Herpes Simplex (HSV) & Human Papilloma Virus (HPV) Review

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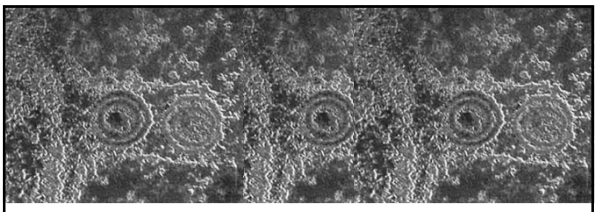


Genital Herpes

Herpes Simplex Virus Infections

Slides adapted from CDC Deck

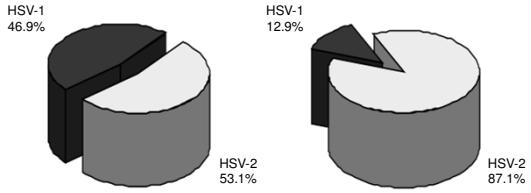
HSV-1 and Genital Infection

- Classically we think of HSV-2 when we think of genital HSV infection
  - "above and below the waist" rule
- Australian MSM study revealed incident HSV-1 infection more common in
  - Younger age
  - Those reporting insertive oral sex with "casual" partners
- US University Health Service
  - HSV-1 more common in females
  - Nearly 50% increase in newly diagnosed HSV-1 between 1993-2001

Jin et al.2006
Roberts et al 2003

Isolation of HSV-1 and HSV-2 According to Sexual Orientation

Initial Episodes of Genital Herpes
(*Harborview Medical Center*)



MSM | Heterosexual Men

Definitions of Infection Types

First Clinical Episode
- Primary infection
  - First infection **ever** with either HSV-1 or HSV-2
  - No antibody present when symptoms appear
  - Disease is more severe than recurrent disease
- Non-primary infection
  - Newly acquired HSV-1 or HSV-2 infection in an individual previously seropositive to the other virus
  - Symptoms usually milder than primary infection
  - Antibody to new infection may take several weeks to a few months to appear

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Definitions of Infection Types

Recurrent symptomatic infection
- Antibody present when symptoms appear
- Disease usually mild and short in duration

Asymptomatic infection
- Serum antibody is present
- No known history of clinical outbreaks

First Episode Primary Infection

- Characterized by multiple lesions that are more severe, last longer (11-12 days), and have higher titers of virus than recurrent infections
- Typical lesion progression:
  - papules → vesicles → pustules → ulcers → crusts → healed
- Often associated with systemic symptoms including fever, headache, malaise, and myalgia
- Illness lasts 2-4 weeks

First Episode Primary Infection without Treatment (continued)

- Local symptoms include pain, itching, dysuria, vaginal or urethral discharge, and tender inguinal adenopathy
- Median duration of viral shedding detected by culture (from the onset of lesions to the last positive culture) is ~12 days
- HSV cervicitis occurs in most primary HSV-2 (70-90%) and primary HSV-1 (~70%) infections

Recurrent Infection

- Prodromal symptoms are common
  - Localized tingling, irritation
  - Begin 12-24 hours before lesions
- Much shorter duration of sx (5-7 days)
- Symptoms tend to be less severe than in primary infection with fewer ulcers and no systemic symptoms
- HSV-2 primary infection more prone to recur than HSV-1

Asymptomatic Viral Shedding

- Most HSV-2 is transmitted during asymptomatic shedding
- Rates of asymptomatic shedding greater in HSV-2 than HSV-1
- Rates of asymptomatic shedding are highest in new infections (<2 years) and gradually decrease over time
- Asymptomatic shedding episodes are of shorter duration than shedding during clinical recurrences
- Medications reduce but DO NOT eradicate shedding

Comparison of HSV-2 vs. HSV-1

- HSV-2 and HSV-1 have different disease courses
- HSV-2 tends be more severe
- HSV-2 More Frequent Recurrences
  - Median ~4 vs. HSV-1 <1
- HSV-2 More Extensive Asymptomatic Shedding
- HSV2 - attenuated by prior infection with HSV1-Ab

Complications of Genital Infection

- Aseptic meningitis
  - More common in primary than recurrent infection
  - Generally no neurological sequelae
- Rare complications include:
  - Stomatitis and pharyngitis
  - Radicular pain, sacral parathesias
  - Transverse myelitis
  - Autonomic dysfunction

Principles of Management of Genital Herpes

- Counseling should include natural history, sexual and perinatal transmission, and methods to reduce transmission
- Antiviral chemotherapy
  - Partially controls symptoms of herpes
  - Does not eradicate latent virus
  - Does not affect risk, frequency or severity of recurrences after drug is discontinued

Management of First Clinical Episode of Genital Herpes

- Manifestations of first clinical episode may become severe or prolonged
- Antiviral therapy should be used
  - Dramatic effect, especially if symptoms <7 days and primary infection (no prior HSV-1)

