Urogenital viral infection

Genital and Perirectal Herpes Simplex Virus Infection

Herpes Simplex Virus (HSV) Type 2

Background and Burden of Disease

- Genital herpes is a chronic, lifelong viral infection
- Two HSV serotypes – HSV-1 & HSV-2
- HSV-2 causes the majority of cases of recurrent genital herpes in the U.S.
- Approximately 1 million new cases occur each year

Transmission

- HSV-2 is transmitted sexually and perinatally
- Majority of genital herpes infections are transmitted by persons who are
  - unaware they are infected with HSV-2 or
  - asymptomatic when transmission occurs
- Efficiency of sexual transmission is greater from men to women than from women to men

Transmission (continued)

- Likelihood of transmission declines with increased duration of infection
- Incubation period after acquisition is 2-12 days (average is 4 days)
- Drying and soap and water readily inactivate HSV; fomite transmission unlikely

HSV-2 and HIV Infection

- HSV-2 infection increases the risk of acquiring HIV infection at least 2 fold
- HSV-2 infection is also likely to facilitate transmission of HIV infection from persons co-infected with both viruses

Virology

- HSV-1 and HSV-2 are members of the human herpes viruses (herpetoviridae)
- All members of this species establish latent infection in specific target cells
- Infection persists despite the host immune response, often with recurrent disease

Pathology

- The virus remains latent indefinitely
- Reactivation is precipitated by multiple known and unknown factors and induces viral replication
- The re-activated virus may cause a cutaneous outbreak of herpetic lesions or subclinical viral shedding
- Up to 90% of persons seropositive for HSV-2 antibody have not been diagnosed with genital herpes

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

First Episode Primary Infection without Treatment

- Characterized by multiple lesions that are more severe, last longer, 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)

- Numerous, bilateral painful genital lesions; last an average of 11-12 days
- 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 Without Treatment

- Prodromal symptoms are common (localized tingling, irritation) - begin 12-24 hours before lesions
- Illness lasts 5-10 days
- Symptoms tend to be less severe than in primary infection
- Usually no systemic symptoms
- HSV-2 primary infection more prone to recur than HSV-1

