

Genital Human Papillomavirus (HPV)

Learning Objectives

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

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

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

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

Introduction

- Genital HPV is one of the most common STDs
- More than 40 HPV types can infect the genital tract

Introduction

- HPV types are divided into two groups based on their association with cancer.
 - Low-risk types (nononcogenic) associated with genital warts and mild Pap test abnormalities
 - High-risk types (oncogenic) associated with moderate to severe Pap test abnormalities, cervical dysplasia and cervical cancer, and other cancers
- Most genital HPV infections are transient, asymptomatic, and have no clinical consequences.

Incidence in the U.S.

- Estimated annual incidence of sexually-transmitted HPV infection is 14.1 million
- Estimated \$1.7 billion spent annually in direct medical costs to treat conditions associated with genital HPV infection

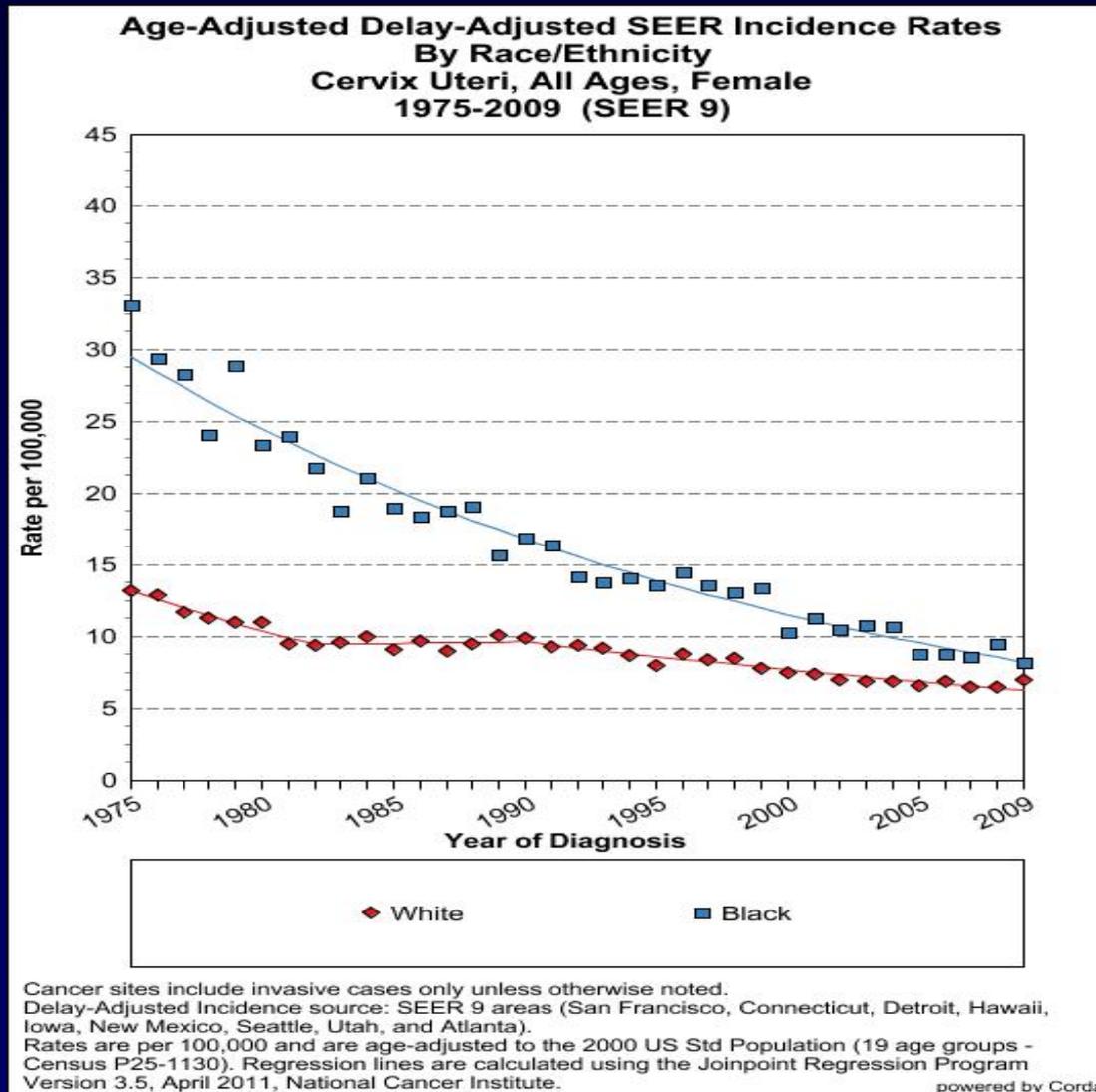
Prevalence in the U.S.

