

Ready-to-Use

STD Curriculum for Clinical Educators

Genital Human Papillomavirus (HPV) Module

Target Audience - Faculty in clinical education programs, including those programs that train advanced practice nurses, physician assistants, and physicians

Contents - The following resources are provided in this module:

- **Faculty Notes** (Microsoft Word and Adobe Acrobat formats) - Includes notes that correspond to the slide presentation, a case study with discussion points, and test questions with answers
- **Slide Presentation** (Microsoft PowerPoint and Adobe Acrobat formats)
- **Student Handouts**
 - **Case Study** (Microsoft Word format)
 - **Test Questions** (Microsoft Word format)
 - **Slides Handout** (Adobe Acrobat format)
 - **Resources** (Microsoft Word format)

Suggested Time Allowance - The approximate time needed to present this module is 60-90 minutes.

These materials were developed by the Program and Training Branch, Division of STD Prevention, CDC. They are Based on the curriculum developed by the National Network of STD/HIV Prevention Training Centers (NNPTC) which includes recommendations from the 2010 CDC STD Treatment Guidelines

Information on the NNPTC can be accessed at:
<http://www.nnptc.org/>
The 2010 CDC STD Treatment Guidelines can be accessed at:
<http://www.cdc.gov/std/treatment/>



March 2013

Centers for Disease Control and Prevention
Division of STD Prevention
Program and Training Branch

[Slide 1]

Genital Human Papillomavirus (HPV) Infection

[Slide 2]

Learning Objectives

Upon completion of this content, the learner will be able to;

- Describe the epidemiology of genital HPV infection in the U.S.;
- Describe the pathogenesis of genital HPV;
- Discuss the clinical manifestations of genital HPV infection;
- Identify methods used to diagnose genital warts and cervical cellular abnormalities;
- Discuss the CDC-recommended treatment regimens for genital warts;
- Summarize appropriate prevention counseling messages for genital HPV infection;
- Describe public health measures for the prevention of genital HPV infection.

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Lessons

- I. Epidemiology of genital HPV infection in the U.S.
- II. Pathogenesis
- III. Clinical manifestations and sequelae
- IV. Diagnosis of genital warts and cervical cellular abnormalities
- V. Patient management
- VI. Patient counseling and education
- VII. Partner management and public health measures

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Lesson I: Epidemiology of Genital HPV Infection in the U.S.

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Introduction

- Genital HPV infection is one of the most common STDs.
- More than 40 types of HPV are sexually transmitted and can infect the genital tract.

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Introduction

- Genital HPV types are divided into two groups, based on their association with cancer.
 - Infections with low-risk types (nononcogenic types) can cause genital warts and benign or low-grade cellular changes (e.g. mild Pap test abnormalities), but are not associated with increased risk of cancer.
 - Infections with high-risk types (oncogenic types) can cause cervical dysplasia (both low-grade and high-grade cervical cellular changes), moderate to severe Pap test abnormalities, and, in rare cases, cancers of the cervix. In addition, these types of HPV infection have been associated with cancers of the vulva, vagina, anus, penis, and oropharynx (back of the throat including base of tongue and tonsils).
- Most genital HPV infections, whether caused by low-risk or high-risk types, are

transient (go away on their own), asymptomatic, and have no clinical consequences.

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Incidence in the U.S.

- incidence and prevalence estimates on genital HPV infection are limited by the fact that
 - Genital HPV infection is not nationally reportable, as most infections are brief, asymptomatic, or subclinical (have no visible clinical manifestations), and have no clinical consequences.
- Incidence in the U.S.
 - The estimated annual incidence of sexually-transmitted HPV infection is 14.1 million cases.
 - An estimated \$1.7 billion spent annually in direct medical costs to treat conditions associated with genital HPV infection (e.g. warts, cervical dysplasia, cancer).

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Prevalence in the U.S.

- It is estimated that 100% of sexually active men and women acquire genital HPV infection at some point in their lives.
- An estimated 79 million women aged 14–59 years are infected with HPV, with the highest prevalence in those aged 20–24 years.

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Incidence and Prevalence of HPV-associated Diseases

- Genital warts
 - Prevalence estimates for genital warts are relatively imprecise.
 - Limited data suggest that annual incidence may be as high as 100 per 100,000 population.
 - An estimated 1.4 million (1% of the sexually active U.S. population) may be affected at any one time.
- Cervical cancer
 - Rates of cervical cancer have fallen by approximately 75% since the introduction of Pap screening programs.
 - From 2004 to 2008, the age-standardized incidence of cervical cancer for all races in the U.S. was 8.1 per 100,000 women.
 - Approximately 12,200 new cases in 2010
 - Approximately 4,210 deaths in 2010

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Age-Adjusted Delay-Adjusted Incidence of Cervical Cancer by Race: 1975–2009

Graph: Age-Adjusted Delay-Adjusted Incidence of Cervical Cancer by Race: 1975–2009. Although cervical cancer rates continue to decline for both white and black women in the U.S., black women continue to suffer a disproportionate burden of disease.

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Transmission of Genital HPV

- Predominantly associated with sexual activity, including vaginal and anal intercourse, oral sex, a nonpenetrative sexual activity (genital-genital contact). Likely requires contact with viable HPV and microtrauma to skin or mucous membranes to establish infection.
- Can occur from asymptomatic and subclinically infected patients.
- Treatment of warts or cervical cellular abnormalities may reduce, but likely does not eliminate infectiousness.
- Transmission by fomites (inanimate objects such as environmental surfaces and clothing) has never been documented.
- Rarely, genital HPV infection with low-risk types is transmitted from mother to newborn during delivery and can cause respiratory tract warts in the child, known as juvenile-onset recurrent respiratory papillomatosis (JORRP).
 - Estimates of the incidence rate of JORRP are imprecise; they range from 0.4–1.2 cases per 100,000 children.
 - The preventive value of cesarean delivery is unknown and, thus, should not be performed solely to prevent transmission of genital HPV to the newborn.
- Condoms might reduce the risk for HPV-associated diseases (e.g. genital warts and cervical cancer). Consistent and correct condom use also may reduce the risk for genital HPV acquisition. HPV infection can occur in areas that are not covered or protected by a condom (e.g., scrotum, vulva, or perianus)

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Risk Factors for Women

- Risk factors consistently associated with genital HPV infection in women
 - Young age
 - Sexual behavior
 - Risk increases with increasing number of recent and lifetime sex partners
 - Early age of first sexual intercourse
 - Sexual behavior of sex partners
 - Risk increases for women whose sex partners have had multiple sex partners.
 - Immune status
 - HPV is more likely to be detected in immunosuppressed women (e.g., HIV-infected persons, women on dialysis, and after kidney transplant).
 - Risk factors less consistently associated with genital HPV infection in women
 - Smoking
 - Oral contraceptive use
 - Nutritional factors (poor nutrition)
 - Lack of circumcision of male partners

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Risk Factors for Men

- Greater number of recent and lifetime sex partners
- Being uncircumcised increases risk

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Lesson II: Pathogenesis

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Virology

Key features of HPV

- Double-stranded DNA virus that belongs to the *Papillomaviridae* family
- Small, nonenveloped virions
- Over 100 characterized types
- Number of recognized HPV types is gradually increasing as more types are identified and genetically characterized.
- Genital types have specific affinity for genital skin and mucosa.
- Very limited animal models and no widely available system for *in vitro* cultivation
- Infection is identified by the detection of HPV DNA.

