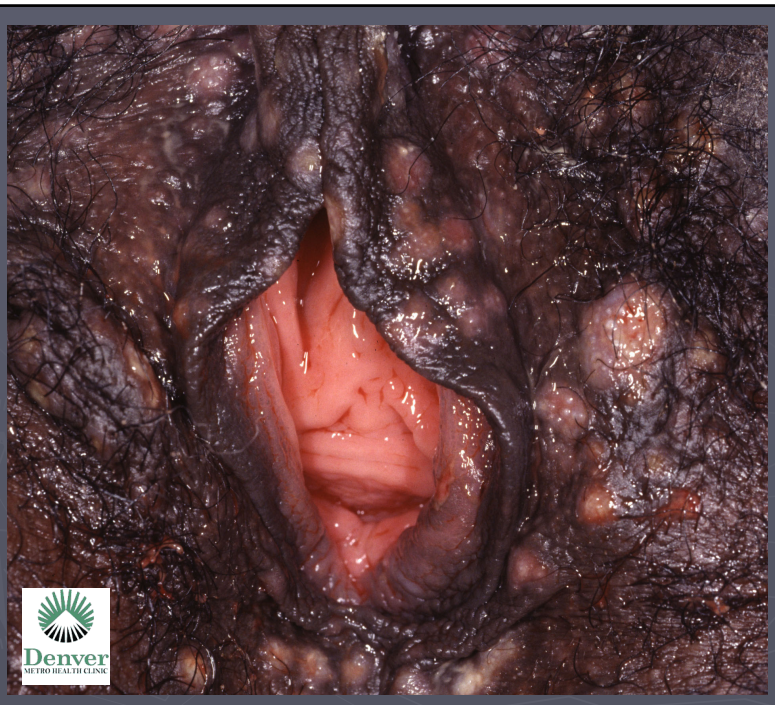
Case

- 28 year-old woman
- Complains of very painful lesions in vulvar area
- Increasing severity since 4 days
- Pain aggravated by urination
- She has a slight fever and also complains of headache and photophobia



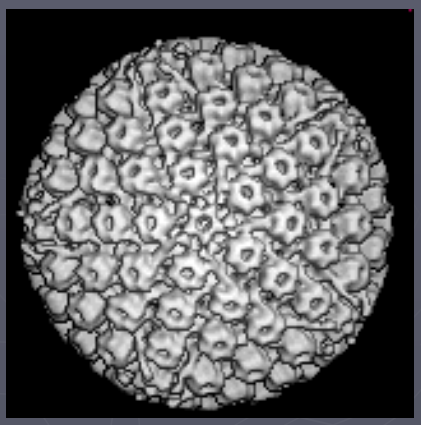
Case 1

- History negative for STI
- In monogamous relationship with husband
- Pt not aware of genital or oral lesions husband
- Both tested HIV negative 6 months ago

Case 1

- Physical exam
  - Multiple erosive lesions vulva on both sides of labia minora
  - Extremely painful to the touch
  - Bilateral inguinal lymphadenopathy

How to proceed?



Genital Herpes

Genital Herpes

- HSV is most common cause of GUD
- Mucocutaneous retrograde infection along sensory nerves characterized by:
  - Recurrent localized vesicular eruption
  - Latent infection in cranial nerve or dorsal ganglia

Genital Herpes

- Two variants
  - HSV-2
    - Most commonly associated with genital herpes
  - HSV-1
    - Most commonly associated with oral/labial herpes
    - However, increasing (up to 25%) cause of genital herpes

Clinical Presentation of Genital HSV

- First Episode Infection
  - Primary: First infection with HSV-1 or -2 (20%)
  - Non-primary: Prior infection with opposite type (40%)
  - First clinical episode of longstanding infection (40%)
- Recurrent genital herpes: second or subsequent recognized outbreak
- Subclinical infection: ~ 60-90% of infections
  - Truly asymptomatic
  - Unrecognized

