HERPES VIRUSES

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Learning Objectives

• To understand the epidemiology, clinical spectrum, diagnosis, and key principles of treatment for the common herpes viruses

• Viruses covered:
  • HSV-1
  • HSV-2
  • Varicella Zoster virus
  • Epstein-Barr virus

Case #1

A 22 year old man presents to clinic complaining of fever, "swollen glands," and severe mouth and throat pain x 24 hours. He has no contact with young children. He has mild anterior cervical LAN and the oral exam shown. He has no skin rash or neurologic findings. Liver and spleen are normal.
The most likely cause is...

1. Herpes zoster
2. Primary herpetic gingivostomatitis (HSV)
3. Group A Streptococcus
4. Mononucleosis (EBV)

Oral HSV: Primary Infection

- **Epidemiology:**
  - Children, young adults
  - Majority are HSV-1, only rarely HSV-2

- **Clinical:**
  - Asymptomatic in 70-90% of cases
  - Gingivostomatitis or pharyngitis (may not have classic HSV lesions!)
  - Can have fever, malaise, LAN
  - Duration of symptoms 10-14d

Case #2

A 30 year old man presents to clinic complaining of “fever blisters” for the past 24 hours. He has moderate pain but mostly feels a great degree of stress and embarrassment about the lesions. This is his 5th episode in the last year.

Oral antivirals (e.g. acyclovir):

1. Shorten the time for lesions to heal
2. Prevent HSV recurrences
3. Both #1 and #2
4. Have no treatment effect
HSV-1 Seroprevalence: Declining over Time

- Contact with active lesions
- Most is by salivary transmission
- Asymptomatic shedding 5-10% of days
- Median duration of shedding = 24h
- Shedding is increased with:
  - Prodromal symptoms
  - Active HSV lesions
  - Immunosuppression
  - Oral surgery, trauma, URI

HSV-1: Transmission

Epidemiology:
- Occurs in 20-40% of HSV-1+ patients
- Average of 1.6 recurrences/year

Clinical
- Prodrome in ~50%
- 25% do not proceed beyond the prodrome or maculopapular phase
- Duration of symptoms 1-10 days

Recurrent Oral HSV: Herpes Labialis

Triggers for Reactivation

- Fever
- Ultraviolet light exposure
- Viral URI
- Emotional stress, fatigue
- Immunosuppression, chemotherapy
- Oral/facial surgery or trauma
- Iron deficiency
- Menstruation
Oral HSV: Treatment

- Sunscreen for all: Limited data but may decrease recurrences
- Topical antivirals: Conflicting data but may shorten time to heal (0.5-2.5 days)
- Oral antivirals
  - Primary infection: time to heal by 6 days
  - Intermittent episodic therapy for recurrences: time to heal by 0.5-2.5 days, but not effective in aborting lesions
  - Suppressive therapy: reduce recurrences by 40-50% (in pts with ≥4-6 recurrences/year)
- See Appendix 1 for specific drug regimens

Oral HSV: Take Home Points

- Primary HSV-1 can be a cause of pharyngitis in young adults (and may not present with vesicles)
- The seroprevalence of HSV-1 is decreasing over time, especially in teenagers
- Oral antivirals have a modest treatment effect but can shorten healing time and be used as suppressive therapy to prevent recurrences

Case #3

A 22 year old man presents with fever, inguinal lymphadenopathy, and painful blisters at the base of his penis. He is sexually active with 2 female partners.

You should determine HSV type because:

1. HSV-1 is a rare cause of genital herpes
2. HSV-1 causes a less severe primary infection
3. HSV-1 is less likely to cause recurrences
Case #4 (continued)

- He is diagnosed with HSV-2 by culture of one of the lesions. He wants to know how likely this is to recur in the next 12 months.

You tell him the likelihood of recurrence in the next 12 months is:

1. 10%
2. 30%
3. 50%
4. >70%

He wants to know about the benefits of suppressive therapy. You tell him:

1. It doesn’t prevent recurrences.
2. It ↓ # of recurrences and risk of transmission.
3. It ↓ # of recurrences but has no effect on transmission.