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HPV Genotyping System

- Types are distinguished by different DNA sequences (>10% difference), primarily those which express L1 capsid (surface) protein.
- Genital HPV types are generally characterized in terms of their oncogenic potential (ability to cause cancer).
 - **Low-risk types (nononcogenic types)**, e.g. HPV types 6 and 11
 - Associated with genital warts and benign or low-grade cervical cellular changes (associated with mild Pap test abnormalities)
 - Most genital warts are caused by HPV types 6 and 11.
 - Recurrent respiratory papillomatosis, a rare condition, is usually associated with HPV types 6 and 11.
 - **High-risk types (oncogenic types)**, e.g. HPV types 16 and 18
 - Associated with low-grade cervical cellular changes, high-grade cervical cellular changes (mild, moderate, and severe Pap test abnormalities), and cervical dysplasia, and, in rare cases, cancers of the cervix. In addition, HPV infection has also been associated with cancers of the vulva, vagina, anus, penis, and oropharynx (back of throat including base of tongue and tonsils).
 - HPV types 16 and 18 account for 70% of cervical cancers.
 - Most women infected with high-risk HPV types have normal Pap test results and never develop cervical cellular changes or cervical cancer.

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Pathology

- Genital HPV infects the basal cell layer of stratified squamous epithelium and stimulates cellular proliferation.
- Affected cells display a broad spectrum of changes, ranging from benign hyperplasia, to dysplasia, to invasive carcinoma.

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Natural History of HPV

- Most infections are transient, asymptomatic or subclinical, and have no clinical

consequences in immunocompetent individuals.

- Time to development of clinical manifestations is unclear, but most likely
 - 3 weeks to months for genital warts,
 - Several months to years for cervical cellular abnormalities, and
 - Decades for cervical cancers.
 - The median duration of new cervical infections (measured by detection of HPV DNA) is 8 months, but varies.
 - 70% of new infections clear within 1 year.
 - 90% of new infections clear within 2 years.
 - The gradual development of an effective immune response is thought to be the likely mechanism for HPV DNA clearance.

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Natural History of HPV (continued)

- Persistent HPV infection is infection that is not cleared by the immune system and is characterized by persistently detectable type-specific HPV DNA.
 - Persistent oncogenic HPV infection is the most important risk factor for precancerous (high-grade) cervical cellular changes and cervical cancer.
 - Factors associated with persistent infection include
 - Older age,
 - Certain HPV types, and
 - Immune suppression.
 - It is unclear whether HPV infection that becomes nondetectable at mucosal surfaces has completely cleared or remains latent in basal cells with potential for later reactivation.

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Lesson III: Clinical Manifestations and Sequelae

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HPV-associated cancers United States, 2004-2008

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Clinical Manifestations and Sequelae

- In most cases genital HPV infection is transient and has no clinical manifestations or sequelae.
- Clinical manifestations of genital HPV infection include
 - Genital warts,
 - Cervical cellular abnormalities detected by Pap tests,
 - Some anogenital squamous cell cancers,
 - Some oropharyngeal cancers, and
 - Recurrent respiratory papillomatosis
- The two most common clinically significant manifestations of genital HPV infection are
 - Genital warts that are visualized without magnification, and
 - Cervical cellular abnormalities that are detected by Pap test screening.

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Genital Warts—Appearance

Genital warts have four morphologic types.

- Condylomata acuminata
 - Cauliflower-like appearance
 - Skin-colored, pink, or hyperpigmented
 - May be keratotic on skin; generally nonkeratinized on mucosal surfaces.
- Smooth papules
 - Usually dome-shaped and skin-colored
- Flat papules
 - Macular to slightly raised
 - Flesh-colored, with smooth surface
 - More commonly found on internal structures (i.e., cervix), but also occur on external genitalia
- Keratotic warts
 - Thick horny layer resembling common warts or seborrheic keratosis

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Genital Warts—Location

- Genital warts appear most commonly in areas of coital friction.
 - Men—penis, scrotum, urethral meatus, and perianal area
 - Women—introitus, vulva, perineum, and perianal area
- Less common genital warts sites—
 - Cervix and vaginal walls in women
 - Pubic area, upper thighs, or crural folds in men and women
- Perianal warts do not necessarily imply anal intercourse, but may be secondary to autoinoculation, sexual activity other than intercourse, or spread from a nearby genital wart site.
- Intra-anal warts are seen predominantly in patients who have had receptive anal intercourse.
- HPV types causing genital warts can occasionally cause lesions on oral, upper respiratory, upper GI, and ocular locations.
- Patients with visible warts are frequently infected simultaneously with multiple HPV types.

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Genital Warts—Symptoms

- Genital warts usually cause no symptoms.
- Vulvar warts can cause dyspareunia, pruritis, and burning discomfort.
- Penile warts occasionally cause pruritis.
- Urethral meatal warts occasionally cause hematuria or impairment of urinary stream.
- Vaginal warts occasionally cause discharge, bleeding, or obstruction of birth canal (due to increased wart growth in pregnancy).
- Perianal and intra-anal warts occasionally cause pain, bleeding on defecation, or pruritis.

- Most patients have fewer than ten genital warts, with total wart area of 0.5–1.0 cm².

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Genital Warts—Duration and Transmission

- Genital warts may regress spontaneously or persist with or without proliferation.
- Frequency of spontaneous regression is unclear. A few studies indicate a regression rate of 10%–30% within three months.
- Persistence of infection occurs, but frequency and duration is unknown.
- Recurrences after treatment are common (20%–50% recurrence rate at 3–6 months).
- Few studies on transmission, but available information suggests that genital warts are highly transmissible. Partners should be told about diagnosis and appropriate prevention strategies should be used.
 - Abstinence until warts are gone
 - Consistent and correct condom use

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Genital Warts and High-Risk HPV

High-risk HPV types occasionally are found in visible genital warts and have been associated with external genital (i.e., vulvar, penile, and anal) squamous intraepithelial lesions (i.e., squamous cell carcinoma *in situ*, Bowenoid papulosis, Erythroplasia of Queyrat, or Bowen's disease of the genitalia).