Primary HSV-2

Transmission of Genital HSV

- Requires contact of viable HSV and abraded skin/mucous.
- More efficient during primary than recurrent episodes due to higher viral titer
- Can be transmitted from asymptomatic patients
- HSV antibody (prior HSV-1 infection) may offer partial protection against acquisition, although more consistent effect is reducing/preventing symptoms
- Fomite transmission extremely rare
- Incubation period after acquisition: 2-28 days

First Episode Genital Herpes

- More severe in those without prior HSV infection
  - Vesiculopustular lesions
  - Cervicitis, urethritis
  - Lymphadenopathy
  - Neuropathic manifestations
  - Systemic manifestations (fever, headache, etc.)
- Progression of lesions: papules → vesicles → (pustules) → ulcers → crusts → healed
- Local Symptoms last 10-21 days
- Systemic symptoms in 40 - 70%
  - Fever, headache, malaise, myalgias

Recurrent Infection

- 90% of patients with symptomatic primary genital HSV-2 have symptomatic recurrences within 12 months
  - Median recurrence rate 4.5 episode/yr
    - Males: 5.2 episodes/yr
    - Females: 4.0 episodes/yr
  - 38% > 6 episodes / yr
  - 20% > 10 episodes / yr
- Often heralded by prodrome:
  - Tingling, itching, burning (neuralgia)

Recurrent Infection

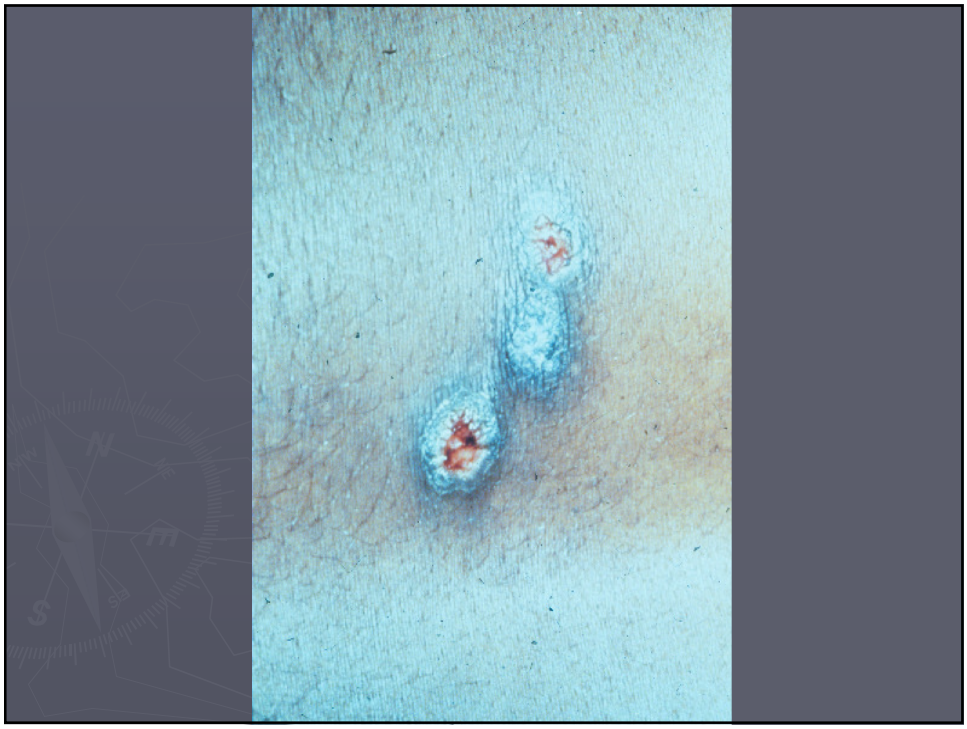
- Rate gradually declines over several years
- Recurrence after initial HSV-1 infection (n=83)
  - 1.3 in Year 1
  - 07. in Years 2 and beyond
  - 38% had no recurrences

