not uncommon, especially in the first 3 months following therapy. With the exception of surgery or other forms of direct destruction or removal, all recommended treatments are only 60% to 80% effective in ablating warts, and none are more effective than others in preventing recurrence.⁵ When a particular treatment is not effective or if warts regrow within 3 months, a different modality should be used. Some experts routinely use combination therapy, such as initial cryotherapy followed by a patient-applied treatment.

Treatment regimens for genital warts are outlined below. Information is summarized from the Centers for Disease Control and Prevention (CDC) 2010 STD treatment guidelines, except where noted.²⁷

Patient-Applied Prescription Treatments

- ▶ Podofilox (Condylox®): Podofilox is a purified derivative of podophyllin resin, and is available as a topical solution or gel.²⁸ Podofilox is applied to genital warts twice a day for 3 days, followed by 4 days of no therapy. This cycle can be repeated up to 4 times. Podofilox use is contraindicated during pregnancy.
- ▶ Imiquimod (Zyclara® 3.75% cream or Aldara® 5% cream): Imiquimod is a topical immune response modifier. Zyclara is applied once daily for up to 8 weeks.²⁹ Aldara can be used 3 times a week (ie, every other night before bed) for up to 16 weeks. Patients should wash their hands after applying imiquimod, and the cream should be washed off approximately 8 hours after application.²⁹ Imiquimod is substantially less effective against warts on dry surfaces than those on moist surfaces (eg, the vulva or under the foreskin). Imiquimod has not been studied in pregnant women.²⁹
- ▶ Sinecatechins (Veregen®): This extract from green tea is a recently approved treatment for genital warts. Available as an ointment, sinecatechins is applied to warts 3 times daily for as long as 16 weeks. Side effects include local irritation including rashes, itching, burning, and ulceration. Sinecatechins is contraindicated during pregnancy.

Provider-Applied Treatments

- ▶ Trichloroacetic acid (TCA) and bichloroacetic acid (BCA): Highly caustic acid compounds that are quite effective in rapidly ablating warts, but occasionally cause short but intense pain.⁵ Care must be taken to prevent contact with normal skin, and some providers protect the area around warts with petroleum jelly.³⁰ Treatment can be repeated weekly, if necessary. Safe to use during pregnancy.²⁸

- Cryotherapy: Freezing tissue (usually liquid nitrogen), which directly destroys wart tissue by thermal injury. After treatment, the outer layer of tissue forms a blister and separates from deeper layers. Cryotherapy is appropriate for both external and internal warts, and for lesions on the cervix. Although pain at the application site is common (and, occasionally, scarring occurs where the treatment was applied to the wart), cryotherapy is generally well tolerated.³⁰
- Podophyllin resin: Efficacy of podophyllin may vary in part because of poor and variable concentrations of the active compounds.⁵ Podophyllin is applied directly to warts, allowed to dry, and the patient is instructed to wash the compound away after 1 to 4 hours; treatment typically is applied weekly. Podophyllin is limited to external use and is contraindicated during pregnancy.
- Surgery and related methods: For appropriately trained clinicians, direct surgical removal may be appropriate, especially for certain locations (eg, intraurethral warts) or particularly large warts. Other related methods also requiring sophisticated training include laser therapy and electrocautery.

HPV Vaccines

The past decade has seen the development of 2 vaccines to prevent HPV infection. In 2006, a quadrivalent HPV vaccine (Gardasil®) was approved by the Food and Drug Administration (FDA) for use in the United States, followed in 2009 with the approval of a bivalent vaccine (Cervarix®). Both are nearly 100% protective against HPV16 and 18, which cause about 70% of cervical cancers; the quadrivalent vaccine also is nearly 100% effective in preventing infection with HPV6 and 11, which together are responsible for nearly all instances of genital warts.³¹ The characteristics of the 2 vaccines are listed in Table 2.

Vaccine Indications

The quadrivalent vaccine is approved for use in the United States in girls and young women aged 9 to 26 years for the prevention of cervical, vulvar, and vaginal cancers and precancers caused by HPV types 16 and 18.² The vaccine is also licensed for use in both males and females aged 9 to 26 years to prevent genital warts (condyloma acuminata) associated with HPV types 6 and 11, and anal cancers, precancers, and dysplasia caused by HPV types 6, 11, 16, and 18.^{32,33} The bivalent vaccine is approved for use in females aged 10 to 25 years for the prevention of cervical cancers and precancers associated with HPV16 and HPV18.³¹ The emphasis on preteen and teenage groups is intended to maximize protection, because many HPV infections are acquired soon after onset of sexual activity.²¹

Table 2.