Genital Herpes: Primary Lesions

Source: Cincinnati STD/HIV Prevention Training Center

Genital Herpes: Multiple Ulcers

Source: Cincinnati STD/HIV Prevention Training Center

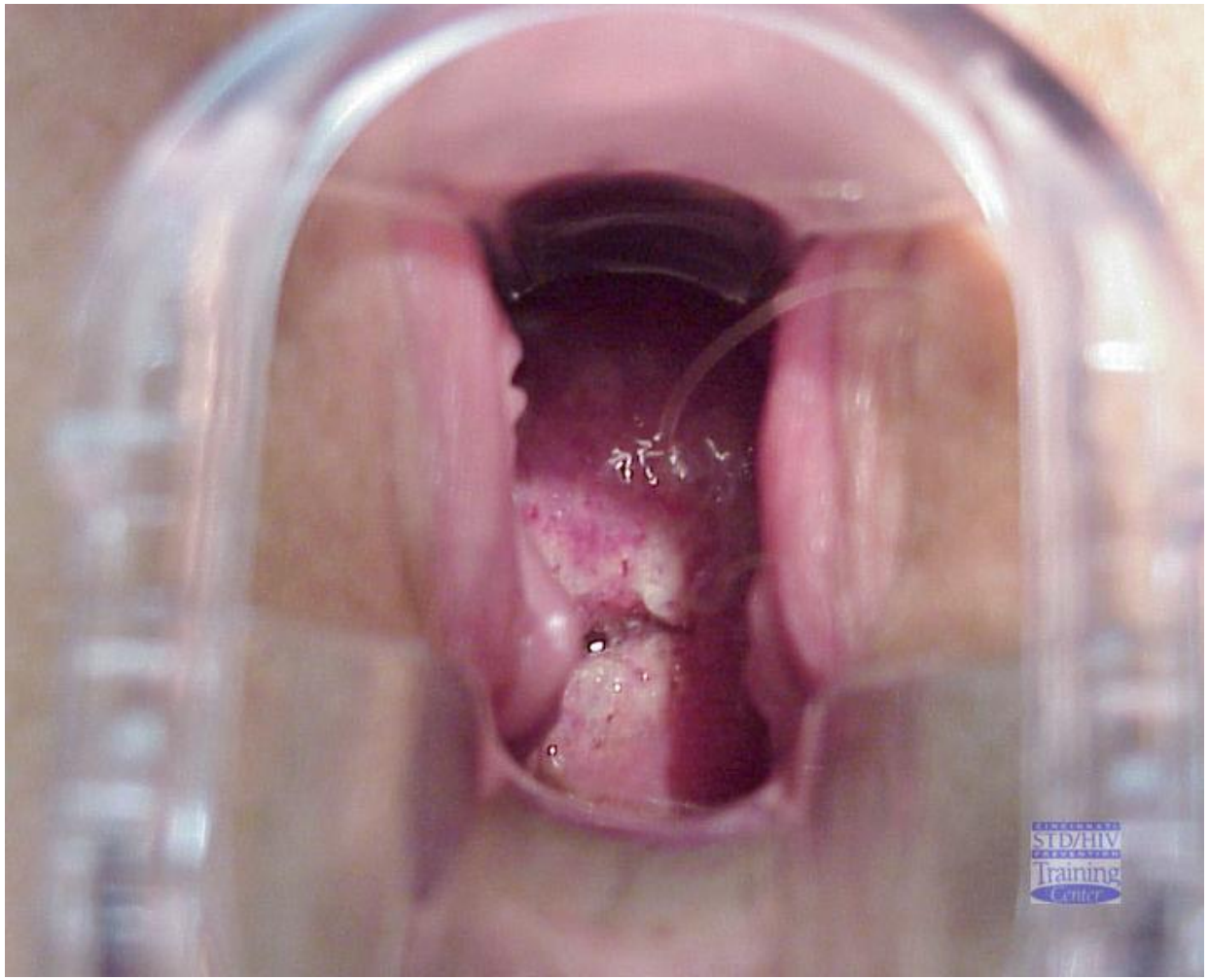
Genital Herpes: Recurrent Ulcer

Source: Cincinnati STD/HIV Prevention Training Center

Genital Herpes: Periurethal Lesions

Source: Cincinnati STD/HIV Prevention Training Center

Genital Herpes: Cervicitis



Source: Cincinnati STD/HIV Prevention Training Center

Herpes on the Buttock

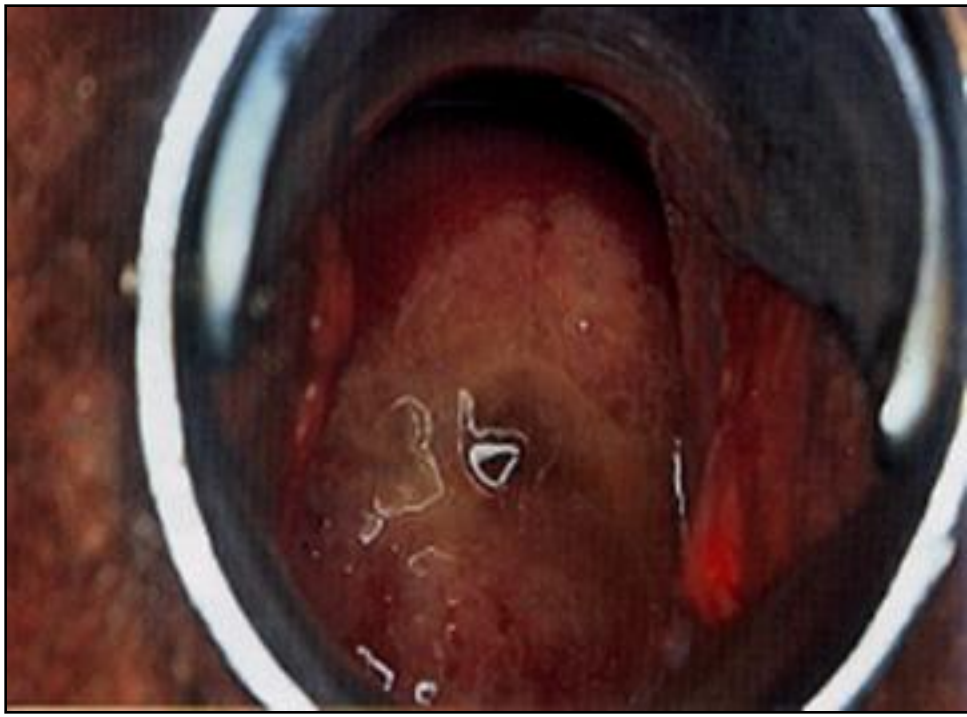
Source: Cincinnati STD/HIV Prevention Training Center

Male Herpes

Female Herpes

Female HSV (external lesion)

Female HSV (cervix)



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

Asymptomatic Viral Shedding (continued)

- Most common sites of asymptomatic shedding are vulva and perianal areas in women and penile skin and perianal area in men
- Antiviral suppressive therapy dramatically reduces, but does not eradicate shedding

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

HSV Diagnosis

- Clinical diagnosis is insensitive and nonspecific
- Clinical diagnosis should be confirmed by laboratory testing:
  - Virologic tests
  - Type-specific serologic tests

Virologic Tests

- Viral culture (gold standard)
  - Preferred test if genital ulcers or other mucocutaneous lesions are present
  - Highly specific (>99%)
  - Sensitivity depends on stage of lesion; declines rapidly as lesions begin to heal
  - Positive more often in primary infection (80%–90%) than with recurrences (30%)
  - Cultures should be typed
- Polymerase Chain Reaction (PCR)
  - More sensitive than viral culture; has been used instead of culture in some settings; however PCR tests are not FDA-cleared or widely available
  - Preferred test for detecting HSV in spinal fluid

Virologic Tests
(continued)