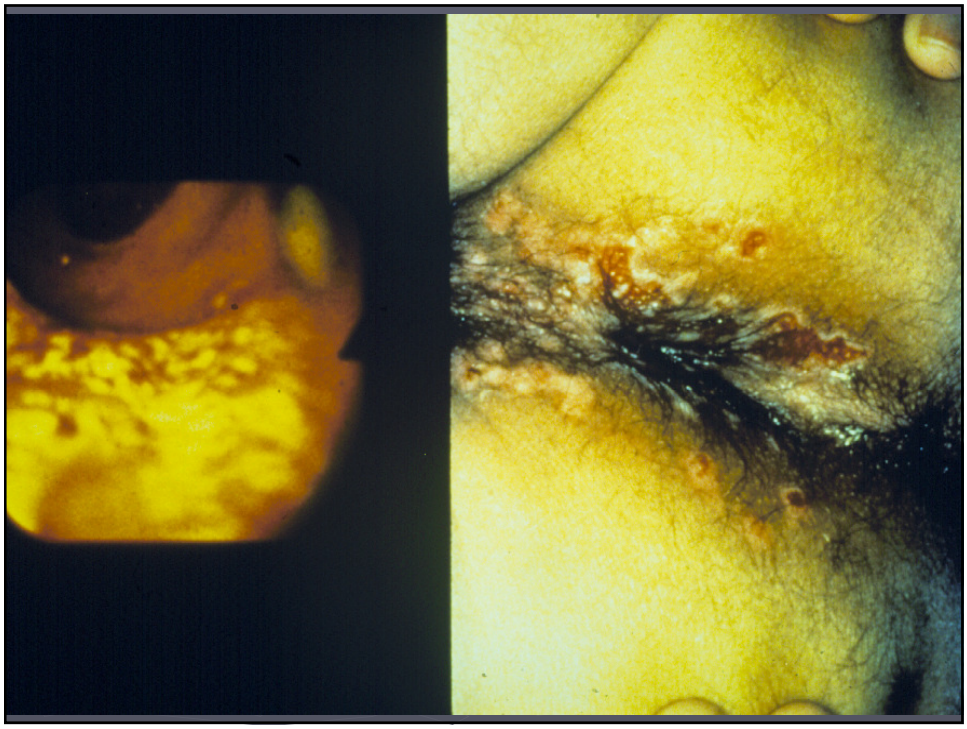
Primary HSV-2


STD/HIV
Training
Center

Recurrent gluteal HSV-2

From Genital Skin Disorders, Fisher & Margesson, 1998



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Herpes
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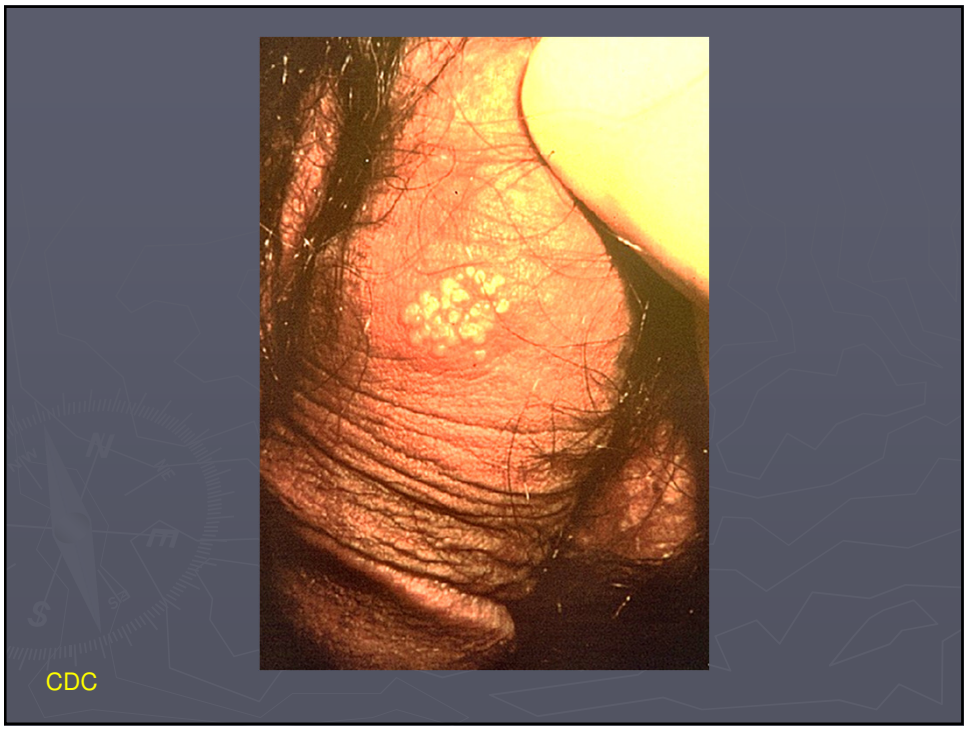