Characteristics of Bivalent and Quadrivalent Prophylactic HPV Vaccines³¹

	Quadrivalent	Bivalent
Vaccine composition	20 µg HPV6 40 µg HPV11 40 µg HPV16 20 µg HPV18	20 µg HPV16 20 µg HPV18
Manufacturing process	Bread yeast (Saccharomyces)	Insect cells (baculovirus)
Adjuvant	225 µg aluminum hydroxyphosphate sulfate	500 µg aluminum hydroxide with 50 µg 3-deacylated monophosphoryl lipid A (AS04)
Preservatives	None	None

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While the full duration of protection is not known, both vaccines produce antibody titer levels greater than the natural HPV infection, which appears to be protective.^{2,34} With both of the currently available vaccines, immunogenicity and efficacy against diseases related to vaccine types of HPV have been demonstrated for at least 5 years, but further research will be required to determine whether or not there is a role for booster immunization after that time.^{34,35}

Efficacy

Both the quadrivalent and bivalent HPV vaccines are highly efficacious against significant cervical diseases (CIN 2/3 and adenocarcinoma in situ [AIS]) related to the HPV types they help build immunity against (Table 3). The efficacy figures shown reflect the per-protocol analysis of those who received all 3 doses of the respective HPV vaccine and were seronegative and HPV DNA–negative at baseline.

The quadrivalent vaccine is also effective in preventing vaginal intraepithelial neoplasia (VaIN), vulvar intraepithelial neoplasia (VIN), genital warts, and anal intraepithelial neoplasia (AIN) caused by the 4 covered HPV types, as summarized in Table 4. The bivalent vaccine has not been studied in relation to these particular outcomes, but likely is similarly effective against lesions like VIN, VaIN, and AIN caused by HPV16 or 18. However, the bivalent vaccine provides no significant protection against genital warts or other lesions caused by HPV6 or 11.

The quadrivalent vaccine is efficacious in males in preventing AIN and genital warts (Table 5).

HPV Vaccine Recommendations

The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination with either the quadrivalent or bivalent vaccine for all females aged 11 and 12, with catch-up for those aged 13 to 26

Table 3.

Bivalent and Quadrivalent HPV Vaccines: Efficacy in Females for Prevention of CIN and AIS³¹

Vaccine/End Point/HPV Type	Vaccine Efficacy (confidence intervals)
Bivalent vaccine	
CIN 2/3 or AIS	
HPV16 and/or 18	92.9 (79.9-98.3)
HPV16	95.7 (82.9-99.6)
HPV18	86.7 (39.7-98.7)
Quadrivalent vaccine	
CIN 2/3 or AIS	
HPV16 and/or 18	98.2 (93.3-99.8)
HPV16	97.6 (91.1-99.7)
HPV18	100.0 (86.6-100.0)

Table 4.

Quadrivalent HPV Vaccine: Efficacy in Females for Prevention of Vulvar VIN, VaIN, and Genital Warts³¹

Vaccine/End Point/HPV Type	Vaccine Efficacy (confidence intervals)
VIN 2/3 or VaIN 2/3	
HPV6, 11, 16, and/or 18	100.0 (82.6-100.0)
HPV16	100.0 (76.5-100.0)
HPV18	100.0 (<0-100.0)
Genital warts	
HPV6 and/or 11	99.0 (96.2-99.9)

years who have not previously been vaccinated.

For males, ACIP guidelines call for permissive use (at the discretion of healthcare providers) of the quadrivalent vaccine to reduce the risk of genital warts.

ACIP has yet to issue recommendations on use of the quadrivalent vaccine for the prevention of anal cancers and precancers. Current ACIP guidelines for HPV vaccines may be reviewed at <http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv>.

HPV vaccines are recommended for use in adolescents for several reasons:

- The cervical transformation zone in girls and young women is particularly vulnerable to HPV infection³⁶
- HPV infection is most prevalent in females under 25 years of age; hence the obvious value of vaccinating against the virus prior to sexual debut²²
- Immunogenicity is higher in younger girls (9 to 15 years), as compared with 16 to 26 year olds²

Dosing schedules with the vaccines are at 0, 1 to 2 months, and 6 months. Minimum intervals are 4 weeks between doses 1 and 2, 12 weeks between doses 2 and 3, and 24 weeks between the first and third doses. It is likely that variations in scheduled doses do not seriously impair the vaccines' effectiveness; therefore, the vaccine series should not be restarted if the schedule is interrupted.