Genital Herpes: Changing Epidemiology

- Historically, HSV-2 has accounted for 75% of all GH
- However, HSV-1 now accounts for >50% of primary GH
  - And 80% of GH visits for college students
- Increase in HSV-1 because:
  - ↑ HSV-1 seroprevalence in childhood
  - ↑ rates of oral sex in young adults
- HSV-1 and HSV-2 are clinically identical but HSV-1 recurrence rate is ↓↓ c/w HSV-2

HSV-2 Seroprevalence: Steady over Time

- Only 10-25% of those with GH are aware they have it
- Most transmission occurs from persons unaware they have herpes or who are asymptomatic
- Asymptomatic shedding occurs on 20-25% of all days, median duration 13h

Genital Herpes: Transmission

- Clinical:
  - Incubation 4-7 days
  - Most infections are asymptomatic
  - Systemic sx: fever, HA, myalgias, dysuria, inguinal LAN
  - Can get new lesions for up to 3 weeks
  - Complications:
    - Aseptic meningitis, proctitis, urinary retention

Primary Genital Herpes

- Classic “scalloped” border

Recurrent Genital Herpes

<table>
<thead>
<tr>
<th>Type of HSV primary infection</th>
<th>% with a recurrence within 1 year</th>
<th>Median # recurrences in 1st year</th>
<th>Subsequent # in recurrences/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-1</td>
<td>20-50%</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>HSV-2</td>
<td>70-90%</td>
<td>4-5</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*Strong predictor of recurrence risk is severity of primary infection

Photo courtesy of Laura Pincus.
### HSV: Diagnostics

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (Recurrence)</th>
<th>Specificity</th>
<th>Take home points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Culture</strong></td>
<td>Vesicle 70-90% Ulcer 30-40%</td>
<td>100%</td>
<td>Gold standard Moderate sensitivity Takes 1-2 days</td>
</tr>
<tr>
<td><strong>DFA</strong></td>
<td>Vesicle 70-90% Ulcer 30% Crusted 10%</td>
<td>99%</td>
<td>Rapid (hours) Sensitivity c/w culture</td>
</tr>
<tr>
<td><strong>PCR</strong></td>
<td>~90% overall</td>
<td>99%</td>
<td>Most sensitive test But not routinely available</td>
</tr>
</tbody>
</table>

When to order HSV-2 Serology

- CDC guidelines:
  1. Recurrent (or atypical) genital symptoms and (-) HSV cultures
  2. A partner with genital herpes (to assess risk for acquisition)
  3. Consider for patients presenting for an STD evaluation or MSM at increased risk for HIV acquisition

- Sensitivity and specificity >95%

CDC, STD Treatment Guidelines 2010, MMWR 59 (No. RR-12).

Utility of IgM Antibodies

- Can IgM be used to determine primary vs recurrent infection?

- Concerns:
  - Limited sensitivity: IgM develops ~10 d after exposure and lasts 1-2 wks
  - Limited specificity: IgM can be found in recurrent disease, up to 70% in older studies
  - But in theory, IgM+IgG- should indicate primary infection

- What does the data show?
  - In patients presenting with “new” episode of GH, IgM had intermediate sensitivity (~80%) but was very specific (~100%) for a diagnosis of primary GH


Genital HSV Rx: General Principles

- Screen for HIV and other STIs

- Treatment:
  - Topical antivirals: of minimal benefit
  - Orals antivirals are the mainstay of treatment

- Counseling, including:
  - Abstinence during prodrome or lesions
  - Educate patients re: risk of asymptomatic shedding
  - Encourage patients to inform sex partners

Treatment Regimens: Episodic Therapy

Primary infection
- 🍎 sx duration by 2-4 days
- No impact on recurrences
- See appendix 2 for specific drug regimens

Recurrent episodes
- Initiate in prodrome or <1d of lesion onset
- Can abort lesions entirely in 20-30% or 🍎 symptom duration by 1-2d
- Does not reduce rate of transmission to uninfected partners
- See appendix 2 for specific drug regimens

CDC, STD Treatment Guidelines 2010, MMWR 59 (No. RR-12); Mertz et al, JAMA 1984; 252:1147.
Suppressive Therapy for Genital Herpes

- ↓ recurrences by 70-80%
- ↓ shedding dramatically and ↓ transmission to negative partner by ~50% (but absolute risk reduction of ~2%)
- Use in patients with “frequent” episodes (? ≥ 6)
- Consider in discordant couples
- Trial off therapy qyear


A New Drug for HSV?

