Sexually Transmitted Infection: A Case Based Update

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Case # 1

A 25 year old MSM presents to your clinic with the complaint of a painless ulcer on his penis (pictured).

Question # 1

The pathogen most likely responsible for this is:

A. Herpes Simplex  
B. Chlamydia Trachomatis  
C. Treponema Pallidum  
D. Human Papilloma Virus
**ANSWER #1**

The pathogen most likely responsible for this is:

C. *Treponema pallidum*

*T. pallidum* is the spirochete (a bacterium) that causes syphilis, the topic of the first case based discussion.

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**Syphilis**

*Treponema pallidum*

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**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
Granuloma inguinale
Syphilis
LGV
HSV

Non Infectious GUD

Reactive Arthritis Syndrome
Behcet’s Syndrome

Bad News 2001

- P&S syphilis cases increased in 2001
- Increase in men
  - 3.5 fold higher
  - >40% of cases in MSM
- Decrease in women and non-Hispanic blacks
- Similar increase in rate and M:F ratio
- No clear effect on HIV or GC transmission
  - Interpret with caution!
Syphilis — Reported cases by stage of infection: United States, 1941–2006

Increase in syphilis by 11% Between 2005-2006

Primary and secondary syphilis by Sex and Sexual activity

64% of cases in MSM

Recognize syphilis

- Primary
  - Chancre
  - 3 week incubation
  - Non tender
  - Indurated
  - Non-purulent
  - Heal with no Rx
Case #2

Your patient reports that he has one sexual partner, who is luckily waiting in the waiting room for him. He comes to be evaluated and reports that he does not recall a genital ulcer, but that he does have a rash around his anus (pictured).

Syphilis testing is pending.

Question #2

The differential diagnosis of these lesions includes:
A. Condyloma acuminatum
B. Herpes Simplex
C. Condyloma lata
D. Skin tags
E. A and B
F. A and C
G. None of the above

ANSWER #2

The differential diagnosis of these lesions includes:
F. A and C

Condyloma lata—a secondary syphilitic eruption of flat-topped papules, found at the anus and wherever contiguous folds of skin produce heat and moisture

Condyloma acuminatum—a warty growth on the external genitals or at the anus, consisting of fibrous overgrowths covered by thickened epithelium showing koilocytosis, due to sexually transmitted infection with human papilloma virus; malignant change is associated with particular types of the virus.
Recognize syphilis

- Secondary
  - 4-10 weeks after chancre
  - Disseminated rash
    - Macular
    - Protean
    - Usually NOT vesicles
  - Protean Manifestations

The Great Imposter!

- Fever
- Malaise
- Sore throat
- Mucous patch
- Meningismus
- Condyloma lata
- Uveitis
- Proctitis
- Alopecia

Natural History
Types of Syphilis Serologic Testing

  - Rapid Plasma Reagin (RPR)
  - Venereal Disease Research Lab (VDRL)
  - Toluidine Red Unheated Serum Test (TRUST)
- Treponemal Test: Detection of anti T. pallidum antibodies. Qualitative (pos or neg)
  - Fluorescent treponemal antibody absorption (FTA-ABS)
  - Microhemagglutination test (MHA-TP)
  - Treponema pallidum particle agglutination assay (TP-PA)
  - Treponema pallidum enzyme immunoassay (TP–EIA)

Making the Diagnosis

- Clinical
- Darkfield & DFA—rarely done
- Nontreponemal Test
  - RPR or VDRL
  - Sensitivity
    - Primary 78-86%
    - Secondary nearly 100%
    - Latent 95-98%
    - Prozone effect
- Treponemal Test for confirmation
- New syphilis IgG tests... special caution
Testing Algorithms

- Traditional: Start with non-treponemal test; if positive confirm with treponemal test. If treponemal test was negative...false pos non treponemal test
- Non Traditional:
  - Low cost automated Treponemal IgG led to REVERSAL of testing in high throughput labs in NYC
  - Treponemal Testing (IgG) first
  - Then Non-Treponemal Testing
  - Has led to new patterns of testing that are often confusing.