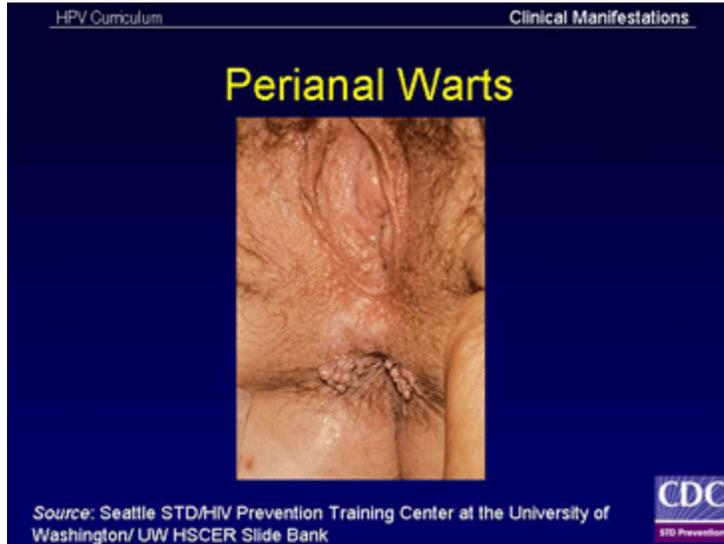
- The most commonly recognized clinical manifestation of external genital squamous intraepithelial lesions (SIL) is Bowenoid papulosis, dome-shaped or flat papules that are often hyperpigmented.
- These lesions can sometimes be clinically indistinguishable from genital warts, but on biopsy demonstrate high-grade SIL.
- They occur in what is usually macroscopically normal epithelium and mucosal tissue.

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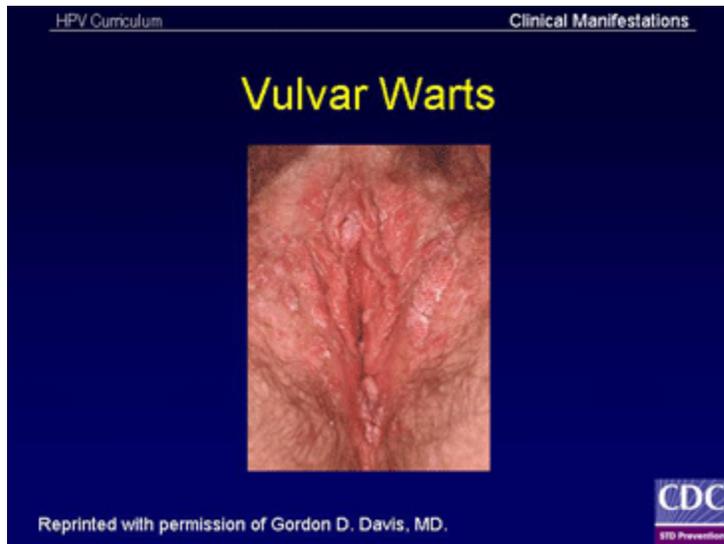
Genital Warts in Preadolescent Children

- May be due to sexual abuse although this condition is not diagnostic for sexual abuse. Their appearance should prompt an evaluation by a clinician.
- May also result from vertical transmission, transmission of nongenital HPV types to genital surface, and possibly fomite transmission, although fomite transmission has never been documented.

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Perianal Warts



[Slide 30]
Vulvar Warts



[Slide 31]
Penile Warts



[Slide 32]
Intrameatal Wart



[Slide 33]
Cervical Cellular Abnormalities

- Cervical cellular abnormalities are usually subclinical.
 - Lesions associated with these abnormalities can be detected by Pap test or colposcopy, with or without biopsy.
 - Magnification by colposcopy can enhance detection of cervical cellular abnormalities; biopsy and histology are used to confirm and stage cervical intraepithelial neoplasia.
 - Cervical cellular abnormalities are usually caused by HPV
- Low gradecervical cellular abnormalities attributed to HPV often regress spontaneously without treatment.

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Classification of Cervical Cellular Abnormalities

- The [2001 Bethesda System](#) classifies cervical cellular abnormalities into one of several categories.
 - Atypical squamous cells (ASC) are cells that do not appear to be completely normal.
 - ASC–US—atypical squamous cells of undetermined significance. These changes are often caused by HPV infection. ASC–US changes are usually mild abnormalities.
 - ASC–H—atypical squamous cells cannot exclude a high-grade squamous intraepithelial lesion. ASC–H changes are more likely to be associated with precancerous abnormalities than ASC-US.
 - Low-grade squamous intraepithelial lesion (LSIL) generally are transient, and caused by infection with HPV.
 - High-grade squamous intraepithelial lesion (HSIL) generally are changes due to persistent infection with a high-risk HPV type. Lesions associated with HSIL may have a higher risk for progression to cervical cancer.
 - See the American Society for Colposcopy and Cervical Pathology Consensus Guidelines on Management of Women with Cytological Abnormalities for more information on the Bethesda Classification System.
<http://www.asccp.org/consensus/cytological.shtml>

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Anogenital Squamous Cell Cancers

- HPV infection is causally associated with cervical cancer and other anogenital squamous cell cancers (e.g., anal, penile, vulvar, vaginal).
- Over 99% of cervical cancers have HPV DNA detected within the tumor.
- Persistent infection with a high-risk HPV type (e.g., infection which is not cleared by the immune system and which is characterized by persistently detectable HPV DNA) is necessary, but not sufficient, for the development of cervical cancer.
 - There have been other risk factors that increase risk of developing cervical cancer precursors and cervical cancer, including immune suppression, specific HPV types, and possibly others.

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Recurrent Respiratory Papillomatosis

- HPV infections in infants and children may present as laryngeal papillomatosis, also known as juvenile onset recurrent respiratory papillomatosis (JORRP).
- Respiratory papillomatosis is a rare condition, usually associated with HPV types 6 and 11.

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Lesson IV: Diagnosis of Genital Warts and Cervical Cellular Abnormalities

[Slides 39-40]

Diagnosis of Genital Warts

- Diagnosis is usually made by visual inspection with bright light. Usually the diagnosis is made clinically.
- Diagnosis can be confirmed by biopsy.
 - Consider biopsy when
 - Diagnosis is uncertain;
 - Patient is immunocompromised;
 - Warts are pigmented, indurated, or fixed;
 - Lesions do not respond or worsen with standard treatment; or
 - There is persistent ulceration or bleeding.
 - Use of type-specific HPV DNA tests for routine diagnosis and management of genital warts is not recommended.
 - Application of acetic acid to evaluate external genitalia is not routinely recommended, but may be useful in some settings.
- Low specificity (many false positives)
- Acetowhitening will occur at sites of prior trauma or inflammation.
 - External genital warts are not an indication for cervical colposcopy or increased frequency of Pap test screening (assuming patient is receiving screening at intervals recommended by her healthcare provider).