CDC

Predictors of Recurrent Genital Herpes

- HSV-2 > HSV-1
- Prolonged primary episodes
- No good data to support role of
  - Stress
  - Diet
  - Menstruation

Asymptomatic Genital HSV-2

- 25-40% of sexually active adults in the U.S. are HSV-2 Antibody positive
  - 50% with no history of clinical genital herpes
- Asymptomatic infections can recur symptomatically
  - Majority (65%) will note lesions after education/counseling

HSV Viral Shedding

- HSV-2 shedding
  - Occurs in 60-65% of both symptomatic and asymptomatic patients
  - Similar in women and men
  - Occurs on 3% (0-15%) of asymptomatic days
  - Most common within first year of primary symptomatic herpes (5-6% of days)
  - Low probability of transmission, but responsible *for the majority* of new genital HSV-2 infections
- HSV-1 shedding
  - Relatively uncommon

Genital Herpes - Diagnosis

- Ulcer
  - Culture
  - PCR (including multiplex PCR)
  - Cytology (Tzanck): insensitive - don't use
- Serology
  - Based on glycoprotein G
  - Type-specific
  - Caveat: Because of high HSV-2 sero-prevalence, the negative predictive value of serology is greater than the positive predictive value in the differential diagnosis of GUD

Are serologies useful?

- Type specific (Glycoprotein G1 and G2) have relatively good sensitivity and specificity 92-98%
- Immunity noted to wane over time
  - HSV 2 >> HSV 1
- HSV immunity waned in up to 20% of persons with confirmed HSV 2 infection (assay variable)

HSV: management of first episode

- HSV-2 vs. HSV-1
- Antiviral therapy
  - Acyclovir 400 mg tid x 7-10 d
  - Acyclovir 200 mg 5x/d x 7-10 d
  - Famcyclovir 250 mg tid x 7-10 d
  - Valacyclovir 1 g bid x 7-10 d
  - Rx may be extended if healing is incomplete after 10 d

HSV: management of first episode

- Counseling
  - Natural history of genital herpes
    - Potential for recurrent episodes
    - Asymptomatic viral shedding
    - Sexual transmission
  - Sexual and perinatal transmission
    - Sexual transmission can occur during asymptomatic periods
    - Risk of neonatal infection should be explained. Patient should inform the HCW caring for her during pregnancy
  - Methods to reduce transmission
    - Abstain from sexual activity when symptomatic
    - Inform sex partners
    - Use of condoms

Herpes

- Episodic vs suppressive
  - Multiple options
    - Acyclovir generic
    - Valacyclovir and famciclovir less frequent dosing schedules
- Discordant couples- considerations
- Type specific serology
  - Glycoprotein G1 (HSV 1) and G2 (HSV 2)