NYC Experience

Complex interpretation
- 6% of tests Syphilis IgG +
- 56% RPR non reactive!
- 83% of RPR NR were positive using a second treponemal test!
  - Treatment indicated if no history of treatment
- 17% of RPR NR were negative for a second test
  - No treatment OR
  - A third treponemal test to resolve issue

So what do I do?
- Know the algorithm at your lab
  - Traditional or non-traditional?
- Obtain patient history of prior testing and treatment

<table>
<thead>
<tr>
<th>INTERPRETATION/ACTION</th>
<th>TP IgG</th>
<th>RPR</th>
<th>TPPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current or Past Syphilis (treated or untreated)—treat if not treated or indicated by RPR titer if prior rx</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
</tr>
<tr>
<td>Current or Past Syphilis (treated or untreated)—treat if not treated</td>
<td>POS</td>
<td>NEG</td>
<td>POS</td>
</tr>
<tr>
<td>No Syphilis</td>
<td>NEG</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>More testing? Probably Negative</td>
<td>POS</td>
<td>NEG</td>
<td>NEG</td>
</tr>
</tbody>
</table>
Case #2a

The patient with the lesions around his anus has a positive Tp-IgG and an RPR that is NR. His TPPA is also positive. He had been treated with one shot of penicillin based on his exposure to the patient from Case #1 and the possibility of condyloma lata. You are convinced that this is a manifestation of the secondary stage of syphilis.

He had a prior negative syphilis test (IgG) 6 months ago.

Question #2a

The reason that the RPR is non-reactive is likely because:

A. A false positive result on the IgG and TPPA
B. The lab needs to dilute the RPR to check for the prozone effect
C. The RPR is not a good test
D. The penicillin that he was given on the day of the test made the RPR non-reactive

ANSWER #2a

The reason that the RPR is non-reactive is likely because:

B. The lab needs to dilute the RPR to check for the prozone effect
ANSWER #2a

- The prozone reaction refers to nonvisualization of agglutination, which normally occurs when antigen and antibody bind together to form a complex.
- When antibody titers are high (as in secondary syphilis), an overabundance of antibodies interferes with clumping of antigen-antibody complexes.
- Experienced laboratory technologists may suspect the prozone phenomenon when an apparent nonreactive test exhibits a rough or granular appearance.
- When such a specimen is diluted, sufficient agglutination can be seen and the true sample reactivity becomes apparent.

Question #2b

Is one IM shot of Benzethine Penicillin G at 2.4 million units enough to treat this stage of syphilis?

A. Yes
B. No
C. I’m not sure

ANSWER #2b

Is one IM shot of Benzethine Penicillin G at 2.4 million units enough to treat this stage of syphilis?

A. Yes
Treatment of Syphilis

- **Primary, secondary, early latent**
  - Benzathine penicillin G 2.4 million units IM x 1
  - 2nd line: doxycycline 100mg PO BID x 14 days
  - Early latent defined as <1y
  - Evidence that azithromycin 2000mg is effective

- **Late latent, unknown duration, tertiary**
  - Benzathine penicillin G 2.4 million units IM q week x 3
  - 2nd line: doxycycline 100mg PO BID x 28 days

- **Neurosyphilis, eye and ear disease**
  - Aqueous crystalline penicillin G 18-14 MU/day div q 4 x 10-14 d
  - Procaine Penicillin 2.4 MU IM QD + probenecid 500mg PO QID x 10-14 days
  - Desensitize penicillin allergic patients

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**Question #2c**

Would you have given this contact of a current case of primary syphilis (remember the chancer from case #1??) a single dose of penicillin on your first meeting with him?

A. Yes  
B. No  
C. I would wait for his syphilis testing  
D. I don’t know

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**ANSWER #2c**

Would you have given this contact of a current case of primary syphilis (remember the chancer from case #1??) a single dose of penicillin on your first meeting with him?

A. Yes
Exposed Individuals

- Persons who were exposed within the 90 days preceding the diagnosis of primary, secondary, or early latent syphilis in a sex partner might be infected even if seronegative; therefore, such persons should be treated presumptively.
- Persons who were exposed >90 days before the diagnosis of primary, secondary, or early latent syphilis in a sex partner should be treated presumptively if serologic test results are not available immediately and the opportunity for follow-up is uncertain.
- Contacts of unknown duration patient with titer >1:32 should be considered exposed.
- Sexual partners of infected patients should be considered at risk and provided treatment if they have had sexual contact with the patient within 3 months plus the duration of symptoms for patients diagnosed with primary syphilis, 6 months plus duration of symptoms for those with secondary syphilis, and 1 year for patients with early latent syphilis.

Case #3a

An HIV positive woman with T cells of 400 was screened for syphilis and was found to have the following pattern of results:

<table>
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<tr>
<th>TP IgG</th>
<th>RPR</th>
<th>TPPA</th>
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<tbody>
<tr>
<td>POS</td>
<td>1:16</td>
<td>POS</td>
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</table>

Prior syphilis testing 11 months ago was negative. She has no neurologic or ocular symptoms in her history, nor did she have any findings on her exam.