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Differential Diagnosis of Genital Warts

- Other infections
 - Condylomata lata—tend to be smoother, moist, more rounded, and darkfield-positive for *Treponema pallidum*. This is a manifestation of secondary syphilis and serologic tests for syphilis are typically positive.
 - Molluscum contagiosum—papules with central dimple, caused by a pox virus; rarely involves mucosal surfaces.
- Acquired dermatologic conditions
 - Seborrheic keratosis
 - Lichen planus
 - Fibroepithelial polyp, adenoma
 - Melanocytic nevus
 - Neoplastic lesions
- Normal anatomic variants
 - “Pink pearly penile papules”
 - Vestibular papillae (micropapillomatosis labialis)
 - Skin tags (acrochordons)
- External genital squamous intraepithelial lesions (SIL)
 - Squamous cell carcinoma *in situ*
 - Bowenoid papulosis
 - Erythroplasia of Queyrat
 - Bowen’s disease of the genitalia

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Diagnosis of Cervical Cellular Abnormalities

- Cytology (Pap test)
 - A useful screening test to detect cervical dysplasia (not HPV *per se*)
 - Provides indirect evidence of HPV because it detects squamous epithelial cell changes that are almost always due to HPV
 - No need for more frequent Pap test screening if external genital warts are present (assuming patient is receiving screening at intervals recommended by her healthcare provider).
 - Limitations of Pap tests
 - Specimen adequacy—Pap test occasionally must be repeated when the laboratory judges the specimen unsatisfactory for evaluation.
 - Variable sensitivity (estimates suggest the sensitivity of a single Pap test is 60%–80% for high-grade lesions, and lower for low-grade lesions).
 - Technologies using liquid collection media (ThinPrep® Pap Test™, Autocyte Prep™) and computer-assisted reading may enhance sensitivity, but reduce specificity.
- Nucleic acid tests
 - A definitive diagnosis of HPV is based on detection of viral nucleic acid (DNA or RNA).
 - Clinical tests that detect high-risk types of HPV DNA in cells scraped from the cervix are commercially available.
 - The FDA has approved these tests for:
 - To triage women with atypical cells of undetermined significance (ASC-US) Pap test results
 - As an adjunct to the Pap test screening for cervical cancer in women 30 years or older
 - Use of HPV DNA tests for women with Pap abnormalities worse than AS-CUS (e.g. LSIL or HSIL) is unnecessary because the vast majority of these women are infected with high-risk HPV.
 - External genital warts are not an indication for HPV DNA testing.
 - Use of HPV testing in women 20 years and younger is not recommended, primarily because these women will frequently have HPV that is transient in nature.
 - HPV tests are not FDA-approved for use in men, or as a general test for STDs.
- Colposcopy
 - Indication for colposcopy is guided by physical exam and Pap test findings, with or without HPV DNA test findings.
 - External genital warts are not an indication for cervical colposcopy.
- Histology (biopsy)
 - Indications for cervical biopsy include
 - Visible exophytic lesions on the cervix;
 - Pap test with HSIL; and
 - Pap test with ASCUS and HPV-positive, ASC-H or LSIL with colposcopic abnormalities.
- For more information on guidelines for managing women with cervical cytologic abnormalities, refer to the 2006 Consensus Guidelines for the Management of Women with Cervical Cytologic Abnormalities.

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Lesson V: Patient Management

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General Treatment of Genital Warts

- Primary goal is removal of warts.
- If left untreated, visible genital warts may regress spontaneously or persist with or without proliferation.
- In most patients, treatment can induce wart-free periods.
- Currently available therapies may reduce, but probably do not eradicate, infectivity.
- Effect of current treatment on future transmission is unclear.
- No evidence that presence of genital warts or their treatment is associated with development of cervical cancer.
- Because of uncertainty regarding the effect of treatment on future transmission and the possibility for spontaneous resolution, some patients may choose to forgo treatment and await spontaneous resolution.
- Consider screening persons with newly diagnosed genital warts for other STDs (e.g., chlamydia, gonorrhea, HIV, syphilis).
- The presence of genital warts is not an indication for HPV testing, a change in the frequency of Pap tests, or cervical colposcopy.

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Treatment Regimens

- Patient-applied and provider-administered treatment regimens are available.
- Providers should be knowledgeable about, and have available, at least one patient-applied and one provider-administered treatment.
 - Choice of treatment should be guided by
 - Patient preference,
 - Available resources,
 - Experience of the healthcare provider,
 - Location of the lesion(s), and
 - Pregnancy status.
 - Factors that may influence selection of treatment include
 - Wart size,
 - Number of warts,
 - Anatomic site of wart,
 - Wart morphology,
 - Patient preference,
 - Cost of treatment,
 - Convenience, and
 - Adverse effects.

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Treatment Response

- Affected by
 - Number, size, duration, and location of warts; and
 - Immune status (pregnancy, HIV infection).
 - In general, warts located on moist surfaces and in intertriginous areas respond better to topical treatment than do warts on drier surfaces.
- Many patients require a course of therapy over several weeks to months rather than a single treatment.
 - Nonsurgical, locally destructive techniques may require multiple treatments.
 - Evaluate the risk-benefit ratio of treatment throughout the course of therapy to avoid over-treatment.
- There is no evidence that any specific treatment is superior to any of the others.
 - No treatment is ideal for all patients or for all warts.
 - The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes.

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Recurrence After Treatment

- As many as two-thirds of patients will experience recurrences of warts within 6–12 weeks of therapy; and after 6 months most patients have clearance.
 - Consider biopsy if
 - Diagnosis is uncertain;
 - Lesions do not respond to standard therapy;
 - Disease worsens during therapy;
 - Patient immunocompromised; or
 - Warts are pigmented, indurated, fixed, bleeding, or ulcerated.
 - Treatment modality should be changed if patient has not improved substantially.
 - The majority of genital warts respond within three months of therapy.
 - Response to treatment and its side effects should be evaluated throughout the course of therapy.

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Complications

- Complications rarely occur, if treatments for warts are employed properly.
 - Depressed or hypertrophic scars are uncommon, but can occur, especially if the patient has had insufficient time to heal between treatments.
 - Rarely, treatment can result in disabling chronic pain syndromes (e.g., vulvodynia or hyperesthesia of the treatment site).
- Patients should be warned that persistent hypopigmentation or hyperpigmentation are common with some treatments.

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CDC-Recommended Regimens For External Genital Warts (Patient-Applied)

- Podofilox 0.5% solution or gel
 - Patients should apply podofilox solution with a cotton swab, or podofilox gel with a finger, to visible genital warts twice a day for three days, followed by four days of no therapy.

- This cycle may be repeated as necessary for up to four cycles.
- Total wart area treated should not exceed 10 cm², and a total volume of podofilox should be limited to 0.5 mL per day.
- If possible, the healthcare provider should apply the initial treatment to demonstrate the proper application technique and identify which warts should be treated.
- *The safety of podofilox during pregnancy has not been established.*
- or**
- Imiquimod 5% cream
 - Patients should apply imiquimod cream once daily at bedtime, three times a week for up to sixteen weeks.
 - The treatment area should be washed with soap and water 6–10 hours after the application.
 - *The safety of imiquimod during pregnancy has not been established.*
- or**
- Sinecatechins 15% ointment
 - Patients should apply sinecatechins ointment three times daily for up to sixteen weeks.
 - **Do not wash off** post-application
 - *The safety of sinecatechins has not been established in pregnancy or HIV- or HSV-coinfected individuals*
- Using patient-applied treatments
 - Provider should identify warts for treatment and teach patients how to apply substance.
 - Patient must be able to identify and reach warts to be treated.
 - Podofilox 0.5% solution or gel, an antimitotic drug that destroys warts, is relatively inexpensive, easy to use, and safe.
 - Most patients experience mild or moderate pain or local irritation after treatment with podofilox.
 - Imiquimod is a topically active immune enhancer that stimulates production of interferon and other cytokines.
 - Local inflammatory reactions are common with use of imiquimod and sinecatechins; these reactions include redness and irritation and are usually mild to moderate.
 - Follow-up is not required, but may be useful several weeks into therapy to determine appropriateness of medication use and response to treatment.