- Dose escalation study for treatment of HSV-2 genital herpes
- ↓ viral shedding and # days with genital lesions by ~90%
- Has potential to treat resistant virus and be used in combination therapy
- No adverse effects but development halted by FDA due to toxicity in monkeys


Genital Herpes: Take Home Points

- HSV-1 now accounts for >50% of cases of primary genital herpes
- HSV-1 and HSV-2 are clinically identical, but HSV-2 is much more likely to recur
- Most transmission occurs in patients who are asymptomatic or are unaware they have genital herpes
- HSV culture +/- DFA are the diagnostic methods of choice
- Oral antivirals can shorten symptom duration, abort lesions entirely, and can be used as suppressive therapy to decrease the number of recurrences as well as transmission

Case #4

64 year old man presents with a blistering rash on the left side of his face in the V3 distribution that started 48 hours ago. He says the pain is severe and debilitating.
What is the best therapy to decrease the risk of PHN?

1. Prednisone
2. Valacyclovir
3. Valacyclovir and prednisone

To confirm the diagnosis, the most sensitive test is:

1. VZV DFA
2. VZV culture

VZV: Epidemiology

- Lifetime incidence 10-20%
- Risk factors:
  - Age (risk doubles each decade >50)
  - Immunosuppression
  - Trauma, especially of the head → 28x increased risk for cranial HZ
  - Statins? (HR of 1.18)
- Second episodes of HZ in ≤5% (in immunocompetent)

Disseminated VZV: Pathophysiology

- Reactivation of VZV in sensory ganglia
- Viremia
- Immune competent or receiving antiviral rx
- Immunocompetent or receiving antiviral rx
- Viremia is cleared
- Viremic spread and skin dissemination
- Visceral infection (rare)

**Zoster: Clinical**

- 80% have prodrome preceding lesions by 2-3 days
- Characteristic rash:
  - New vesicles appear for 2-4 days
  - Lesions tend to be clustered
- <20% have systemic symptoms


**Zoster: Dermatomes**

- Zoster (Greek) and shingles (French) both mean belt
- Dermatomes:
  - 54% thorax
  - 15% face (CNV or VII)
  - 14% cervical
  - 13% lumbar
  - 3% sacral
- Overlap into adjacent dermatomes in 20% (normal variation in innervation)


**Post-Herpetic Neuralgia**

- Defined as pain lasting >3 months after zoster episode
- About 10-20% with zoster develop PHN
- Risk factors:
  - Older age
  - Greater severity of acute pain during zoster
  - Greater severity of rash
  - Proxome of dermatomal pain
- Seems to get better over time, but 3-40% will still have long term difficulty with pain


**Zoster: Diagnosis**

- DFA
  - Test of choice
  - Sensitivity 90%, Specificity 95%
  - Rapid (hours)
- PCR
  - Most sensitive, but not widely available
- Culture
  - Sensitivity 60-75%, Specificity 100%
  - Takes 1-2 weeks to grow

Review of HSV/VZV Diagnostics

<table>
<thead>
<tr>
<th>Virus</th>
<th>Test of Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-1 or HSV-2</td>
<td>Culture &gt; DFA</td>
</tr>
<tr>
<td>VZV</td>
<td>DFA</td>
</tr>
</tbody>
</table>

Zoster Treatment: General principles

- **Goals of therapy:**
  1. Treatment of acute pain
  2. Prevention of spread (by eliminating viral replication)
  3. Prevention of PHN

- **Types of therapy:**
  - Topical Antiviral Rx: no efficacy
  - Systemic Antivirals are drugs of choice

Benefits of Antivirals

- Multiple clinical trials show that antivirals:
  - **↓** duration of viral shedding and new lesion formation (by 1-2 days)
  - Accelerate rash healing
  - **↓** severity and duration of acute pain

- Most (but not all) studies show a **↓** risk of PHN
  - Mechanism: antivirals inhibit viral replication and neural damage, which is thought to play a major role in risk for PHN

Strong recommendation:

1. Patients ≥ 50 years of age
2. Patients with moderate or severe pain
3. Patients with moderate or severe rash
4. Patients with nontruncal involvement

- But consider in EVERYONE even with mild disease because the benefit (preventing PHN) likely outweighs the risk (as the drugs are very safe)
Timing of Therapy

- **Timing:**
  - All RCTs initiate therapy within 72 hours
  - Starting therapy at >72h hasn’t been well studied, but it is possible there may be some benefit up to 7d

- If a patient presents at >72 hrs, consider treating if:
  - Presence of new vesicles (indicating viral replication)
  - Cutaneous, motor, ocular, neurologic complications
  - Advanced age, severe pain (since these are RF for PHN)


Zoster: Antiviral Regimens

- **Drug options**
  - Acyclovir 800 mg 5 times daily for 7-10 days
  - Famciclovir 500 mg tid daily for 7 days
  - Valacyclovir 1000 mg tid daily for 7 days