- Antigen detection (DFA or EIA)
  - Fairly sensitive (>85%) in symptomatic shedders
  - Rapid (2-12 hours)
  - May be better than culture for detecting HSV in healing lesions
- Cytology (Tzanck or Pap)
  - Insensitive and nonspecific and should not be relied on for HSV diagnosis

Type-specific Serologic Tests

- Type-specific and nonspecific antibodies to HSV develop during the first several weeks to few months following infection and persist indefinitely
- Presence of HSV-2 antibody indicates anogenital infection
- Presence of HSV-1 does not distinguish anogenital from orolabial infection

Uses of Type-specific Serologic Tests

- Type-specific serologic assays might be useful in the following scenarios:
  - Recurrent or atypical genital symptoms with negative HSV cultures
  - A clinical diagnosis of genital herpes without laboratory confirmation
  - A sex partner with herpes
  - As part of a comprehensive evaluation for STDs among persons with multiple sex partners, HIV infection, and among MSM at increased risk for HIV acquisition

Evaluation of Genital Ulcer

- All patients with genital ulcers should be evaluated with a serologic test for syphilis and a diagnostic evaluation for genital herpes
- In settings where chancroid is prevalent, a test for *Haemophilus ducreyi* should also be performed

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

Antiviral Medications

- Systemic antiviral chemotherapy includes 3 oral medications:
  - Acyclovir
  - Valacyclovir
  - Famciclovir
- Topical antiviral treatment is not recommended

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

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

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

Severe Disease

- IV acyclovir should be provided for patients with severe disease or complications requiring hospitalization

- CDC-Recommended Regimen:
  - Acyclovir 5-10 mg/kg IV every 8 hours for 2-7 days or until clinical improvement
  - Follow with oral antiviral therapy to complete at least 10 days total therapy

Counseling: Natural History

- Recurrent episodes likely following a first episode; with HSV-2 more than HSV-1
  - Frequency of outbreaks may decrease over time
  - Stressful events may trigger recurrences
  - Prodromal symptoms may precede outbreaks

- Asymptomatic viral shedding is common and HSV transmission can occur during asymptomatic periods

Human Papillomavirus (HPV)

What is HPV ?

- HPV stands for the Human papillomavirus.
- HPV is the most common family of viruses.
- HPV is the most common sexually transmitted infection.
- Chances are you will contract some form of the HPV virus in your lifetime and not have any signs or symptoms.

So Why Worry About HPV?

- There are over 100 different types of the HPV virus - most types are totally harmless.
- Over 30 types of the HPV virus are sexually transmitted and affect the area between the genitals and the anus.
- Some types are considered “low risk” and can cause warts on the anus, vagina, vulva, penis and thighs.
- Other types are considered “high risk” and can cause pre-cancerous lesions and can lead to cancer of the cervix, anus and other genital areas.

How Do You Get HPV?

- Anyone who has ever had a sexual encounter, even without penetration, can contract HPV.
- Most common transmission is by skin-to-skin contact with the penis, scrotum, vagina, vulva, or anus of an infected person.
- Kissing or touching a partner's genitals with the mouth can also transmit the HPV virus.

How Do You Know You Have HPV?

- There are no tests to detect the HPV virus.
- Most people who contract HPV will never know they have it.
- Having HPV does not mean you have a disease – most people don't have any signs or symptoms.
- Some low risk types cause genital and anal warts.
- In rare instances, the virus persists, especially the high risk types of the HPV virus that can develop pre-cancerous lesions and cancer.

What Are Genital Warts?

- Genital warts are unsightly cauliflower-like growths.
- In women, genital warts can appear on the vulva, urethra, cervix, vagina, anus or thighs.
- In men, warts can appear on the penis, scrotum, anus or thighs.
- Genital and anal warts are very contagious and are spread during oral, vaginal or anal sex with an infected partner.

What If You Have Genital or Anal Warts?

- Genital and anal warts sometimes disappear without treatment.
- Sometimes genital warts last for years.
- There are many treatments that can be done at home or in your doctor's office.
- On average it takes about 8 months to get rid of warts.
- Genital and anal warts can sometimes come back.

Genital Warts: Appearance

- Condylomata acuminata
  - Cauliflower-like appearance
  - Skin-colored, pink, or hyperpigmented
  - May be keratotic on skin; generally non-keratinized 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

- Warts 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.
- Patients with visible warts can be simultaneously infected with multiple HPV types.

Genital Warts: Symptoms

- Genital warts usually cause no symptoms other than the warts themselves.
- Vulvar warts--dyspareunia, pruritis, burning discomfort
- Penile warts--occasional itching
- Urethral meatal warts--occasional hematuria or impairment of urinary stream
- Vaginal warts--usually asymptomatic; occasional discharge/bleeding, obstruction of birth canal (secondary to increased wart growth during pregnancy)
- Perianal warts--usually asymptomatic; pain, bleeding on defecation, itching
- Most patients have fewer than 10 genital warts, with total wart area of 0.5-1.0 $cm^{2.}$

Genital Warts: Duration

- May regress spontaneously or persist with or without proliferation.
  - Frequency of spontaneous regression is unclear.
  - Persistence of infection occurs, but frequency and duration are unknown.
  - Recurrences after treatment are common.

