Condyloma Acuminatum

See also Cervical cancer

Background

1. Definition
    - Flat, papular or pedunculated growths on anal & genital mucosa caused by human papilloma virus (HPV)
2. General information
    - Caused by Human Papilloma Virus (HPV), dsDNA virus
    - Highly species-specific
        - HPV only infects humans
    - Over 100 serotypes
        - Approx. 35 types infect ano-genital epithelium
        - Infection usually involves multiple serotypes
    - Serotypes 16, 18 assoc with high-grade intraepithelial neoplasia, Bowen's Dz
    - Serotypes 6, 11 assoc with condyloma acuminata, respiratory papillomatosis
        - Infrequently low-grade intraepithelial neoplasia

Pathophysiology

1. Pathology
    - Virus induces changes in DNA of host cells that alter regulatory mechanisms leading to overgrowth
        - Large percentage of infected individuals asymptomatic
        - May have long latency period after infection
    - Condyloma acuminata (Genital warts): types 6, 11
        - Most common manifestation
        - Single or multiple papules
        - Most common sites
            - Women: posterior introitus, labia majora, labia minor
            - Men: penile shaft in circumcised, glans, coronal sulcus, frenulum, foreskin uncircumcised
2. Incidence/prevalence
    - Genital HPV
        - Most common viral STD in US
            - Estimated 1 million new cases diagnosed every year
        - Approx. 1% of sexually active US population has genital warts
        - 25% of HPV positive women will be high-risk for intraepithelial neoplasia (serotype 16 or 18)
        - 15% of cervical HPV infections will progress to cervical intraepithelial neoplasia or carcinoma within 2-3 years if left untreated
        - Peak incidence: 20-24 yo
        - Transmission rate after single sexual encounter up to 26%
        - Prevalence
            - Peak: 17-33 yo
            - Women: 39% in women 10-40 yo
            - Men: 28%

- Cutaneous warts (not anogenital)
  - 10% of children
  - Peak incidence ages 12-16

3. Risk factors
   - Unprotected sex
   - Multiple sex partners
   - Immunosuppressed
   - Presence of other STDs
   - Penetration not required for infection
     - Contact with infected area sufficient for transmission
   - Source of infection is typically asymptomatic
4. Morbidity/mortality
   - Depends upon serotype and general health of pt.
   - Increased risk of intraepithelial cancers serotypes 16 & 18

Diagnostics

1. History
   - Pt history of raised lesions in anogenital region
   - Most lesions are asymptomatic
   - Can be associated with pruritus, tenderness, burning, pain, vaginal discharge or bleeding
   - Hx of sexual contacts
     - Most pts do not know where infection was contracted
   - Hx of possibility of immunosuppression
2. Physical exam
   - Anogenital (condyloma acuminata)
     - Pedunculated or papular growths
     - Flesh- to gray-colored papules
     - Hyperkeratotic, exophytic
     - Smooth or jagged surface
     - 1 mm to several centimeters in size
   - Flat warts
     - 3-5% acetic acid solution can be used to delineate lesions
     - HPV associated lesions develop acetowhite appearance
     - Not recommended for routine diagnosis
     - Typically used to guide biopsy
3. Diagnostic testing
   - Test for other STDs
   - HPV nucleic acid test is not recommended for routine diagnosis
   - Biopsy required:
     - (anoscope / sigmoidoscope/ colposcope guided)
     - Diagnosis not certain
     - No response to standard treatment or worsens with treatment (3 treatments or 6 months of treatment)
     - Indurated, friable, bleeding or ulcerated

Differential Diagnosis

1. Condyloma lata
    - Flat and velvety lesions caused by Treponema pallidum
2. Herpes simplex
    - Multiple painful ulcers and vesicles caused by herpes simplex virus (HSV)
3. Squamous cell carcinoma
    - Plaque like or fungating lesions
4. Paget disease
    - Red, crusted, sharply demarcated lesions caused by infiltration of epidermis with large, anaplastic vacuolated tumor cells
5. Molluscum contagiosum
    - 1-5 mm umbilicated papules, often in clusters, expressible caseous material from center, caused by poxvirus

Therapeutics

1. Goal of treatment:
    - Removal of warts, but no evidence that this reduces future transmission of warts
2. No evidence that one treatment method is superior to another
3. Response to Tx affected by:
    - Compliance
    - Immunosuppression
4. Factors influencing selection of method of treatment:
    - Size
    - Number of warts
    - Anatomic site
    - Morphology
    - Adverse effects
    - Patient preference & convenience
    - Cost of treatment
    - Provider experience
5. **External warts**: patient applied
    - Podofilox 0.5% solution or gel
        - Extract from podophyllum peltatum
        - Applied twice a day for 3 days and then 4 days off
        - Can repeat for a total of 4 cycles
        - Area of application should not exceed 10cm (can cause neurotoxicity and pain)
        - No more than 0.5 ml of podofilox should be applied per day
        - Teratogenic (not recommended for use in pregnancy)
        - Superior to podophyllin
    - Imiquimod 5% cream
        - Apply 3x week at bedtime, for 16 weeks
            - Wash after 6-10 hours
        - Can cause local erythema, excoriations and erosions
        - Not recommended for use during pregnancy
        - Not for internal use (Cervix, urethra)
        - Superior to podophyllin