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CDC-Recommended Regimens for External Genital Warts (Provider Administered)

- Cryotherapy with liquid nitrogen or cryoprobe
 - Repeat applications every one to two weeks.
 - May be used on internal or external warts and during pregnancy.
- or**
- Podophyllin resin 10%–25% in compound tincture of benzoin
 - Apply a small amount to each external wart and allow to air dry.
 - The treatment can be repeated weekly if needed.

- To avoid the possibility of complications associated with systemic absorption and toxicity, two important guidelines should be followed.
 - Application should be limited to < 0.5 mL of podophyllin or < 10 cm² of warts per session.
 - No open lesions or wounds should exist in the area to which treatment is administered.
- Some specialists suggest that the preparation area be thoroughly washed off one to four hours after application to reduce local irritation. Local irritation is common.
- Podophyllin resin preparations differ in the concentration of active components and contaminants. The shelf life and stability of podophyllin preparations is uncertain.
- *The safety of podophyllin during pregnancy has not been established.*
- or**
- Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%
 - Apply a small amount only to warts and allow to air dry (white “frosting” develops).
 - If excess amount of acid is applied, powder the treated area with talc or sodium bicarbonate (i.e., baking soda), or with liquid soap preparations to remove unreacted acid.
 - Repeat weekly if necessary.
 - Can be used on vaginal and anal warts as well as on external warts and during pregnancy.
- or**
- Surgical removal—tangential scissor excision, tangential shave excision, curettage, or electrosurgery
 - Surgical therapy is most beneficial for patients who have large numbers or areas of genital warts.
 - Can be used on accessible internal warts and during pregnancy
 - Can usually eliminate warts at a single visit
 - Requires substantial clinical training, additional equipment, and a longer office visit

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Alternative Treatment Regimens

- Intralesional interferon
 - Systemic interferon is not effective.
 - Intralesional interferon is probably effective because of antiviral and/or immunostimulating effects. Administration of intralesional interferon is associated with stinging, burning, and pain at the injection site, and sometimes systemic effects.
 - Not recommended as a modality because of inconvenient routes of administration, frequent office visits, and the association between its use and a high frequency of systemic adverse effects.
- Carbon dioxide laser and surgery, topical cidofovir might be useful in management of extensive warts or intraurethral warts, particularly for those that have not responded to other treatments. Topical cidofovir has challenges as the preparation is

not readily available and must be formulated by a pharmacist.

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CDC-Recommended Regimens for Cervical Warts

- For women who have exophytic cervical warts, high-grade SIL must be excluded before treatment is initiated.
- Management should include biopsy and consultation with a specialist.

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CDC-Recommended Regimens for Vaginal Warts

Treat only if symptomatic, since most treatments also affect normal tissue and could cause scarring and pain.

- Cryotherapy with liquid nitrogen
 - The use of a cryoprobe in the vagina is not recommended because of risk for vaginal perforation and fistula formation.
- or**
- TCA or BCA 80%–90% applied to warts
 - Apply small amount only to warts and allow to air dry (white “frosting” develops).
 - If an excess amount of acid is applied, powder the treated area with talc, sodium bicarbonate (i.e., baking soda), or with liquid soap preparations to remove unreacted acid.
 - Repeat weekly, if needed.

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CDC-Recommended Regimens for Urethral Meatal Warts

- Cryotherapy with liquid nitrogen
- or**
- Podophyllin 10%–25% in compound tincture of benzoin
 - Treatment area must be dry before contact with normal mucosa.
 - Repeat weekly if needed.
- Note:** *The safety of podophyllin during pregnancy has not been established.*
- Although data evaluating the use of podofilox and imiquimod for the treatment of distal meatal warts are limited, some specialists recommend their use in certain patients.

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CDC-Recommended Regimens for Anal Warts

- Cryotherapy with liquid nitrogen
- or**
- TCA or BCA 80%–90% applied to warts
 - Apply small amount only to warts and allow to dry (white “frosting” develops).
 - If an excess amount of acid is applied, powder the treated area with talc, sodium bicarbonate (i.e., baking soda), or with liquid soap preparations to remove unreacted acid.
 - Repeat weekly if needed.
- or**

- Surgical removal
 - Warts on the rectal mucosa should be managed in consultation with a specialist.
 - Many persons with warts on the anal mucosa also have warts on the rectal mucosa, so persons with anal warts can benefit from an inspection of the rectal mucosa by digital examination or anoscopy.

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Management in Pregnancy

- Genital warts can proliferate and become more friable during pregnancy.
- Cytotoxic agents (podophyllin, podofilox, imiquimod) should not be used.
- Cryotherapy, TCA, BCA, and surgical removal may be used.
- HPV types 6 and 11 can cause recurrent respiratory papillomatosis in children. The route of transmission (i.e., transplacental, perinatal, or postnatal) is not completely understood.
- The prevention value of cesarean delivery is unknown; thus, C-section should not be performed solely to prevent transmission to neonate.
 - Cesarean delivery may be indicated for women with genital warts, if the pelvic outlet is obstructed, or if vaginal delivery would result in excessive bleeding.

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Genital Warts in HIV-Infected Patients

General considerations

- No data suggest that treatment modalities for external genital warts should be different.
- Might have larger or more numerous warts
- Might not respond as well to therapy
- Might have more frequent recurrences after treatment
- Squamous cell carcinomas arising in or resembling genital warts might occur more frequently, therefore, requiring biopsy for confirmation of diagnosis.

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Pap Test Screening in Immunodeficient Patients

- Provide cervical Pap test screening every six months for one year, then annually for all HIV-infected women with or without genital warts.
- Anal Paps
 - There is an increased incidence of anal cancer in HIV-infected MSM. Some experts screen for anal intraepithelial neoplasia by cytology—however, this is not routinely recommended, because evidence is limited on natural history of anal intraepithelial neoplasias, reliability of screening methods, safety and response to treatments, and programmatic considerations.

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Squamous Cell Carcinoma *in situ*

- Patients in whom squamous cell carcinoma *in situ* of the genitalia is diagnosed should be referred to a specialist for treatment.
- Ablative modalities usually are effective, but careful follow-up is essential.

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Genital Wart Follow-up

- Counsel patients to
 - Watch for recurrences (most frequent in first three months after treatment), and
 - Continue regular Pap screening at the same intervals as recommended for women **without** genital warts. The presence of genital warts is not an indication for increase in frequency of Pap test screening (assuming patient is receiving screening at intervals recommended by her healthcare provider), or for cervical colposcopy.
 - Communicate to current sex partners about genital warts and the risk of transmission. Patients should have no sexual activity until warts are gone.
- External genital warts can be difficult to identify, so it might be useful for patients to have a follow-up evaluation three months after treatment.
- Earlier follow-up visits also might be useful for some patients to
 - Monitor or treat complications of therapy,
 - Document the absence of warts, and
 - Reinforce patient education and counseling messages.
- Patients concerned about recurrences should be offered a follow-up evaluation three months after treatment.