HPV & Cancer

- High risk types of the HPV virus are linked to cervical cancer as well as cancers of the penis, of the anus and other genital cancers.
- In women, pre-cancerous cells can be detected in the cervix by a Pap test.
- It is unlikely that a young girl will be diagnosed with cervical cancer as it takes many years for a cancer to develop.

What is a Pap Test ?

- A Pap test is an examination of a woman's internal genital organs.
- It is the only way to detect abnormal cells in the cervix that could potentially develop into cancer later in life.
- A girl should have her first Pap test within 3 years of becoming sexually active.

Screening

- PAP Smear
  - Detects precancerous cells
  - Should begin by age 21 or within 3 years of onset of first sexual intercourse
- If abnormal
  - HPV DNA testing
  - Colposcopy and Biopsy

Can You Prevent HPV?

1. Absolutely no skin-to-skin sexual contact.
2. One sexual / intimate partner forever.
3. The more sexual partners, the higher the chance of contracting HPV.

Can You Prevent HPV?

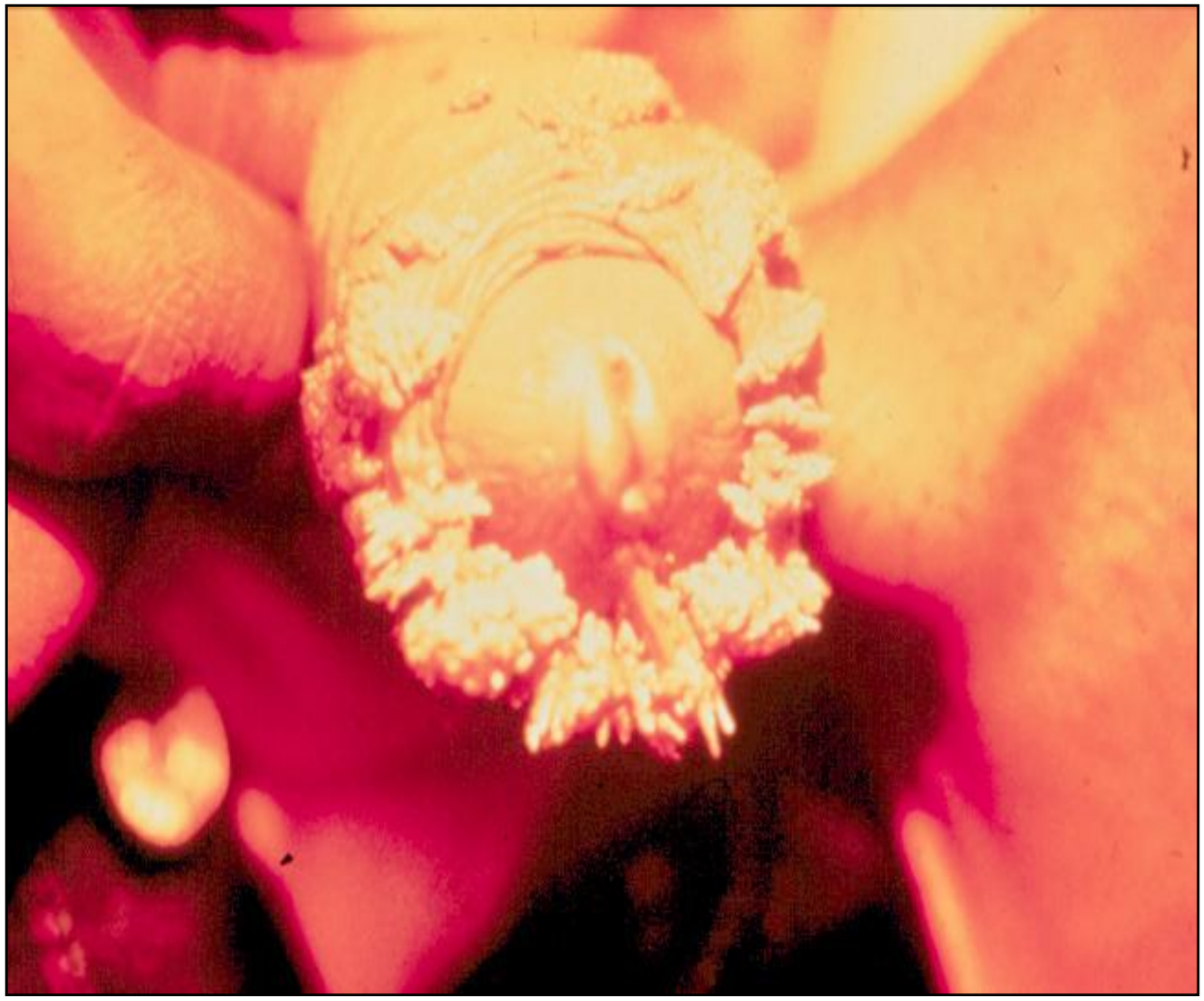
4. Using condoms is excellent protection against STI, but does not cover all the skin.