Question #3a

Should this patient have a lumbar puncture:
A. Yes, all HIV infected people with syphilis should have an LP
B. No, her T cells are too high and her RPR is too low to predict neurological involvement
C. No, she is early latent
D. No, she has no neurological symptoms
E. B, C, and D in combination
ANSWER #3a

Should this patient have a lumbar puncture:
E. B, C, and D in combination

To tap or not to tap

- Neurologic/Ocular symptoms or signs
- Late latent or unknown duration in HIV+ (guidelines)
- HIV CD4<350 RPR > or = 1:32
- Active tertiary syphilis
- Failure of therapy in non-neurosyphilis
- What is a + CSF? NOT STANDARD
  - HIV+
    - + CSF FTA-Ab with no visible blood contamination
    - And <5-20 WBC
    - Alternative: CD4<350, RPR>1:32
  - HIV Neg
    - + CSF FTA-Ab
    - And EITHER CSF pleocytosis OR elevated protein >45

Case #3b

The patient from case #3 was treated with one shot of 2.4 million units of penicillin and returned for follow up testing at 3, 9, and 24 months. Her RPR results were:
At treatment- 1:16
Month 3- 1:8
Month 9- 1:8
Month 24- 1:64

She has not had any sexual partners since being treated.
Question # 3b

This increase in titer:
A. Represents a serofast state, we should do nothing but observe
B. The patient is possibly re-infected
C. The patient may have experienced treatment failure because of inadequate therapy for her stage of treponemal disease
D. The patient may have asymptomatic neurosyphilis and should have a lumbar puncture.
E. B, C, and D are all possible

ANSWER # 3b

This increase in titer:
E. B, C, and D are all possible

Follow Up

• Repeat non-treponemal test at 6 and 12 months in HIV negative patients
• HIV positive should have titer checked at 3, 9, and 24 months
• If Neurosyphilis, repeat CSF 3, 6 and then q 6 months until normal
Failure

- Treatment failure definition
  - Signs and sx
  - Failure of nontreponemal tests to decline 4-fold or sustained 4-fold increase in treponemal test after rx within 6 months of Rx
- Management
  - Check CSF
    - If + treat for neurosyphilis
    - If neg treat for late latent

The Serofast State

- While a majority of treated patients with syphilis experience declines in nontreponemal titers to nonreactive, that is not always the case. Patients whose nontreponemal antibody titers remain reactive after treatment are said to be "serofast".
- The serofast state is seen in approximately 15 to 20 percent of patients but usually does not indicate treatment failure.
- In virtually all such cases, the nontreponemal titer stabilizes at a low level (eg, a titer of <1:8), and periodic rechecking of nontreponemal titers is advised. Detection of a fourfold increase above the serofast baseline would suggest reinfection

Case # 3c

You elect to pursue a lumbar puncture and you find that the patient has 2 WBC, a normal protein, and a negative VDRL in her CSF.

The next step in her management is:
A. Treat for neurosyphilis
B. Treat for late latent infection (3 shots)
C. Monitor only
D. Both A and B
ANSWER #3c

The next step in her management is:

B. Treat for late latent infection (3 shots)

Genital Herpes

Herpes Simplex Virus Infections

HSV Epidemiology

- HSV-1 and HSV-2 are common infections worldwide; at least 50 million persons have genital herpes in the United States alone
- Genital HSV is frequently under-recognized because infection is often not recognized by the patient
- In a population-based cross-sectional survey of adults living in New York City:
  - 28 percent were infected with HSV-2
  - 68 percent had no prior knowledge of their diagnosis
- Prior infection with HSV-1 also leads to a three-fold increase in asymptomatic HSV-2 infection
Age-Adjusted Herpes Simplex Virus Type 2 Seroprevalence According to the Lifetime Number of Sex Partners, by Race/Ethnicity and Sex on NHANES in 1999-2004


HSV Epidemiology (2)

- Trends in HSV over time
  - 19% decrease of HSV-2 seroprevalence when comparing a population-based crosssectional study capturing 1988-94 and 1999-2004
  - 7% decrease in HSV-1 prevalence
  - More GENITAL infections caused by HSV-1 alone
  
  Ross et al. 1993
  Roberts et al. 2003

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)

- HSV-1
  - MSM: 46.9%
  - Heterosexual Men: 12.9%
- HSV-2
  - MSM: 53.1%
  - Heterosexual Men: 87.1%

Question A

A herpes virus infection can be eradicated by the immune system or medications.
A. True
B. False

Answer A

A herpes virus infection can be eradicated by the immune system or medications.
B. False
Pathogenesis