Safety and Side Effects

In studies with tens of thousands of males and females worldwide, HPV vaccines have been shown to be effective, safe, and well tolerated. Adverse events (AEs) are no greater in those receiving an HPV vaccine than background rates of other vaccines for this age group. There is no difference between vaccine and control groups in serious AEs, new onset chronic disease and autoimmune disorders, or deaths.³⁴

The most common local symptoms reported are pain, swelling, and redness at the injection site. The most common general symptoms include headache, nausea, and fever.³¹ To avoid syncope (fainting), patients should sit or lie down for 15 minutes after the vaccine has been administered and before leaving the office or clinic.³¹

Contraindications include^{31,34}:

- Pregnancy
- Those with a severe allergic reaction (eg, anaphylaxis) after previous dose
- With the quadrivalent vaccine, a history of immediate hypersensitivity to yeast
- Prefilled syringes of the bivalent vaccine are contraindicated for those with anaphylactic latex allergy (single-dose vials of the bivalent vaccine have no latex)

Table 5.

Quadrivalent HPV Vaccine: Efficacy in Males for Prevention of AIN and Genital Warts^{32,33}

Vaccine/End Point/HPV Type	Vaccine Efficacy (confidence intervals)
Quadrivalent vaccine	
AIN 1/2/3	
HPV6, 11, 16, and 18	77.5 (39.6-93.3)
AIN 2/3	
HPV6, 11, 16, and 18	74.9 (8.8-95.4)
Genital warts	
HPV6, 11, 16, and 18	89.3 (65.3-97.9)

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While there is no evidence of impaired fertility/harm to the fetus in animal studies, HPV vaccines are contraindicated during pregnancy.³⁴ If a woman becomes pregnant after initiation of vaccination, the remainder of the series should be delayed until postpartum. Lactating women can receive the HPV vaccine.³¹

Psychosocial Aspects of HPV

A diagnosis of HPV and/or a related disease often carries a large psychosocial burden. Research indicates that having genital warts, for example, is associated with lower quality of life scores. Anxiety, depression, pain, and discomfort have been shown to be greater for patients with warts.³⁷ Specific complaints include frustration with treatment regimens, feelings of shame, and worries about relationships.³⁸

Clinicians should be mindful that HPV diagnosis carries shame and stigma. In the 2010 STD treatment guidelines, the CDC recommends sharing the following information in patient counseling, as appropriate²⁷:

- Anogenital HPV infection is ubiquitous among those who are sexually active, with a majority of men and women likely to have an HPV infection at some point; having genital HPV is a

normal and expected consequence of human sexuality

- The risk of HPV is similar in everyone, regardless of number of sex partners and history of other STDs; for this reason, Pap tests are equally important for all women, regardless of sexual history
- The virus is usually harmless, causes no warts, abnormal Pap test, or any other apparent abnormality, and in most cases will clear naturally over a few months; however, it is difficult to determine how long an individual may be able to transmit the virus to new partners
- Cancer is an uncommon outcome of infection, even with the oncogenic HPV genotypes

For many patients the psychosocial impact of HPV is significant. Patient counseling should address common causes of anxiety, including partner communication.

- HPV diagnosed within a relationship should not be construed as an indication of infidelity
- It is rarely possible to determine when and from whom any particular HPV infection was acquired; in general, it is not important to identify the source of infection
- HPV does not impact fertility and is unlikely to prevent a pregnant woman from having a normal vaginal delivery
- Latex condoms are moderately effective at reducing the risk of HPV transmission for any single exposure; however, because condoms do not cover all vulnerable skin areas, they do not completely eliminate the risk, and many consistent condom users—perhaps most of them—acquire genital HPV somewhere along the line
- Sex partners of persons with diagnosed HPV infections do not need to be professionally examined and do not need to seek medical care unless and until they notice an abnormality, such as genital warts
- Immunization should be routine for all sexually active young persons in order to prevent infection with the most troublesome HPV types



CASE: Counseling for an 18-Year-Old Female Patient and Her Partner

Presentation

An 18-year-old female patient comes to see you and brings her reluctant 19-year-old boyfriend. She is increasingly concerned about a cluster of slightly raised bumps on the coronal sulcus of his penis. He says they have been there for as long as he can remember. The couple occasionally uses condoms and does not utilize any other type of contraception.

Her first intercourse was at age 15, and she has had 3 male sex partners prior to her current monogamous partnership for the last 6 months. Eighteen months earlier, she had warts detected around the anus, which were treated with cryotherapy and resolved.