- 100% of sexually active men and women acquire genital HPV at some point in their lives.
- An estimated 79 million females aged 14–59 years are infected with HPV infection.

Incidence and Prevalence of HPV-associated Diseases

- Genital warts
 - Incidence may be as high as 100/100,000.
 - An estimated 1.4 million 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.
 - Incidence is estimated at 8.1/100,000.

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



Transmission of Genital HPV

- Predominantly associated with sexual activity
- Can occur from asymptomatic and subclinical patients
- Infectivity after treatment of genital warts or cervical cellular abnormalities is unknown
- Condoms may reduce risk

Risk Factors for Women

- Young age
- Sexual behavior
 - Risk increases with increasing number of recent and lifetime sex partners
- Sexual behavior of sex partners—risk increases for women whose sex partners had multiple sex partners
- Immune status—HPV more likely to be detected in immune-suppressed women

Risk Factors for Men

- Risk increases with increasing number of recent and lifetime sex partners
- Being uncircumcised increases risk

Lesson II: Pathogenesis

Virology

- Double-stranded DNA virus that belongs to the *Papillomaviridae* family
- Genital types have specific affinity for genital skin and mucosa
- Infection identified by the detection of HPV DNA

HPV Genotyping System

Genital HPV types are generally characterized in terms of oncogenic potential.

- Low-risk types (nononcogenic types)
 - Most genital warts caused by HPV types 6 and 11
 - Recurrent respiratory papillomatosis associated with HPV types 6 and 11
- High-risk types (oncogenic types)
 - HPV types 16 and 18 found in 70% of cervical cancers
 - Most women with high-risk HPV infection have normal Pap test results and never develop cellular changes or cervical cancer.

Pathology

- 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.

Natural History of HPV

- Most genital HPV infections are transient, asymptomatic (subclinical), and have no clinical consequences in immunocompetent individuals.
- Time to development of clinical manifestations is variable.
- Median duration of new cervical infections is 8 months, but varies.
 - 90% of infections clear within 2 years
 - Gradual development of an effective immune response is the likely mechanism for HPV DNA clearance.

Natural History of HPV-continued

- Persistent HPV infection
 - Not cleared by the immune system
 - Characterized by persistently detectable type-specific HPV DNA
 - Persistent oncogenic HPV infection is most important risk factor for precancerous cervical cellular changes and cervical cancer.

Lesson III: Clinical Manifestations and Sequelae

HPV-associated cancers United States, 2004-2008

Anatomic Area	Average annual number of cases*	Estimated+	
		HPV attributable	HPV 16/18 attributable
Cervix	11,967	11,500	9,100
Vagina	729	500	400
Vulva	3,136	1,600	1,400
Anus (F)	3,089	2,900	2,700
Oropharynx (F)	2,370	1,500	1,400
Total (Females)	21,291	18,000	15,000
Penis	1,046	400	300
Anus (M)	1,678	1,600	1,500
Oropharynx (M)	9,356	5,900	5,600
Total (Males)	12,080	7,900	7,400

* Defined by histology and anatomic site; Watson M et al. Cancer 2008. Data source: National Program of Cancer Registries and SEER, covering 100% coverage of US population. + Gillison ML, et al. Cancer 2008. Ref: Human Papillomavirus-Associated Cancers MMWR 2012;61(15):258-261.

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.

*Two most common clinically significant manifestations of genital HPV infection

Genital Warts-Appearance

- 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 that can resemble common warts or seborrheic keratosis

Genital Warts-Location

- Most commonly occur in areas of coital friction
- Perianal warts do not necessarily imply anal intercourse.
 - May be secondary to autoinoculation, sexual activity other than intercourse, or spread from 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 simultaneously infected with multiple HPV types.