- For immunocompromised patients: treat until all lesions have crusted given the risk of relapse (this may take longer than 7-10 days)


Steroids in Acute Zoster: Controversial

- **Studies:**
  - 3 RCTs comparing ACV+steroids vs ACV+placebo within 7-96h of rash onset
  - Patients >50-60 with HZ, no contraindications to steroids

- The addition of steroids to ACV:
  - Accelerated healing and reduced acute pain (by ~1.5-3 fold)
  - Improved quality of life
  - But no decrease in PHN

- Steroid Regimen (example from Whitley et al):
  - Prednisone 60 mg/d x 7d, then 30 mg/d x 7d, then 15 mg/d x 7d


Steroid Use: Guidelines

- **Consider if:**
  - Moderate to severe pain
  - Facial nerve paralysis
  - Ocular VZV with significant edema
  - No contraindications to steroid use

- Must carefully weigh the risks and benefits of steroid use in elderly patients

VZV Ophthalmicus

- Defined as HZ in the V1 distribution
- Without treatment, 50% will develop ocular complications
  - Conjunctivitis
  - Anterior uveitis
  - Keratitis
  - Corneal ulcer
  - Orbital apex syndrome


VZV Ophthalmicus: Management

- Ophtho consult
  - For all patients with eye symptoms, with lesions on the tip or side of the nose, or who are immunocompromised
- Antivirals:
  - All patients should be treated irrespective of the duration of symptoms
  - Treat with intravenous ACV in immunocompromised patients or with eye involvement
  - Consider systemic steroids if there is significant edema, which can cause orbital apex syndrome via pressure on nerves entering the orbit

Dworkin et al, Clin Infect Dis 2007; 44 (Suppl2): S1

Case #5

A 59 year old woman on an anti-TNF inhibitor for RA presents with fever and rash on her trunk, arms, and legs. VZV DFA is positive.

How would you treat her?

1. High dose PO valacyclovir and close follow-up
2. Admission and IV acyclovir
Zoster: Complications

• Disseminated VZV = lesions outside the primary or adjacent dermatomes

• CNS complications
  • Aseptic Meningitis
  • Encephalitis (small vessel vasculopathy)
  • Necrotizing Arteritis (large vessel vasculopathy)
  • Transverse Myelitis
  • Ocular involvement

• Other complications:
  • Ramsay-Hunt syndrome
  • Motor nerves involved in 5-15% (bystander effect)

VZV Encephalitis

• Usually occurs in immunocompromised patients

• Clinical:
  • HA, fever, AMS, seizures
  • Rash can be absent (in up to 1/3)

• CSF profile:
  • Lymphocytic pleocytosis (median 107 cells/mm³)
  • Elevated protein (median 262 mg/dL)
  • Glucose normal to slightly low (median 55 mg/dL)
  • Positive VZV PCR (sensitivity 80-100%, specificity 98%)
  • Positive VZV Abs (may be more sensitive than PCR for chronic cases)

Disseminated VZV

• Usually in immunocompromised, occurs via viremic spread to the skin

• Patients may have new lesions for up to 2 weeks

• Patients are at high risk for pneumonitis, hepatitis, DIC

Other complications:

• Ramsay-Hunt syndrome
• Motor nerves involved in 5-15% (bystander effect)

Treatment of Complicated Zoster

• When to admit patients for IV acyclovir?
  • Disseminated disease or CNS complications
  • Severely immunocompromised patients with localized disease (to prevent dissemination)
  • Strongly consider in VZV Ophthalmicus, Ramsay Hunt
  • Exception: HIV+ patients can be treated with PO therapy

• How long to treat and when can you switch to PO?
  • Total duration 2-3 weeks
  • Use IV for at least 7 days (and until all lesions are crusted over)
  • Can switch to PO valacyclovir on a case by case basis


Cohen, NEJM 2013, 369:255.


VZV: Infection Control Issues

- Immunocompetent:
  - Localized HZ: Standard (cover lesions)
  - Disseminated disease: Airborne and Contact
- Immunocompromised:
  - Localized HZ: Airborne and Contact until disseminated disease is ruled out (then can de-escalate to standard precautions)
  - Disseminated disease: Airborne and Contact
- Continue until all lesions are dry and crusted


VZV: Take Home Points

- DFA is the diagnostic method of choice for cutaneous zoster
- Antivirals decrease symptom severity and duration, and may have some benefit in risk of PHN
- Steroids provide no additional benefit in risk of PHN
- Admit patients for IV acyclovir if they have disseminated disease, CNS complications, or are severely immunocompromised

Case #6

A 19 year old college freshman presents to clinic requesting advice because his girlfriend was just diagnosed with “mono.” He wants to know when it will be safe for them to resume kissing in terms of his risk of contracting the infection. He has never had “mono” to his knowledge.