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Treatment of Cervical Dysplasia

- Detailed discussion of treatment of cervical dysplasia is beyond the scope of this educational offering.
- For more information on managing women with cervical dysplasia refer to the following sources:
 - 2006 Consensus Guidelines for the Management of Women with Cervical Cytologic Abnormalities <http://www.asccp.org/consensus/cytological.shtml>
 - CDC National Breast and Cervical Cancer Early Detection Program <http://www.cdc.gov/cancer/nbccedp/index.htm>

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Lesson VI: Patient Counseling and Education

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The Nature of HPV Infection

- Genital HPV infection is common in sexually active adults.
- The majority of sexually active adults will have HPV infection at some point in their lives, although the majority of them will never know because the infection usually has no symptoms and clears on its own.
- Natural history of HPV infection is usually benign.
 - Low-risk genital HPV types are associated with mild Pap test abnormalities and genital warts.
 - High-risk types are associated with mild to severe Pap test abnormalities, and rarely, cancers of the cervix, vulva, vagina, anus, penis, and oropharynx.

- Most women infected with HPV infection do not develop cervical cancer.
- Recurrence of genital warts within the first several months after treatment is common.

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Transmission Issues

- Genital HPV infection is usually sexually transmitted (through vaginal intercourse, anal intercourse, oral sex, and also possible through nonpenetrative sexual activity such as genital-genital contact).
- Infection is often shared between partners
 - The incubation period (i.e., the interval between initial exposure and established infection or disease) is variable, and determining the timing and source of infection is frequently difficult.
 - Within ongoing sexual relationships, sex partners are usually infected by the time of the patient's diagnosis, although they may have no symptoms or signs of infection.
- Recurrences usually are not reinfection.
- Treatment for genital warts can reduce HPV infection, but whether treatment results in a reduction in risk for transmission of HPV to sex partners is unclear. The duration of infectivity after wart treatment is unknown.
- The value of disclosing a past diagnosis of genital HPV infection to future partners is unclear, although candid discussions about past STD should be encouraged and attempted whenever possible.
- HPV testing is not indicated for partners of persons with genital warts or cervical cellular abnormalities due to HPV.

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Risk Reduction

- Assess patient's behavior-change potential.
- Develop individualized risk-reduction plans with the patient for lasting results.
- Discuss prevention strategies such as abstinence, mutual monogamy, condoms, limiting number of sex partners, etc.
- Consistent and correct male condom use reduces the risk for genital HPV acquisition and HPV-associated diseases (e.g., genital warts and cervical cancer).
 - HPV infections can occur in male and female genital areas that are not covered by a latex condom (e.g., scrotum, vulva, or perianus).

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Patient Counseling and Education Resources

- Division of STD Prevention. Available at: <http://www.cdc.gov/std/hpv/default.htm>
- American Sexual Health Association, National HPV and Cervical Cancer Prevention Resource Center. Available at: <http://www.ashastd.org/std-sti/hpv.html>
- CDC Cervical Cancer Screening Fact Sheet
http://www.cdc.gov/cancer/cervical/pdf/cc_basic.pdf
- National Cancer Institute Cervical Cancer Screening Information For Patients
<http://www.cancer.gov/cancertopics/pdq/screening/cervical/Patient>

- American Society of Colposcopy and Cervical Cancer Pathology
<http://www.asccp.org/EducationLearning/EducateTheEducatorsbrHPVResourceCenter/tabid/5980/Default.aspx>

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Lesson VII: Partner Management and Public Health Measures

[Slide 74]

Partner Management for Patients with Genital Warts

- Sex partner examination is not necessary for management of genital warts. There are no data to indicate that reinfection plays a role in recurrences.
- No recommended uses of the HPV test to diagnose HPV infection in sex partners have been established. HPV infection is commonly transmitted to partners but usually resolves on its own.
- Providing treatment solely for the purpose of preventing future transmission cannot be recommended because the value of treatment in reducing infectivity is not known.
- The counseling of sex partners provides an opportunity for these partners to
 - Learn about the implications of having a partner who has genital warts, and about the potential for future disease transmission; and
 - Receive STD and Pap screening, if necessary.

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Cervical Cancer Screening

- The key strategy to prevent cervical cancer is regular cervical cancer screening (Pap test screening) for sexually active women 21 years and older.
- New technologies, including liquid-based cytology and testing for high-risk HPV types, may offer some benefits
- Liquid-based cytology is an alternative to conventional Pap tests; it has a higher sensitivity for detection of SIL and can facilitate HPV testing in women with ASC-US. However, liquid-based cytology has a lower specificity, resulting in more false-positive tests.
- Recommendations for cervical cancer screening intervals vary in the U.S., but the American Cancer Society (ACS) and the American College of Obstetricians and Gynecologists (ACOG) guidelines recommend screening to begin at age 21 years. The recommendations for intervals and use of HPV tests vary.
 - American Cancer Society
http://www.cancer.org/docroot/PED/content/PED_2_3X_ACS_Cancer_Detection_Guidelines_36.asp?sitearea=PED
 - ACOG www.acog.org CDC Cervical Cancer and Pap Test Information
http://www.cdc.gov/cancer/cervical/basic_info/
 - National Cancer Institute Screening for Cervical Cancer Health Professional Information
<http://www.cancer.gov/cancertopics/pdq/screening/cervical/healthprofessional>
 - U.S. Preventive Services Task Force Cervical Cancer Screening Recommendations
<http://www.uspreventiveservicestaskforce.org/uspstf/uspscerv.htm>

- American Society for Colposcopy and Cervical Pathology Consensus Guidelines on Management of Women with Abnormal Cervical Cancer Screening Tests for more information on the Bethesda Classification System and on management of cervical cellular abnormalities: <http://www.asccp.org/consensus/cytological.shtml>
- CDC recommendations for cervical cancer screening for women who attend STD clinics or have a history of STDs <http://www.cdc.gov/std/treatment/2010/cc-screening.htm>

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Special considerations:

- Pregnant women should have a Pap test as part of routine prenatal care.
- Anal Pap test screening in HIV-infected persons
 - Because of the increased incidence of anal cancer in HIV-positive persons, screening for anal cancer by cytology in this population is recommended by some specialists.
 - However, evidence is limited concerning the natural history of anal intraepithelial neoplasias, the reliability of screening methods, the safety and response to treatments, and the programmatic considerations that would support this screening approach.
 - Until additional data are generated, this screening approach is not routinely recommended.

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Reporting Requirements

- Genital HPV infection is not a reportable infection.
- Genital warts are reportable in some states.
- Some states have made cervical precancer reportable.
- Check with state or local health department for reporting requirements for HPV associated outcomes in your area.