The boyfriend's sexual debut was at age 13 or 14, and he recalls a history of at least 4 female sex partners and 1 male sex partner. He is reluctant to describe further details of his past sexual relationships, but confirms his partner's history of mutual monogamy in the last 6 months. He recalls having a human immunodeficiency virus (HIV) test a few years ago but never returned for results.

Physical Examination

The male's penile symptoms appear to be hirsutoid papillomas (pearly penile papules), a normal anatomic variant unrelated to HPV.

Laboratory Findings

The female's most recent cervical cytology (10 months ago at another clinic) detected mildly abnormal lesions (LSIL). She has had no follow up.

Clinical Decision Point

Given the recent abnormal Pap test, what would be a reasonable next step in managing the female patient?

- Offer a Pap test now
- Offer a Pap test in 12 months
- Add HPV testing with any Pap test
- Combine colposcopy with the Pap test

Comment

While the recommendation is to delay cervical cancer screening until age 21, adolescent females are still sometimes given Pap tests. Given that HPV infections and related abnormalities typically regress naturally in young women, those younger than age 21 with borderline or mildly abnormal cervical cytology results should be followed with repeat Pap testing at 12 months rather than an immediate referral for colposcopy. If no high-grade disease (HSIL) is detected with the follow-up Pap test, repeat cytology again in 12 months.²⁰

HPV testing is not recommended, given her age and the fact that a positive test result would not alter clinical management.

Additionally, the couple may benefit from:

- Birth control and STD counseling
- HIV testing
- Pregnancy and chlamydia tests for the female—annual chlamydia testing is recommended for all sexually active females under age 25²⁷

Clinical Decision Point

To which of these 2 patients could you offer an HPV vaccine?

- Female only
- Male only
- Both male and female
- Neither

Comment

Both males and females can be vaccinated against HPV, although this is impacted in part by the type of HPV vaccine you offer. The bivalent vaccine is only approved for use in females aged 10 to 25 years, whereas the quadrivalent vaccine is approved for males and females aged 9 to 26 years. Regulatory standards do not prevent immunization in persons outside the approved population groups, although in some instances medical insurance may not cover such use.

The female patient has a previous diagnosis of 2 HPV-associated diseases (abnormal cervical cytology and anal warts), but by receiving either HPV vaccine, she benefits from protection against the HPV types covered by the vaccine to which she may not have been exposed. It is statistically unlikely that she has already been infected by all the HPV types covered by the 2 vaccines.

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Frequently Asked Questions About HPV

Q. Why aren't males tested for HPV?

A. Collecting an adequate specimen from male genital skin is trickier than when sampling moist tissue from the cervix. Also, keep in mind that even with women, HPV testing has limited use strictly as a specific component of cervical cancer screening: it is not used as a general means of checking infection status, for example. The high prevalence of HPV among sexually active men, coupled with the infrequency of diseases in men attributed to oncogenic HPV genotypes, means that knowing a male's HPV status will seldom have any clinical utility.

Q. Should a partner of someone diagnosed with HPV be examined?

A. It is not commonly recommended that someone be examined when their partner is diagnosed with HPV, unless they notice any symptoms. Since the vast majority of HPV are asymptomatic, and testing for the virus has limitations as previously discussed, there is typically no need for a partner to be evaluated.

Q. Within an established relationship, when only 1 partner is diagnosed with any HPV disease, what potential impact can that have on their sex life?

A. The couple almost certainly will share an HPV infection, which could have been present indefinitely prior to any diseases being diagnosed. There seems little point for those in ongoing relationships to be fearful over continuing to be sexually active. Condom use probably is not necessary in relationships where HPV is shared. That HPV may be present for an extended interval before diagnosis of either the virus or related diseases is especially important for patients to understand, given that HPV detected within an established relationship often raises questions about sexual fidelity.

Q. What about disclosing an HPV diagnosis to future partners?

A. No data indicate that disclosing an HPV diagnosis to a future partner prevents transmission. There seems to be little rationale that supports having someone discuss with a new partner a resolved HPV infection that no longer is causing problems.

Q. Are HPV infections acquired from fomites?

A. Most experts believe HPV transmission from inanimate objects is rare. Certainly there is no reason for concern over the types of interactions people commonly think about when asking this question, such as using a bathroom, tub or shower, or a swimming pool or hot tub. Sex toys pose a theoretical risk, so clean sex toys thoroughly after each use and do not share, especially when lesions are present.