5. Pap testing will detect abnormal cells.

6. Vaccination is now available to prevent certain low risk types that cause genital warts certain high risk types that cause cancer.

Female HPV

Male HPV infection



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

Source: Cincinnati STD/HIV Prevention Training Center

Intrameatal Wart

Source: Cincinnati STD/HIV Prevention Training Center

Differential Diagnosis of Genital Warts (continued)

- 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)

General Treatment of Genital Warts

- Primary goal is removal of symptomatic 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 eradicate infectivity.
- Effect of current treatment on future transmission is unclear.

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 rather than a single treatment.
  - Evaluate the risk-benefit ratio of treatment throughout the course of therapy to avoid over-treatment.
- 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

- Up to 2/3 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.

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

CDC-Recommended Alternative Regimens

- Intralesional interferon

OR

- Laser surgery

Routine HPV Vaccination Recommendations

- ACIP recommends routine vaccination of females 11 or 12 years of age
- The vaccination series can be started as young as 9 years of age at the clinician's discretion
- "Catch-up" vaccination recommended for females 13 through 26 years of age

***MMWR* 2007;56(RR-2):1-24**

HPV Vaccination Schedule

- Routine schedule is 0, 2, 6 months
- Third dose should follow the first dose by at least 24 weeks
- An accelerated schedule using minimum intervals is not recommended
- Series does not need to be restarted if the schedule is interrupted

Human Papillomavirus Vaccine

- Quadrivalent HPV vaccine is not currently* approved for males, or for females younger than 9 years or older than 26 years

- Studies of safety and efficacy among males and females older than 26 years are ongoing

***as of May 2009**

HPV Vaccine
Special Situations*

- Equivocal or abnormal Pap test
- Positive HPV DNA test
- Genital warts
- Immunosuppression
- Breastfeeding

***Vaccine can be administered**

HPV Vaccine
Adverse Reactions

- Local reactions 84%
  (pain, swelling)
- Fever 10%*
- No serious adverse reactions reported

***similar to reports in placebo recipients (9%)**

Syncope Following Vaccination

- An increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS)
- 11-18 year old females have contributed most of the increase
- Serious injuries have resulted
- Providers should strongly consider observing patients for 15 minutes after they are vaccinated

HPV Vaccine
Contraindications and Precautions

- Contraindication
  - Severe allergic reaction to a vaccine component or following a prior dose
- Precaution
  - Moderate or severe acute illnesses (defer until symptoms improve)

HPV Vaccination During Pregnancy

- Initiation of the vaccine series should be delayed until after completion of pregnancy
- If a woman is found to be pregnant after initiating the vaccination series, remaining doses should be delayed until after the pregnancy
- If a vaccine dose has been administered during pregnancy, there is no indication for intervention

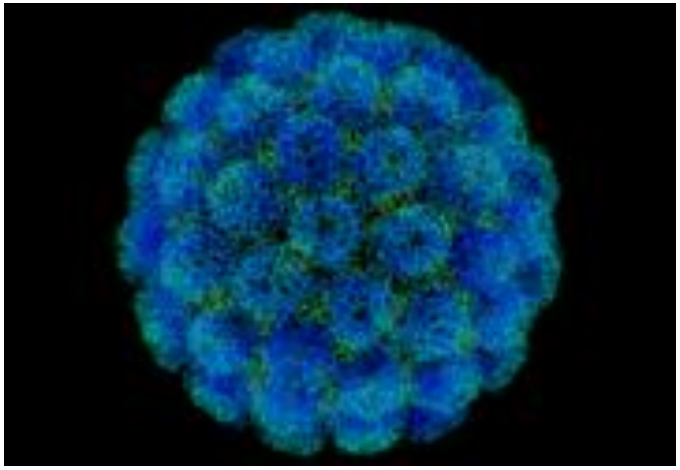
…And Now The Good News

- 70% of women infected with HPV clear the infection through natural means within two years.
- It may take 10 to 15 years for an HPV infection to develop into cancer.
- Vaccines are currently in development against oncogenic strains.

Polyoma Viruses

- 2 major clinical manifestations are known
  - BK virus
  - JC virus
  - both of these are members of the papovaviridae family
- JC virus is primarily associated with progressive multifocal leukoencephalopathy in AIDS pt's
- BK virus is primarily associated with nephropathy and ureteral obstruction
- Both are asymptomatic infections acquired in childhood that remain latent