CDC-Recommended Regimens for First Clinical Episode

- Acyclovir 400 mg orally 3 times a day for 7-10 days,

or

- Acyclovir 200 mg orally 5 times a day for 7-10 days,

or

- Famciclovir 250 mg orally 3 times a day for 7-10 days,

or

- Valacyclovir 1 g orally twice a day for 7-10 days

Recurrent Episodes of Genital Herpes

- Most patients with symptomatic, first-episode genital HSV-2 experience recurrent outbreaks
- Episodic and suppressive treatment regimens are available
- Treatment options should be discussed with ALL patients

Suppressive Therapy for Recurrent Genital Herpes

- Reduces frequency of recurrences
  - By 70%-80% in patients with > 6 recurrences per year
  - Also effective in those with less frequent recurrences
- Reduces but does not eliminate subclinical viral shedding
- Periodically (e.g., once a year), reassess need for continued suppressive therapy

CDC-Recommended Regimens for Suppressive Therapy

- Acyclovir 400 mg orally twice a day, or
- Famciclovir 250 mg orally twice a day, or
- Valacyclovir 500 mg orally once a day, or
- Valacyclovir 1 g orally once a day

Episodic Treatment for Recurrent Genital Herpes

- Ameliorates or shortens duration of lesions
- Requires initiation of therapy within 1 day of lesion onset
- Provide patient with a supply of drug or a prescription and instructions to self-initiate treatment immediately when symptoms begin

CDC-Recommended Regimens for Episodic Therapy

- Acyclovir 400 mg orally 3 times a day for 5 days, or
- Acyclovir 800 mg orally twice a day for 5 days, or
- Acyclovir 800 mg orally 3 times a day for 2 days, or
- Famciclovir 125 mg orally twice a day for 5 days, or
- Famciclovir 1000 mg orally twice a day for 1 day, or
- Valacyclovir 500 mg orally twice a day for 3 days, or
- Valacyclovir 1 g orally once a day for 5 days

Herpes in HIV-Infected Persons

- HIV-infected persons may have prolonged, severe, or atypical episodes of genital, perianal, or oral herpes
- HSV shedding is increased in HIV-infected persons
- Treatment guidelines are a bit different

CDC-Recommended Regimens for Daily Suppressive Therapy in HIV-Infected Persons

- Acyclovir 400-800 mg orally twice a day or three times a day, or
- Famciclovir 500 mg orally twice a day, or
- Valacyclovir 500 mg orally twice a day

CDC-Recommended Regimens for Episodic Infection in HIV-Infected Persons

- Acyclovir 400 mg orally 3 times a day for 5-10 days, or
- Famciclovir 500 mg orally twice a day for 5-10 days, or
- Valacyclovir 1 g orally twice a day for 5-10 days

Patient Counseling and Education

- Goals
  - Help patients cope with the infection
  - Prevent sexual and perinatal transmission
- Counsel initially at first visit
- Education on chronic aspects may be beneficial after acute illness subsides
- HSV-infected persons may express anxiety about genital herpes that does not reflect the actual clinical severity of their disease

Patient Counseling and Education

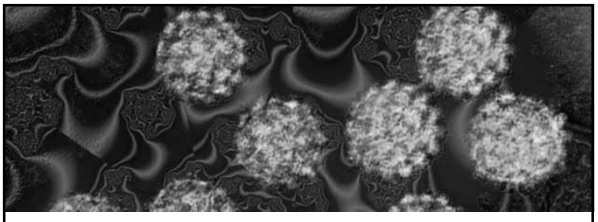
- Counseling should include:
  - Natural history of the infection
  - Treatment options
  - Transmission and prevention issues
  - Neonatal HSV prevention issues
- Emphasize potential for recurrent episodes, asymptomatic viral shedding, and sexual transmission even without symptoms!
- Discuss symptoms and preventive therapy
- Same counseling for asymptomatic people

Counseling: Transmission and Prevention

- Inform current and future sex partners about genital herpes diagnosis
- Abstain from sexual activity with uninfected partners when lesions or prodrome present
- Correct and consistent use of latex condoms might reduce the risk of HSV transmission
- Valacyclovir suppressive therapy decreases HSV-2 transmission in heterosexual couples in which source partner has recurrent herpes

Partner Management

- Symptomatic sex partners
  - Evaluate and treat in the same manner as patients who have genital lesions
- Asymptomatic sex partners
  - Ask about history of genital lesions
  - Educate to recognize symptoms of herpes
  - Offer type-specific serologic testing



Human Papilloma Virus

Human Papilloma Virus
Warts and Cancers

Introduction

- HPV types are divided into 2 groups based on their association with cervical cancer:
  - Low-risk types associated with genital warts and mild Pap test abnormalities
  - High-risk types associated with mild to severe Pap test abnormalities and cervical cancer
- Most genital HPV infections are transient, asymptomatic, and have no clinical consequences.