Genital Warts-Symptoms

- Genital warts usually cause no symptoms. Symptoms that can occur include:
 - Vulvar warts-dyspareunia, pruritis, burning discomfort;
 - Penile warts-occasional itching;
 - Urethral meatal warts-hematuria or impairment of urinary stream;
 - Vaginal warts-discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy); and
 - Perianal and intra-anal warts-pain, bleeding on defecation, itching
- Most patients have fewer than ten genital warts, with total wart area of 0.5–1.0 cm².

Genital Warts-Duration and Transmission

- May regress spontaneously, or persist with or without proliferation.
 - Frequency of spontaneous regression is unclear, but estimated at 10–30% within three months.
 - Persistence of infection occurs, but frequency and duration are unknown.
 - Recurrences after treatment are common.

Genital Warts and High-Risk HPV

- High-risk HPV types occasionally can be found in visible warts and have been associated with squamous intraepithelial lesions (squamous cell carcinoma *in situ*, Bowenoid papulosis, Erythroplasia of Queyrat, or Bowen's disease of the genitalia).
- The lesions can resemble genital warts.
- Unusual appearing genital warts should be biopsied.

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.

Perianal Warts



Source: Seattle STD/HIV Prevention Training Center at the University of Washington/ UW HSCER Slide Bank

Vulvar Warts

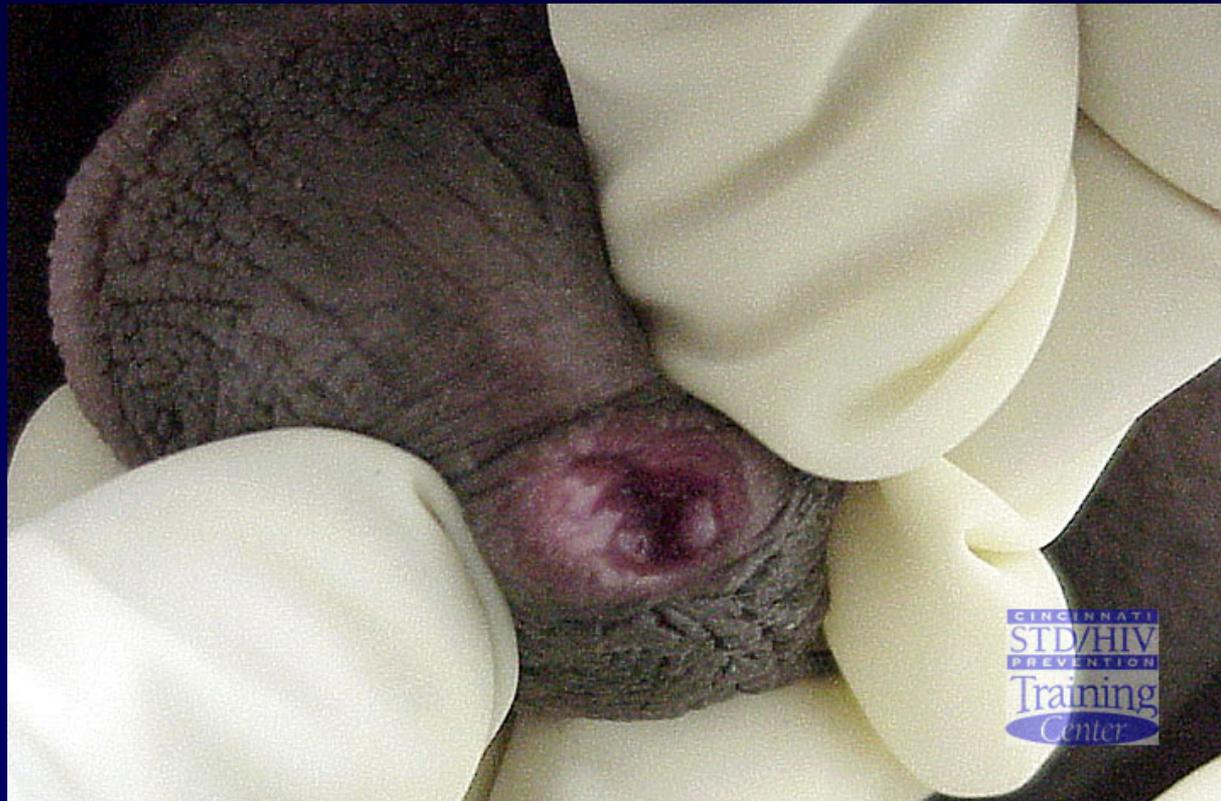


Source: Reprinted with permission of Gordon D. Davis, MD.