6. **External warts**: provider administered
    - Cryotherapy with liquid nitrogen or cryoprobe
        - Applications can be repeated every 1-2 weeks
        - Provider training required
        - Office procedure
        - Ice ball should not extend beyond 2-3 mm in external warts and 5 mm in cervical warts
        - Superior to podophyllin
    - Podophyllin 10%- 25%
        - Apply sparingly to lesion and wash after one to four hours
        - Apply weekly until lesions clear
        - Not for use over cervix, vagina, open areas (chemical burns)
        - Side effects: pain, local irritation, ulceration
    - Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80%--90%
        - Apply sparingly to affected area and after it dries a white frosting will appear
        - Surrounding healthy tissue can be protected by application of petroleum jelly and excess medication can be neutralized with talc, sodium bicarbonate or washed with liquid soap
            - Apply weekly for six weeks or until lesions clear
            - Can be used internally
            - Can be used in pregnancy
            - Side effects are: local irritation
    - Surgical removal
        - Excision under local anesthesia, with cauterization of base
        - Curettage
        - Electrosurgery
        - All these may cause scarring and strictures
        - Superior to podophyllin
    - Other treatments
        - Intralesional interferon
            - Can cause stinging, burning and pain at site of injection
            - Not recommended as primary mode of treatment because of systemic side effects, route of administration and number of office visits
        - Laser surgery
            - Requires specific training
            - Co2/NdYag
            - Destruction should not extend beyond 1 mm in depth
            - Expensive
            - Risk of development of mucosal warts in operator
            - Side effects: pain, scarring
7. **Vaginal warts Tx**
    - Cryotherapy with liquid nitrogen
    - Cryoprobe is not recommended because of the risk of perforation and formation of fistulas
    - TCA or BCA

8. **Urethral meatus warts Tx**
    - Cryotherapy with liquid nitrogen
    - Podophyllin 10% --25%
9. **Anal warts Tx**
    - Inspection of rectal mucosa for rectal warts by digital exam or anoscopy should be performed to rule out rectal warts
    - Cryotherapy with liquid nitrogen
    - TCA or BCA 80%-90%
    - Surgical removal
10. Management of sex partners
    - Counsel about HPV infection, and safe sex practices
    - Evaluation for other STDs and Pap screening for women

Follow-Up

1. As needed based on response to treatment
    - Recurrences common during first 3 months
2. Documented serotype 16 & 18 infections require close f/u
3. See also Cervical cancer screening

Special Circumstances

1. Pregnant women
    - Decreased cell mediated immunity can exacerbate viral infections
    - TCA has no systemic absorption and no known fetal effects
    - Cryotherapy
    - C-section not routinely recommended but indicated if pelvic outlet is obstructed or if there is a risk of excessive bleeding
    - Imiquimod, podophyllin and podofilox should not be used
2. Post menopausal
    - Greater risk of vulvar intraepithelial neoplasia or vulvar cancer, biopsy should be considered before treatment
3. HIV
    - Biopsy recommended because high-grade dysplasia is more common
    - 5% Imiquimod topically
    - Surgical therapy if medical therapy fails or presence of extensive or bulky disease

Prognosis

1. Depends on
    - Immune status
        - HPV infections are transient in most immunocompetent patients
        - Immunocompromised women are at higher risk of developing cervical and vaginal dysplasia
    - HPV type
        - Types 16 & 18 more likely to develop into malignancy
    - Duration of infection
        - Persistent infection assoc with increased risk of malignancy
    - Viral load
        - Larger amounts of virus assoc with increased risk of malignancy

Prevention

1. Avoidance of contact with infected individuals
    - Unlikely that condoms prevent transmission
2. Vaccine
    - HPV recombinant vaccine (Gardasil)
        - HPV types 6, 11, 16, 18
        - Recommended for females between 9- 26 yrs
        - Recommended age of administration is 11-12 yrs
        - 0.5 ml IM in 3 doses, 2nd dose 2 months after 1st dose and 3rd dose 6 months after first dose
        - Reduces incidence of CIN 2 & CIN 3
3. PAP smear is essential screening tool in women
4. See also Cervical cancer screening

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Evidence-Based Inquiry

1. What is the most effective treatment for external genital warts?
2. Does vaccination for HPV prevent cervical intraepithelial neoplasia?

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