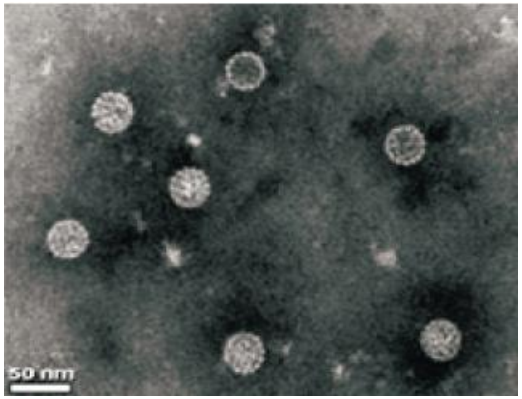
BK virus



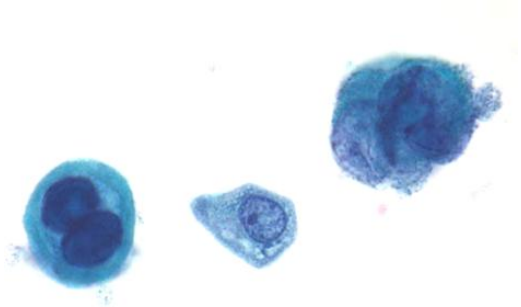
BK virus

- A human polyomavirus;

  non-enveloped, DNA virus
- Seroprevalence in adults is between 60 – 80%
- primary infection in childhood
- latent infection in renal tubules and urothelial cells
- Reactivation, mostly asymptomatic viruria, with decoy cells in urine



BK virus



Decoy cells

BK virus

- First recognized in 1971, not truly appreciated until mid 1990's when recognized as a cause for renal allograft loss (~5% incidence)

- Has a tropism for the urogenital tract, tends to affect "diseased" kidneys

- Clinical manifestations
  - asymptomatic hematuria
  - hemorrhagic cystitis
  - ureteral stenosis
  - interstitial nephritis (nephropathy)

Epidemiology

- Estimated that 80-90% of adult population has been exposed to BK virus
- Probably multiple routes of transmission, but respiratory secretions predominate
- Primary infection may be asymptomatic, mild URI, cystitis…
- Enters latent phase, in urogenital tract, lymphoid tissue, brain

Pathogenesis

- BK replication (viruria) occurs during states of immune suppression
  - Pregnancy
  - Malignancy
  - HIV
  - Diabetes
  - Transplantation
- Viremia (13-20%) & nephropathy (5-8%) are unique to the post-kidney transplant setting

BK virus

- Viruria can be detected in many populations, but the most clinically important is renal transplant recipients
- Exact pathogenesis of the infection is poorly understood
- Diagnosis must be made histologically (biopsy)
  - Special stains and PCR can help solidify the diagnosis

BK virus

- Treatment
  - Only effective therapy is immune reconstitution (i.e. reduction of immunnosuppressant therapy)
  - Cedofivir and leflunomide are effective in reducing viral load, but do very little to change the course of disease, and are both nephrotoxic

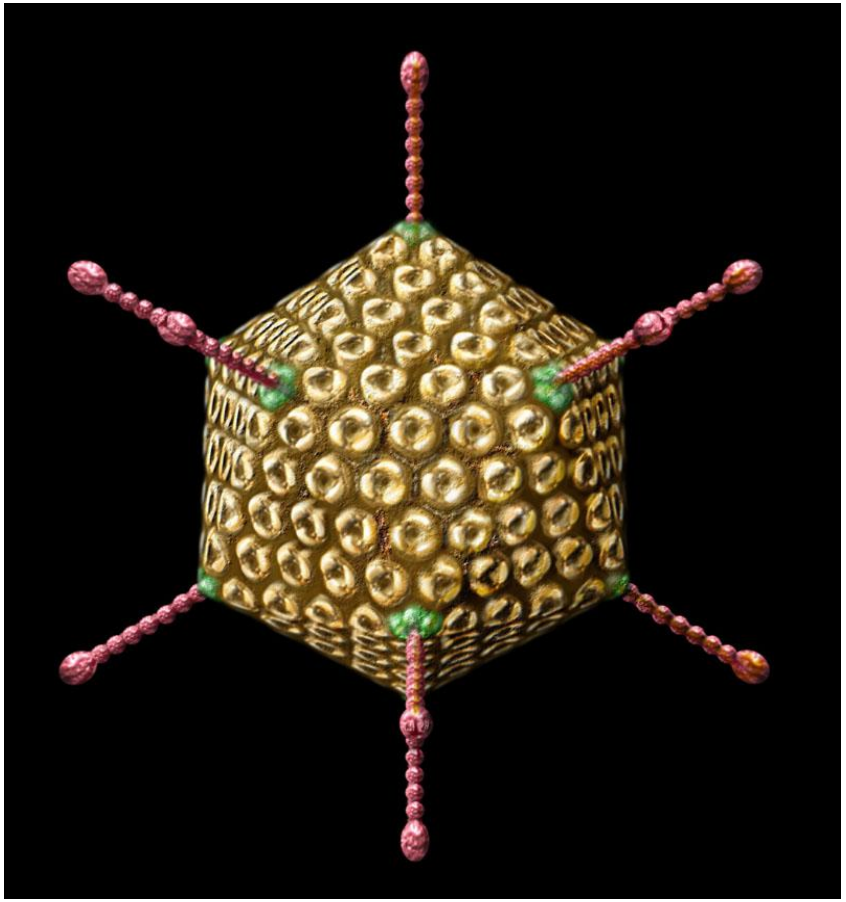
- One must effectively walk the tightrope between progressive renal destruction secondary to infection, and acute rejection causing graft loss