Penile Warts



Intrameatal Wart



Cervical Cellular Abnormalities

- Usually subclinical
- Lesions associated with these abnormalities can be detected by Pap test or colposcopy, with or without biopsy.
- Can be caused by HPV
- Low-grade lesions often regress spontaneously without treatment.

Classification of Cervical Cellular Abnormalities

2001 Bethesda System

- **Atypical Squamous Cells (ASC-US and ASC-H)** are cells that do not appear to be completely normal
 - **Atypical Squamous Cells of Undetermined Significance (ASC-US)**
 - Changes are often caused by HPV infection.
 - Changes are usually mild.
 - **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.

Classification of Cervical Cellular Abnormalities-continued

- **Low-grade squamous intraepithelial lesion (LSIL)**
 - Usually transient, caused by HPV infection
- **High-grade squamous intraepithelial lesion (HSIL)**
 - Generally changes due to persistent infection with a high-risk HPV type
 - Lesions associated with HSIL have a higher risk for progression to cervical cancer.

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 is necessary, but not sufficient, for the development of cervical cancer.

Recurrent Respiratory Papillomatosis

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

Lesson IV: Diagnosis of Genital Warts and Cervical Cellular Abnormalities

Diagnosis of Genital Warts

- Diagnosis is usually made by visual inspection with bright light.
- 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.

Diagnosis of Genital Warts-continued

- 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 due to its low specificity.
- 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).

Differential Diagnosis of Genital Warts

- Other infections
 - Condylomata lata
 - Tend to be smoother, moist, more rounded, and darkfield-positive for *Treponema pallidum*
 - 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

Differential Diagnosis of Genital Warts-continued

- 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

Diagnosis of Cervical Cellular Abnormalities

- Cytology (Pap test)
 - Useful screening test to detect cervical cell changes
 - Provides indirect evidence of HPV because it detects squamous epithelial cell changes that are almost always due to HPV

Diagnosis of Cervical Cellular Abnormalities-continued

- HPV DNA tests
 - FDA-approved:
 - To triage women with ASC-US Pap test results, and
 - As an adjunct to Pap test screening for cervical cancer in women 30 years or older.
- HPV DNA tests should not be used
 - In men,
 - In adolescents <21 years,
 - To screen partners of women with Pap test abnormalities,
 - To determine who will receive HPV vaccine, or
 - STD screening for HPV.

Diagnosis of Cervical Cellular Abnormalities-continued

- Colposcopy
 - Indication guided by physical exam or Pap test findings with or without HPV DNA test findings
- Cervical biopsy
 - May be indicated if there is/are
 - Visible exophytic lesions on cervix
 - Pap test with HSIL, ASC-H, or other findings
- For more information on guidelines for managing women with cervical cytologic abnormalities, refer to 2006 Consensus Guidelines for Management of Women with Cervical Cytologic Abnormalities
<http://www.asccp.org/consensus/cytological.shtml>

Lesson V: Patient Management

General Treatment of Genital Warts

- Primary goal is removal of warts.
- If left untreated, 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 eliminate infectivity.
- Effect of current treatment on future transmission is unclear.

General Treatment of Genital Warts-continued

- No evidence that presence of genital warts or their treatment is associated with development of cervical cancer.
- 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).

Treatment Regimens

- Patient-applied and provider-administered therapies 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 lesion(s), and
 - Pregnancy status.

Treatment Regimens-continued

- Factors influencing treatment selection include
 - Wart size,
 - Number of warts,
 - Anatomic site of wart,
 - Wart morphology,
 - Patient preference,
 - Cost of treatment,
 - Convenience, and
 - Adverse effects.