• 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

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
Question B

A clinical scenario consistent with a primary infection with genital HSV-2 is:

A. Multiple HSV-like ulcers/lesions and a positive serology for HSV-2 and negative serology for HSV-1
B. Solitary HSV-like ulcer and a negative serology for HSV-2 and negative serology for HSV-1
C. Multiple HSV-like ulcers and a negative serology for HSV-2 and negative serology for HSV-1
D. Solitary HSV-like ulcer and a positive serology for HSV-2 and negative serology for HSV-1

ANSWER B

A clinical scenario consistent with a primary infection with genital HSV-2 is:

C. Multiple HSV-like ulcers and a negative serology for HSV-2 and negative serology for HSV-1

Remember 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
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

(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

Question C

When compared to HSV-1, HSV-2 is:
A. Less likely to cause recurrences
B. Less severe
C. Associated with more shedding without clinical sx
D. More symptomatic in individuals previously infected with HSV-1
ANSWER C

When compared to HSV-1, HSV-2 is:

C. Associated with more shedding without clinical sx

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
HSV Diagnosis

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

Viral Culture

- 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

HSV Culture Sensitivity

Virus isolated in 80% of primary lesions, but only <50% (<30%) of recurrent lesions
NAAT-based testing

- 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

**QUESTION D #1**

The best test for a patient with an early, active HSV -like lesion to confirm the diagnosis is:

A. Clinical diagnosis, no testing  
B. HSV culture  
C. HSV serology  
D. Tzanck Smear

**ANSWER D #1**

The best test for a patient with an early, active HSV -like lesion to confirm the diagnosis is:

B. HSV culture
QUESTION D #2
The best test for a patient who has never had an outbreak of HSV but has a partner with genital HSV infection is:
A. Clinical diagnosis, no testing
B. HSV culture
C. HSV serology
D. Tzanck Smear

QUESTION D #3
The best test strategy for a patient who has recurrent fissures in the same location of her vulva in the setting of negative HSV culture is:
A. Clinical diagnosis, no testing
B. HSV culture
C. HSV serology
D. Tzanck Smear
**ANSWER D #3**

The best test strategy for a patient who has recurrent fissures in the same location of her vulva in the setting of negative HSV culture is:

C. HSV serology

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**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

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**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
Genital Herpes in Pregnancy

- Majority of mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes
- Risk for transmission to neonate is high (30%-50%) among women who acquire genital herpes near the time of delivery
- Risk is low (<1%) in women with histories of recurrent herpes at term or who acquire genital HSV during the first half of pregnancy

Genital Herpes in Pregnancy (continued)

- Prevention of neonatal herpes depends on:
  ✓ avoiding acquisition of HSV during late pregnancy
  ✓ avoiding exposure of the infant to herpetic lesions during delivery
- All pregnant women should be asked whether they have a history of genital herpes and at the onset of labor:
  - All women should be questioned carefully about symptoms of genital herpes, including prodromal
  - All women should be examined carefully for herpetic lesions
- Women without symptoms or signs of genital herpes or its prodrome can deliver vaginally

Genital Herpes in Pregnancy (continued)

- Safety of acyclovir, valacyclovir, famciclovir in pregnancy not definitively established, but no clear evidence for increased birth defects
- Oral acyclovir may be given for first-episode or severe recurrent herpes; IV acyclovir should be used for severe infection
- Suppressive acyclovir late in pregnancy reduces frequency of cesarean sections in women with recurrent genital herpes; many specialists recommend it
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

Case #4a

Your 32 year old female patient comes to your office distraught because she noticed that she has developed painful genital sores (pictured). She does not recall ever having such lesions before. She is particularly distraught because she is getting married in 2 months and is worried that she obtained this infection from her male partner.

She does not feel ill, and on exam has some regional lymphadenopathy. Notes some itching before the outbreak.

Question 1

You obtain a culture of this lesion that is positive for HSV-2. You also decide to get a serology that is positive for both HSV1 and 2. You would categorize this clinical presentation to most likely be:

A. Primary HSV-2 Infection
B. Non-Primary Infection with a second strain of HSV
C. Recurrence of previous infection
D. I don’t know
ANSWER 1

You obtain a culture of this lesion that is positive for HSV-2. You also decide to get a serology that is positive for both HSV1 and 2. You would categorize this clinical presentation to most likely be:

C. Recurrence of previous infection

HSV culture + with fully positive serology implies a recurrence of old infection

Question 2

Her male partner comes in for testing with his fiancée and you offer him a type specific serology. He is HSV-1 positive and HSV-2 negative. Counseling should include:

A. Condom use
B. Symptom recognition by both partners
C. Avoidance of sex during outbreaks
D. Medications for prevention of HSV transmission
E. Teaching on asymptomatic shedding
F. Perinatal transmission prevention
G. All of the above

Question 2

Her male partner comes in for testing with his fiancée and you offer him a type specific serology. He is HSV-1 positive and HSV-2 negative. Counseling should include

G. All of the above
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.

Incidence in the U.S.