BK virus

- Several case reports exist for BK nephropathy in non-renal transplant recipients
  - Bone marrow
  - Heart
  - Lung

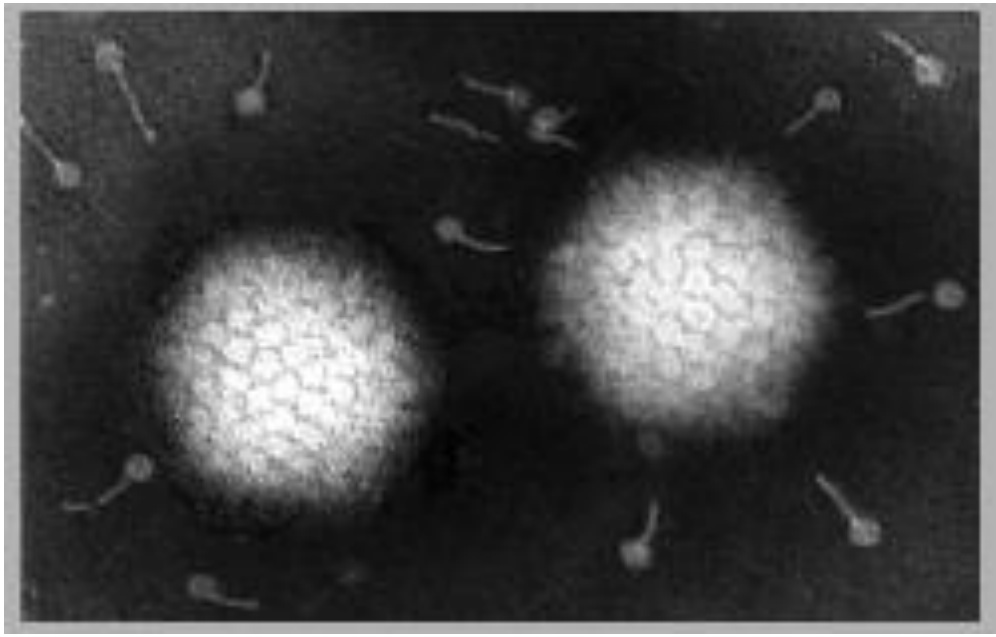
- However, these are rare, and are at level of case report

Adenovirus



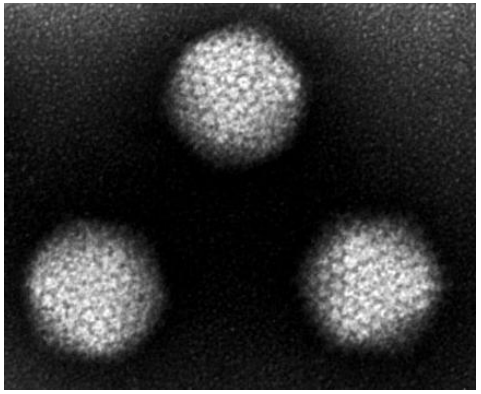
Adenovirus

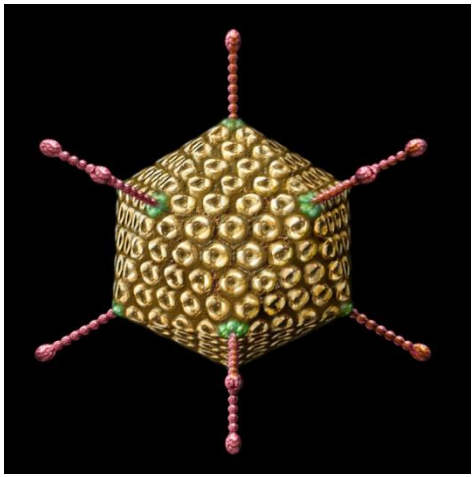
- A group of viruses that infect the membranes (tissue linings) of the respiratory tract, the eyes, the intestines, and the urinary tract, adenoviruses account for about 10% of acute respiratory infections in children and are a frequent cause of diarrhea.



Adenoviruses

- Non-enveloped, DNA viruses; capsid formed by hexons and pentons, fibres project from penton bases
- 51 serotypes grouped into 6 species (formerly sub-groups), A to F
- Primary infection with one or serotype in childhood; site of latency uncertain
- Many serotypes cause disease in immunocompromised patients
- commonest are 1, 2 and 5 (species C) and 34 and 35 (species B)





Adenoviruses

Species	Tissue tropism	Serotypes
A	Gastrointestinal tract	12, 18, 31
B	Urinary tract, lung	3, 7, 11, 14, 16, 21, 34, 35, 50
C	Respiratory tract	1, 2, 5, 6
D	Eye, gastrointestinal tract	8-10, 13, 15, 17, 19, 20 22-30, 32, 33, 36-39, 42-49, 51
E	Respiratory tract	4
F	Gastrointestinal tract	40,41