Treatment Response

- Affected by
 - Number, size, duration, and location of warts, and immune status
 - 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 or months rather than a single treatment.
 - 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.
 - The use of locally developed and monitored treatment algorithms has been associated with improved clinical outcomes

Recurrence After Treatment

- As many as two-thirds of patients will experience recurrences of warts within 6–12 weeks of therapy; after 6 months most patients have clearance.
 - If persistent after 3 months, or if there is poor response to treatment, consider biopsy to exclude a premalignant or neoplastic condition, especially in an immunocompromised person.
- Treatment modality should be changed if patient has not improved substantially after 3 provider-administered treatments or if warts do not completely clear after 6 treatments

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 treatment site).
- Patients should be notified that persistent hypopigmentation or hyperpigmentation are common with some treatments.

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

- **Podofilox 0.5% solution or gel***
 - Apply solution with cotton swab or gel with a finger to visible warts twice a day for 3 days, followed by 4 days of no therapy.
 - Cycle may be repeated as needed up to 4 cyclesor
- **Imiquimod 5% cream***
 - Apply cream once daily at bedtime, 3 times a week for up to 16 weeks.
 - Treatment area should be washed with soap and water 6–10 hours after applicationor
- **Sinecatechins 15% ointment*,****
 - Apply ointment 3 times daily for up to 16 weeks.
 - ***Do not wash off*** post-application

**Safety not established in pregnancy*

***Safety not established in HIV- or HSV-co-infected individuals*

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

- **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.**

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

- **Cryotherapy with liquid nitrogen or cryoprobe**
 - Repeat applications every 1–2 weeks, or
- **Podophyllin resin 10%–25%* in compound tincture of benzoin**
 - Apply a small amount to each wart and allow to air dry
 - To avoid toxicity
 - 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
 - Treatment may be repeated weekly if needed, or
- **Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%–90%**
 - Apply small amount only to warts and allow to dry
 - Treatment may be repeated weekly if needed, or
- **Surgical removal** - tangential scissor excision, tangential shave excision, curettage, or electrosurgery

Alternative Treatment Regimens

- Alternative Treatment Regimens include treatment options that might be associated with more side effects and/or less data on efficacy including
 - Intralesional interferon,
 - Carbon dioxide laser and surgery, and
 - Topical cidofovir.

CDC-Recommended Regimens for Exophytic Cervical Warts

- Biopsy needed, high-grade squamous intraepithelial lesions (SIL) must be excluded before treatment is initiated.
- Management should include biopsy and consultation with a specialist.

CDC-Recommended Regimens for Vaginal Warts

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

- **Cryotherapy with liquid nitrogen**
 - 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 dry (white “frosting” develops).
 - Treatment may be repeated weekly if needed.

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.
 - Treatment may be repeated weekly, if needed.

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).
- Treatment may be repeated weekly if needed.

or

- Surgical removal

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 is not completely understood.
- Prevention value of cesarean delivery is unknown; thus, C-section should not be performed solely to prevent transmission to neonate.

Genital Warts in HIV-Infected Patients

- No data that treatment should be different
- Larger, more numerous warts
- Might not respond as well to therapy
- More frequent recurrence of lesions after treatment
- Squamous cell carcinomas arising in or resembling genital warts might occur more frequently among immunosuppressed persons, therefore, requiring biopsy for confirmation of diagnosis for suspicious cases, and referral to a specialist.

Pap Test Screening in Immunodeficient Patients

- Provide cervical Pap test screening every 6 months for 1 year, then annually for all HIV-infected women with or without genital warts.
- Anal Pap tests and anoscopy
 - 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.

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.

Genital Wart Follow-Up

- Counsel patients to
 - Watch for recurrences,
 - Continue regular Pap screening at same intervals as recommended for women **without** genital warts, and
 - Communicate to current sex partners about genital warts and the risk of transmission. Patients should have no sexual activity until warts are gone.
- After visible warts have cleared, follow-up evaluation is not mandatory, but provides an opportunity to
 - Monitor or treat complications of therapy,
 - Document absence of warts, and
 - Reinforce patient education and counseling messages.
- Offer patients concerned about recurrences a follow-up evaluation 3 months after treatment.⁶⁶

Treatment of Cervical Dysplasia

- 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>

Lesson VI: Patient Counseling and Education

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, although most will never know because infection will be asymptomatic and will clear 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, oropharynx.
 - Most women infected with HPV do not develop cervical cancer.
- Genital warts have a high recurrence rate after treatment.