- Estimated annual incidence of sexually transmitted HPV infection is 6.2 million
- Estimated $1.6 billion spent annually in direct medical costs to treat symptoms of genital HPV infection
- Estimated 20 million people currently have a detectable genital HPV infection
Prevalence in the U.S.

- It is estimated that at least 50% of sexually active men and women acquire genital HPV at some point in their lives.

- A recent estimate suggests 80% of women will have acquired genital HPV by the age of 50.

Clinical Manifestations by HPV Type

<table>
<thead>
<tr>
<th>Type</th>
<th>Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plantar Warts</td>
<td>1</td>
</tr>
<tr>
<td>Common Warts</td>
<td>2, 4, 26, 27, 29</td>
</tr>
<tr>
<td>Flat Warts</td>
<td>3, 10, 28, 49</td>
</tr>
<tr>
<td>Genital Condyloma Acuminate</td>
<td>6, 11</td>
</tr>
</tbody>
</table>
| Ano-genital Intraepith. Neoplasia/ Carcinoma | 16, 18, 6, 11 ...
| Mouth (focal epithelial hyperplasia) | 11, 32        |
| Laryngeal papilloma                 | 6, 11         |
| Head & Neck Carcinoma               | 16, 18, 30    |

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

HPV DNA Prevalence in Cancers Other than Cervical

<table>
<thead>
<tr>
<th>Site</th>
<th>HPV DNA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vulvar Intraepith. Neoplasia</td>
<td>72-100</td>
</tr>
<tr>
<td>Vaginal Intraepith. Neoplasia</td>
<td>82-100</td>
</tr>
<tr>
<td>Penile Intraepith. Neoplasia</td>
<td>90</td>
</tr>
<tr>
<td>Anal Squamous Cell</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Cancers of Head &amp; Neck</td>
<td>33-72</td>
</tr>
</tbody>
</table>
Case #5

A 30 year old woman is screened for cervical cancer with a PAP smear and a HPV type test. The PAP comes back with ATYPICAL CELLS OF UNDETERMINED SIGNIFICANCE (ASCUS). The HPV test is positive for HIGH RISK HPV.

QUESTION #5

The next step in her management should be:

A. Repeat PAP in 1 year
B. Repeat PAP in 3 months
C. Colposcopy
D. Repeat HPV test
E. None of the Above

ANSWER #5

The next step in her management should be:

C. Colposcopy
Guidelines for ASCUS are to repeat cytology in 6 months if HPV testing not available. If ASCUS is in the presence of high risk HPV, the guidelines are to proceed to colposcopy.

Case/Question #6

A 25 year old HIV + MSM presents for a primary care visit. You review his healthcare maintenance and get a sexual history that reveals that he is having anal sex. You decide that screening should include all of the following except:

A. Genital and extra-genital STI tests
B. Syphilis testing
C. Colonoscopy
D. Anal PAP smear
E. Lipids
F. Vaccines

Age appropriate screening should include all of the above. Unless he has a family history of early colon cancer there is no role for routine colonoscopy at this age.

Case/Question #6a

A 25 year old HIV + MSM presents for a primary care visit. You review his healthcare maintenance and get a sexual history that reveals that he is having anal sex. You decide that screening should include all of the following except:

C. Colonoscopy
Case #6b

Results came back:
Oral Gonorrhea: NEGATIVE
Rectal Gonorrhea and Chlamydia: NEGATIVE
Urine Gonorrhea and Chlamydia: NEGATIVE
RPR: 1:2 (serofast)
Lipids: WNL
ANAL PAP: ASCUS

Question #6b

The next step in this patient’s management is:
A. A shot of penicillin
B. A repeat Anal PAP smear immediately
C. A repeat Anal PAP in 6 months
D. A high resolution anoscopy
E. A and D

Answer #6b

The next step in this patient’s management is:
C. A high resolution anoscopy
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 vulval/vaginal or cervical dysplasia
  - solid organ transplant recipients who have an increased risk of anal cancer

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

Treatment

- 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 [23]. The vaccination series can be administered as young as 9 years.
  - "permissive use" of the quadrivalent vaccine in males aged 22 through 26 years.