Leen AM, Rooney CM, Br J Haematol 2005; 128: 135-144

Diseases caused by Adenoviruses

Group Affected	Syndromes	Serotypes
Neonates	Fatal disseminated infection	3, 7, 21, 30
Infants	Coryza, pharyngitis	1, 2, 5 (C)
Children	Upper respiratory disease Pharyngoconjunctival fever Hemorrhagic cystitis Diarrhea Intussusception Meningoencephalitis	1, 2, 4-6 3, 7 (B) 7, 11, 21 (B) 2, 3, 5, **40**, **41** (F) 1, 2, 4, 5 2, 6, 7, 12
Young adults	Acute respiratory disease and PNA	3, 4, 7
Adults	Epidemic keratoconjunctivitis	8, 19, 37 (D)
Immunocompromised patients	PNA with dissemination Liver infection Urinary Tract Infection Intestinal Infection CNS disease including encephalitis	5, 31, 34 1, 2, 5 (C) 35, 39 42-51 (D) 7, 12, 32

Diseases caused by Adenoviruses

Groups Affected	Diseases	Serotypes
HSCT	Gastroenteritis, pneumonitis, hepatitis, hemorrhagic cystitis, encephalitis, disseminated disease	1-3, 5, 7, 11, 31
Liver transplant	Gastroenteritis, hepatitis pneumonitis, disseminated disease	1, 2, 5, 7, 31
Renal transplant	Hemorrhagic cystitis, pneumonitis, GI disease	11, 34, 35
Lung transplant	Pneumonitis, disseminated diseases	2, 5

Adenoviruses

- Adenovirus infections are common in HSCT with reported rates of 5 – 29%
- Incidence higher in children and time of diagnosis is earlier than in adults (less than 30 days cf. more than 90 days)
- Variation in reported rates may be due to:
  - Differences in patient groups (adults/children)
  - Conditioning regimes
  - Diagnostic tests used
  - Testing protocols
  - Lack of accepted case definitions for infection/disease

Adenovirus Vectors

- Vaccine production
  - HIV
  - Malaria
  - Ebola
  - Hepatitis C
  - TB

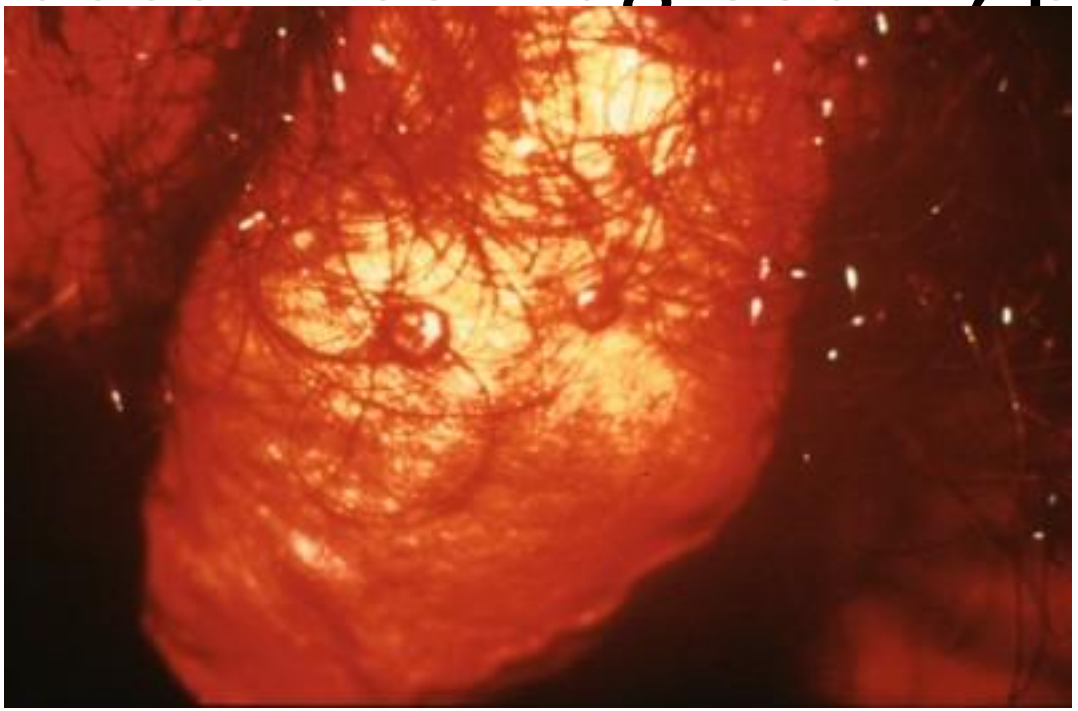
Poxviruses: Parapox

- Molluscum contagiousum
  - Umbilicated firm cutaneous
  - May be more persistent in immunocompromised adults
  - Typically is treated with curettage or cryotherapy.

Molluscum contagiosum

Molluscum contagiosum, vulva and

Molluscum contagiosum, penis



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