Transmission Issues

- Usually sexually transmitted
- Infection is often shared between partners
- Determining source of infection is usually difficult (incubation period variable)
- Recurrences usually are not reinfection
- Transmission risk to current and future partners after treatment is unclear.
- Likelihood of transmission and duration of infectivity with or without treatment are unknown.
- Value of disclosing a past diagnosis of genital HPV infection to future partners is unclear, although candid discussions about past STD should be encouraged.

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 risk for genital HPV acquisition and HPV-associated diseases (e.g., genital warts and cervical cancer).
 - HPV infections can occur in areas that are not covered or protected by a condom (e.g., scrotum, vulva, or perianus).

Patient Counseling and Education Resources

- Division of STD Prevention
<http://www.cdc.gov/std/hpv/default.htm>
- American Sexual Health Association, National HPV and Cervical Cancer Prevention Resource Center
<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>

Lesson VII: Partner Management and Public Health Measures

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.
- Providing treatment solely for the purpose of preventing future transmission cannot be recommended because value of treatment in reducing infectivity is not known.
- 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 disease transmission, and
 - Receive STD and Pap screening, if necessary.

Cervical Cancer Screening

- The key strategy to prevent cervical cancer is regular cervical cancer screening (Pap test screening) for all sexually active women ≥ 21 years.
- 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
- Several organizations provide guidelines for cervical cancer screening, including
 - American Cancer Society (ACS),
 - American College of Obstetricians and Gynecologists (ACOG),
 - U.S. Preventive Services Task Force (USPSTF), and
 - American Society for Colposcopy and Cervical Pathology (ASCCP).

Special Considerations

- Pregnant women should have a Pap test as part of routine prenatal care
- Anal Pap test screening in HIV-positive persons not routinely recommended

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.

HPV Vaccines

- Two types
 - Bivalent vaccine (HPV2) protects against HPV 16 and 18-associated cervical precancers.
 - Quadrivalent vaccine (HPV4) protects against HPV 6, 11, 16, and 18-associated genital warts, cervical precancers, vulvar and vaginal precancers, and anal precancers.
- Administration
 - Either vaccine is recommended for routine vaccination of females aged 11 or 12 years. HPV4 is recommended for routine vaccination of males aged 11 or 12 years. This vaccine can be given at 9 or 10 years of age.
 - 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.

HPV Vaccines (continued)

- Dosing
 - Three-dose series intramuscularly over a six-month period
- Women who have received HPV vaccine should continue routine cervical cancer screening.
 - Thirty percent of cervical cancers are caused by HPV types other than 16 and 18
- CDC has a website with additional vaccine information
<http://www.cdc.gov/vaccines/pubs/ACIP-list.htm#hpv>

Case Study



History

- **Anne Drew:** 34-year-old woman who wants to get "checked out" because Jonathan, her sex partner, has small solid "bumps" on the skin on the shaft of his penis.
- Jonathan told her that he was diagnosed and treated for genital warts about a year ago, and his healthcare provider told him they could recur.
- No history of abnormal Pap smears and no history of STDs
- Last Pap smear performed 4 months ago
- Sexually active with men only since age 16; has had a total of 7 sex partners over her lifetime
- Currently sexually active with 1 partner for the last 8 months
- Uses oral contraceptives for birth control

Question

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

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

Questions

2. What is the differential diagnosis for the papular genital lesions?
3. What is the **most likely** diagnosis based on history and physical examination?
4. Which laboratory tests should be ordered or performed?

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

Questions

5. What is the effect of treatment on future transmission? What is the possibility of recurrence after treatment?
6. What are appropriate counseling messages for Ms. Drew about genital warts and HPV infection?
7. What condition could cause a substantial increase in the number and size of Ms. Drew's genital warts?