Episodic antiviral therapy

- Might shorten the duration of symptoms
  - If initiated during the prodrome or within 24 h of lesions- sooner the better
  - Pt should have prescription and/or drug supply
    - Acyclovir 400 mg tid x 5 d
    - Acyclovir 200 mg 5x/d x 5 d
    - Acyclovir 800 mg bid x 5 d
    - Famcyclovir 1000 mg bid x 1 d
    - Valacyclovir 500 mg bid x 3 d

Suppressive antiviral therapy

- Can ameliorate or prevent recurrent outbreaks
  - Not associated with resistance in immunocompetent pts
  - Reduces asymptomatic viral shedding/ discordant couples
  - Consider DC after 1 yr
    - Acyclovir 400 mg bid
    - Famcyclovir 250 mg bid
    - Valacyclovir 250 mg bid
    - Valacyclovir 500 mg qd
    - Valacyclovir 1 g qd

Some experts recommend discontinuing acyclovir after one year of continuous use so that the recurrence rate can be reassessed. The lowest continuous dose that will suppress recurrences in an individual can only be determined empirically

Topical Acyclovir or Penciclovir for HSV Treatment

- Ineffective: do not use

Genital Herpes Why a Public Health Issue?

- Significant morbidity both physically and psychologically
- Neonatal Herpes
  - Relatively rare
  - Most common when primary infection occurs in vulvo/vaginal region around time of delivery
  - Significant neonatal morbidity and mortality
- Co-factor in HIV transmission

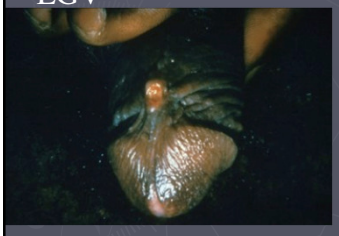
Differential of GUD

- Herpes Simplex Virus (painful)
- Syphilis (usually painless)
- Chancroid (painful)
  - -Haemophilus ducreyi.
- Granuloma Inguinale (painless)
  - Klebsiella granulomatis…formerly Calymmatobacterium granulomatis
- LGV (painless)
  - Chlamydia trachomatis (L1-L3)
- Fixed drug eruption
- Trauma
- Autoimmune
  - Behcet's
  - Reactive Arthritis Syndrome

GUD pictures

Chancroid

LGV



Granuloma inguinale

Syphilis

HSV

Non Infectious GUD

Reactive Arthritis Syndrome

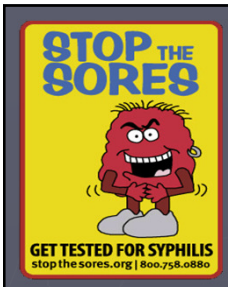
Behcet's Syndrome

Epidemiological Synergy

- Co-infection with HIV prolongs the infectiousness on STDs
- STDs facilitate HIV transmission by increasing genital HIV-RNA/DNA levels
- STDs facilitate HIV acquisition by disrupting epithelial barriers and attracting inflammatory cells
  - GUD increases risk of HIV acquisition 8 fold

Evidence for Genital Tract Compartmentalization

- HIV-1 RNA/DNA detected in semen and CVL across a wide range of plasma levels
- No absolute level of plasma viral load at which genital secretions are undetectable
- Genital levels may be higher than plasma levels or vice versa
- Genotypic differences may exist between plasma and genital virus



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ABCs of Syphilis Serology

- Non treponemal screening blood test
  - VDRL- Venereal Disease Reporting Laboratory
  - RPR-Rapid Plasma Reagin
- Treponemal Blood Tests (confirmatory)
  - TPPA- T. pallidum particle agglutination assay
  - TPHA- T. pallidum hemaglutination assay
  - FTA-ABS- Fluorescent Treponemal Antibody-Absorption
  - MHA-TP-Microhemaglutination assay
  - EIA-Enzyme Immunoassay
  - CLIA/CIA-Chemiluminescense Immunoassay