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HPV Vaccines

- Two HPV vaccines are licensed in the U.S.
 - The bivalent vaccine (HPV2), Cervarix®, protects against two HPV types (16 and 18) which are responsible for 70% of cervical cancers.
 - The quadrivalent vaccine (HPV4), Gardasil®, protects against four HPV types (6, 11, 16, 18), which are responsible for 70% of cervical cancers (16 and 18) and 90% of genital warts (6 and 11).
- Administration
 - Either vaccine is routinely recommended for girls aged 11 or 12 years. HPV4 is routinely recommended for boys aged 11 or 12 years. The vaccines can be administered to boys or girls beginning at age 9 years .
 - Vaccination is also recommended for 13–26-year-old females and 13–21-year-old males who have not had any or all the doses at a younger age.
 - MSM should be vaccinated through age 26 years
 - Immunocompromised persons (including those with HIV-infection) should be vaccinated through age 26 years.

- Ideally, the vaccines should be administered before onset of sexual activity. However, persons who are sexually active also may benefit from vaccination.
 - It is uncommon for young persons to be infected with all HPV types in the vaccines.
 - Currently, there is no test available for clinical use to determine whether a person has had any or all of the HPV types in the vaccines.
- Dosing
 - Three-dose series intramuscularly over a six-month period
 - Second dose 1–2 months after the first dose (minimum of four weeks after first dose)
 - Third dose six months after the first dose (minimum of twelve weeks after second dose, **and** minimum 24 weeks after first dose)
 - The same vaccine product should be used for the entire three-dose series.
 - Available for eligible children and adolescents 19 and younger through Vaccines for Children (VFC) program
- Women who have received HPV vaccines should continue routine cervical cancer screening.
 - Thirty percent of cervical cancers are caused by HPV types other than 16 and 18.
 - Neither vaccine is recommended for persons >26 years.
 - HPV Vaccine Efficacy

CASE STUDY

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Case Study

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History

- Anne Drew is a 34-year-old woman who comes in stating that she wants to get "checked out" because Jonathan, her sex partner, has small solid "bumps" on the skin at the base of his penis. Jonathan told her that he was diagnosed and treated for genital warts about a year ago, and his health care provider told him they could recur.
- No history of abnormal Pap tests and no history of STDs.
- Last Pap test was performed 4 months ago.
- Sexually active since age 16 with men and has had a total of 7 sex partners over her lifetime.
- Currently sexually active with one partner for the last eight months.
- Uses oral contraceptives for birth control.

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Question

1. What should be included in Ms. Drew's evaluation?

Ms. Drew's evaluation should include a pelvic exam with a visual inspection of genitalia. Diagnosis of genital warts is usually made by visual inspection with bright light. If the diagnosis is uncertain, it can be confirmed by biopsy.

Acetic acid evaluation of external genitalia may be of limited value due to its low specificity (many false positives) and is not routinely recommended. Ms. Drew had a normal Pap test four months ago. There is no need for more frequent Pap tests when external genital warts are present.

HPV DNA testing is not recommended for diagnosis and management of external genital warts.

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Physical Examination

- Vital signs: blood pressure 96/74, pulse 78, respiration 13, temperature 37.1° C
- Cooperative, good historian
- Chest, heart, musculoskeletal, and abdominal exams within normal limits
- Pelvic exam is normal
- Visual inspection of the genitalia reveals multiple small (<0.5 cm), flesh-colored, papular lesions in the perineal area

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Questions

2. What is the differential diagnosis for the papular genital lesions?

Correct responses include the following

- Secondary syphilis (condylomata lata)
- Molluscum contagiosum—caused by a pox virus
- Genital warts—caused by HPV
- Sebaceous glands—acquired dermatologic condition
- Skin tags—acquired dermatologic condition
- Melanocytic nevi—acquired dermatologic condition
- Lichen planus—acquired dermatologic condition

3. What is the **most likely** diagnosis based on history and physical examination?

Genital warts are the most likely diagnosis due to her partner's history of genital warts and the appearance of the lesions.

The diagnosis of genital warts is usually based on clinical appearance. No serologic test is commercially available, nor would one be helpful in making the diagnosis of genital warts, since the presence of antibodies does not indicate active infection.

If the lesions appear atypical (pigmented, fixed, indurated, or ulcerated), then biopsy is indicated.

Secondary syphilis is not the most likely diagnosis, given the patient's history and the low incidence of syphilis. However, the condylomata lata of secondary syphilis can mimic genital warts. A serologic test for syphilis should be performed to evaluate for that possibility.

Molluscum contagiosum is not the most likely diagnosis because the lesions are smooth dome-shaped papules with a characteristic central umbilication (dimple).

Sebaceous glands are not the most likely diagnosis. Sebaceous glands are normal anatomical structures that are generally smooth and yellowish-white, and are usually not located on the perineum. It is not a high priority to test for this diagnosis.

Skin tags are not the most likely diagnosis. Skin tags are normal structures. While they may be somewhat pedunculated like warts, they have a smooth instead of a rough surface.

Melanocytic nevi are not the most likely diagnosis. Melanocytic nevi are hyperpigmented lesions.

Lichen planus is not the most likely diagnosis. Lichen planus lesions tend to be hyperpigmented and are violaceous and polygonal.

4. Which laboratory tests should be ordered or performed?

Correct responses include the following:

- Serologic test for syphilis (e.g., RPR – STAT if available)
- Test for *Chlamydia trachomatis*
- Test for *Neisseria gonorrhoeae*
- Counseling and testing for HIV

Screening for other STDs, including HIV, should be considered for all persons newly diagnosed with HPV. A serologic test for syphilis should be performed to rule out secondary syphilis.

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Patient Management

The following genital warts management options are discussed with Ms. Drew:

Patient-applied therapy

- Podofilox 0.5% solution or gel
- Imiquimod 5% cream
- Sinecatechins 15% ointment

Provider-administered therapy

- Cryotherapy with liquid nitrogen or cryoprobe
- Podophyllin resin 10%–25% in compound tincture of benzoin
- Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%

Surgical removal

No intervention

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Questions

5. What is the effect of treatment on future transmission? What is the possibility of recurrence after treatment?

The effect of treatment on future transmission is unknown. Because of uncertainty about the effect of treatment on future transmission and the possibility for spontaneous resolution, some patients may choose to forgo treatment and await spontaneous resolution.

Recurrence of genital warts within the first several months after treatment is common and usually indicates recurrence rather than reinfection. Many patients require a course of therapy rather than a single treatment. Treatment is labor intensive and non-surgical, locally destructive techniques may require multiple treatments. Complications rarely occur if treatments for warts are properly employed.

6. What are appropriate counseling messages for Ms. Drew about genital warts and HPV infection?

Correct responses include the following:

- Genital HPV is a sexually transmitted viral infection which is common in sexually active adults.
- The incubation period is variable and it is often difficult to determine the source of infection.
- Low-risk genital HPV types are associated genital warts. These are different types from those associated with cancers.
- Genital warts can be easily transmitted, so it is important to discuss prevention strategies with a partner (abstinence until warts are gone, consistent and correct condom use).
- Genital warts have a high recurrence rate after treatment.
- The value of disclosing a past diagnosis of genital HPV infection is unclear, although candid discussions about past STD should be encouraged and attempted whenever possible.
- Consistent and correct condom use reduces the risk of HPV transmission. However, HPV infections can occur in male and female genital areas that are covered or protected by a latex condom, as well as in areas that are not covered.
- There is no need for her to have more frequent Pap test screenings after being diagnosed with genital warts (assuming she is receiving screening at intervals recommended by her healthcare provider), since genital warts are associated with low-risk HPV types, not the high-risk types associated with moderate to severe Pap test abnormalities and invasive cancer.