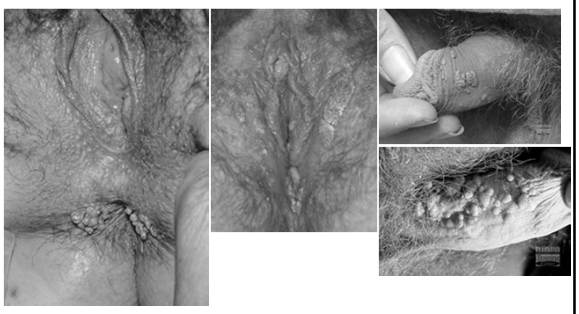
CDC

Clinical Manifestations by HPV Type

Plantar Warts	1
Common Warts	2, 4, 26, 27, 29
Flat Warts	3, 10, 28, 49
Genital Condyloma Acuminate	6, 11
Ano-genital Intraepith. Neoplasia/ Carcinoma	16, 18, 6, 11 …
Mouth (focal epithelial hyperplasia)	13, 32
Laryngeal papilloma	6, 11
Head & Neck Carcinoma	16, 18, 30

Adapted from Sexually Transmitted Diseases, 4th edition; Holmes, Starling, Stamm, etal.

Warts



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

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

- Podofilox 0.5% solution or gel (Condylox™)
  - Patients should 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 cycles.

OR

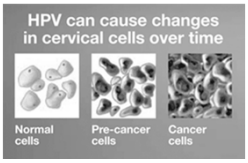
- Imiquimod 5% cream (Aldara™)
  - Patients should apply cream once daily at bedtime, 3 times a week for up to 16 weeks.
  - Treatment area should be washed with soap and water 6-10 hours after application.

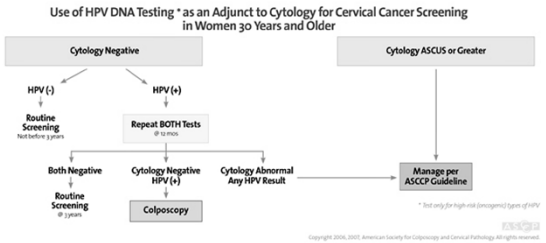
CDC-Recommended Regimens For External Genital Warts (Provider-Administered)

- 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
  - 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

Screening for Cervical Cancer across Guidelines

- Start screening for Cervical cancer at 21 y/o
- Screening recommended
  - Cytology every 3 years for 21-65 y/o
  - HPV detection co-test every 5 years for 30-65 y/o
  - No HPV co-test for <30 y/o
  - Most recommend against HPV screening alone
- Stop screening >65 with adequate history of screening
- Vaccine administration does not change the screening guidelines





- Guidelines for ASCUS are to repeat cytology in 6 months if HPV DNA testing not available.
- If ASCUS is In the presence of high risk HPV DNA, the guidelines are to proceed to colposocopy.

HPV DNA Prevalence in Cancers Other than Cervical

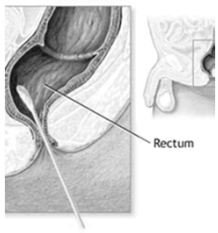
Site	HPV DNA (%)
Vulvar Intraepith. Neoplasia	72-100
Vaginal Intraepith. Neoplasia	82-100
Penile Intraepith. Neoplasia	90
Anal Squamous Cell	>80
Cancers of Head & Neck	33-72

Screening for Anal Dysplasia

- Formal guidelines on screening for anal dysplasia do not exist
- Specialists recommend screening HIV + MSM
- Other populations include:
  - HIV + MSW
  - individuals with perianal HPV lesions
  - HIV+ women
  - women with high-grade vulvar/vaginal or cervical dysplasia
  - solid organ transplant recipients who have an increased risk of anal cancer

Anal Pap Smear

- Insert dacron swab approximately 2 inches into the anus
- May wet swab, no lubricant
- Circular motion as you pull out
  - "peanut butter our of a jar"
- Tap swab into cytology fluid (higher yield)
- Send for ANAL Cytology



Interpreting Results

- Anal PAP smears are technically screening for High Grade Intraepithelial Lesions (HPV-related precursor of anal cancer
- Any positive result (including ASCUS) requires evaluation by HRA…cytology does not necessarily match pathologic grade on biopsy…ASCUS may be found on PAP when HSIL is present

Ablation of HSIL Lesions

- Controversial
- Smaller lesions may be treated with Bichloroacetic or Tricholoracetic Acid
- Some evidence for Imiquimod rx in HIV + MSM on HAART
- Infrared coagulation
- Multistage HRA-guided therapy
- Heightened anal cancer observation for extensive disease

HPV Vaccine

- Bivalent Vaccine (Cervarix™)
  - Type 16 and 18 (High risk)
- Quadrivalent Vaccine (Gardasil™)
  - Type 16 and 18 and wart strains 6 and 11
- Advisory Committee on Immunization Practices recommends offering HPV vaccine to:
  - females between the ages of 11 and 12 years to prevent cervical intraepithelial neoplasia and cervical cancer.
  - males aged 11 or 12 years
  - Permissive use in up to age 26
- Future: 9-valent vaccine in development to target other high risk HPV using the same platform

Thank you!