7. What conditions could cause a substantial increase in the number and size of Ms. Drew's genital warts?

Pregnancy and immunodeficiency can cause a substantial increase in the number and size of genital warts.

TEST QUESTIONS

1. It is estimated that ___ of sexually active adults are infected with genital HPV during their lifetime.
 - a. 10%
 - b. 25%
 - c. 40%
 - d. **100%**
2. All of the following are true about transmission of genital HPV, **except**:
 - a. Transmission is associated with sexual activity.
 - b. **Transmission via fomites has been documented.**
 - c. Transmission can occur from asymptomatic and subclinical patients.
 - d. Transmission probably requires contact with viable HPV and microtrauma to skin/mucous membranes.
3. HPV types ___ and ___ account for more than half of HPV types found in cervical cancers.
 - a. 6 and 11
 - b. 6 and 18
 - c. **16 and 18**
 - d. 11 and 16
4. Genital HPV types are characterized in terms of their oncogenic potential (ability to cause cervical cancer).
 - a. **True**
 - b. False
5. Which of the following is the most important risk factor associated with development of cervical cancer precursors (high-grade cervical cellular changes) and cervical cancer?
 - a. Older age
 - b. High-risk HPV types
 - c. **Persistence of high-risk HPV infection**
 - d. Immunodeficiency
6. If left untreated, visible warts may
 - a. Resolve on their own
 - b. Remain unchanged
 - c. Increase in size and number
 - d. **Any of the above**
7. Which factor should guide genital wart treatment?
 - a. The preference of the patient
 - b. The available resources

- c. The experience of the health care provider
 - d. All of the above**
8. Which of the following is **not** a presentation of genital warts?
- a. Condylomata acuminata
 - b. Smooth papules
 - c. Flat papules
 - d. Keratotic warts
 - e. All of the above are presentations of genital warts**
9. Acetic acid evaluation of external genital warts may be of limited value because:
- a. It has low sensitivity (many false negatives).
 - b. It has low specificity (many false positives).**
 - c. It is not cost effective.
 - d. All of the above
10. Manifestations of genital HPV infection include
- a. Genital warts
 - b. Cervical cellular abnormalities
 - c. Anogenital squamous cell cancers
 - d. Respiratory papillomatosis
 - e. All of the above**
11. Most genital HPV infections are transient and have no clinical manifestations or sequelae.
- a. True**
 - b. False
12. Which HPV types usually cause cervical cancer?
- a. Low-risk types
 - b. High-risk types**
 - c. Both low-risk and high-risk types
 - d. Neither low-risk nor high-risk types
13. Diagnosis of external genital warts is usually made by
- a. Visual inspection**
 - b. Biopsy
 - c. Acetic acid evaluation
 - d. HPV DNA test

14. The FDA has approved HPV DNA testing for use in
- Cervical cancer screening for women under 30 years
 - Triage of women with ASC-US Pap test results**
 - Triage of women with LSIL Pap test results
 - External genital wart diagnosis
15. Cervical cellular abnormalities are detected by which of the following?
- Serologic test
 - Pap test**
 - Wet mount
 - HPV DNA test
16. Which of the following statements is true about the treatment of genital warts?
- In most patients treatment does not induce wart-free periods.
 - Current treatment decreases future transmission.
 - The primary goal is removal of warts.**
 - Available therapies eradicate infectivity.
17. Which of the following is a patient-applied treatment for external genital warts?
- Podofilox**
 - Podophyllin
 - Trichloroacetic acid (TCA)
 - Bichloroacetic acid (BCA)
18. Which of the following is a provider-administered treatment for external genital warts?
- Cryotherapy with liquid nitrogen or cryoprobe
 - Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%
 - Podophyllin resin 10%–25% in compound tincture of benzoin
 - All of the above**
19. All of the following external genital wart treatments may be used in pregnancy, **except**
- Surgical removal
 - Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
 - Imiquimod 5% cream**
 - Cryotherapy
20. Which of the following is true of HPV infection in immunodeficient patients?
- Genital warts occur more frequently.
 - Genital warts are more resistant to conventional therapy.
 - The occurrence of atypical lesions (e.g., oral warts) is more likely.
 - All of the above**

21. Patient counseling and education should cover
- The nature of HPV infection
 - Transmission issues
 - Risk reduction
 - All of the above**
22. All of the following are appropriate patient education messages about the nature of HPV infection **except**
- Genital HPV is a viral infection which is one of the most common STDs.
 - High-risk HPV types are associated with external genital warts.**
 - Genital warts have a high recurrence rate after treatment.
 - The majority of women with high-risk HPV types do not develop cervical cancer.
23. Which of the following is correct about partner management for patients diagnosed with genital warts?
- Sex partner examination is not necessary for management of genital warts because no data indicate that reinfection plays a role in recurrences.
 - Providing treatment solely for the purpose of preventing future transmission cannot be recommended because the value of treatment in reducing infectivity is not known.
 - The counseling of sex partners provides an opportunity for these partners to learn about the implications of having a partner who has genital warts and about the potential for future disease transmission and receive STD and Pap screening if necessary.
 - All of the above**
24. The presence of genital warts is an indication for
- Change in Pap test frequency
 - Cervical colposcopy
 - Both of the above
 - Neither of the above**
25. Which of the following actions should be considered for patients with newly diagnosed genital warts?
- Screening of all current and former sex partners for genital warts
 - Immediate Pap smear, regardless of when last Pap screening was performed
 - Screening for other STDs (e.g., chlamydia, gonorrhea, HIV, syphilis)**
 - HPV DNA test

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Websites and Other Resources

1. CDC Division of STD Prevention: www.cdc.gov/std
2. 2010 CDC STD Treatment Guidelines (including E-book downloadable version): www.cdc.gov/STD/treatment/2010/
3. National Network of STD/HIV Prevention Training: Centers: nnptc.org/
4. STD information and referrals to STD clinics:
 CDC-INFO
 1-800-CDC-INFO (800-232-4636)
 TTY: 1-888-232-6348

In English, en Español

5. CDC National Prevention Information Network (NPIN): www.cdcnpin.org
6. American Sexual Health Association, National HPV and Cervical Cancer Prevention Resource Center: www.ashastd.org/std-sti/hpv.html
7. CDC Cervical Cancer and Pap Test Information:
www.cdc.gov/cancer/cervical/pdf/cc_basic.pdf
8. National Cancer Institute (NCI): www.cancer.gov/
9. U.S. Preventive Services Task Force Cervical Cancer Screening: Recommendations: www.uspreventiveservicestaskforce.org/uspstf/uspscerv.htm
10. American College of Obstetrics and Gynecology: www.acog.org
11. American Society of Colposcopy and Cervical Pathology (ASCCP):
www.asccp.org
12. CDC Advisory Committee on Immunization Practices:
www.cdc.gov/vaccines/acip/index.html
13. American Cancer Society: www.cancer.org/Cancer/CervicalCancer/index