You consider the epidemiology...

The chance he has already been infected with EBV is:

1. 20%
2. 40%
3. 70%
4. 95%
After an acute episode of mononucleosis, most patients shed virus (orally) for:

1. 1 week
2. 1 month
3. 6 months
4. 5 years

EBV: Epidemiology

- 95% of adults in the U.S. are infected with EBV
  - Most infections are acquired in childhood
  - By age 18, 62-75% of adults are EBV seropositive
- Main risk factor in teenagers and adults is kissing (irrespective of sexual intercourse)

EBV and Shedding

- 20% shed virus into their saliva before they develop symptoms, sometimes up to a month before symptom onset
- Most patients with EBV shed virus into the oral cavity for at least 6 months after acute infection, and many at high levels
- Reactivation is common and shedding occurs in healthy adults —25-75% of the time — likely the main reservoir for transmission

EBV and Symptoms

- Incubation period 4-6 weeks
- Infectious mononucleosis = classic triad of sore throat, cervical lymphadenopathy, and fever
- Most infections are acquired in childhood and are asymptomatic or a nonspecific illness
- In contrast, up to 90% of primary infections acquired in college (“delayed primary infections”) are symptomatic

Diagnosis of IM: Heterophile Ab (Monospot)

- Sensitivity:
  - 90-95% after the 1st week
  - But only 75% in the 1st week
- Specificity: 94%
  - False positives have been reported in acute HIV


Diagnosis of IM: Atypical Lymphocytes

- Sensitivity: 75%
- Specificity: 92%


Diagnosis of IM: EBV Serologies

- Sensitivity 84-89%
- Specificity 96-98%


Diagnosis of IM: EBV PCR in Blood

- Not a lot of data for use in IM (as opposed to PTLD)
- Sensitivity of 20-100% in IM depending on method of PCR assay (plasma, whole blood, PMBC)
- Usually undetectable by week 3
- Can be useful in early disease if serologies are inconclusive

**IM Diagnostic Approach**

- IM from EBV can usually be diagnosed in adolescents/young adults by clinical presentation, atypical lymphs, and monospot

- But the monospot is not an antigen-specific test; definitive diagnosis requires antibody testing (and/or PCR)

- Additional diagnostics (for EBV or other etiologies) should be pursued in:
  - Patients at high risk for acute HIV (r/o acute HIV in these patients)
  - Pregnant women who could have significant consequences from alternative diagnoses (check for acute HIV, toxoplasmosis, CMV)

**Complications of EBV Infection**

- Hematologic 25-50%
  - Hemolytic anemia
  - Thrombocytopenia
  - Aplastic anemia
  - TTP/HUS
  - DIC

- Neurologic 1-5%
  - Guillain–Barre syndrome
  - Facial paralysis
  - Aseptic meningitis
  - Encephalitis
  - Transverse myelitis
  - Peripheral neuritis
  - Optic neuritis

- Other rare complications:
  - Splenic rupture 0.5-1% (usually occurs within 3 wks)
  - Upper airway obstruction 1%
  - Trigger for hemophagocytic lymphohistiocytosis (HLH)

**Infectious Mononucleosis: Treatment**

- **Steroids?** → Not for all, maybe in some cases
  - Cochrane review 2006: “insufficient evidence to recommend” for symptom control, lack of research into side effects
  - Consider short course to treat severe complications (e.g., upper-airway obstruction)

- **Antivirals?** → NO
  - ACV: Multiple RCTs show no benefit
  - Valacyclovir: may have slight benefit based on very small study

**EBV and Chronic Fatigue Syndrome**

- >90% with IM become asymptomatic by 28 days

- Fatigue may resolve more slowly, particularly in women

- EBV and chronic fatigue syndrome?
  - Initial studies conflicting, some showed high EBV Ab titers in CFS
  - Since then, multiple PCR studies → no evidence of EBV replication
  - Post-infective fatigue syndromes seem to occur at a similar rate after other viral and non-viral infections

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So, Back to the Case...

A 19 year old college freshman presents to clinic requesting advice because his girlfriend was just diagnosed with “mono.” He wants to know when it will be safe for them to resume kissing in terms of his risk of contracting the infection. He has never had “mono” to his knowledge.

You tell him:
1. Wait 4 weeks to give yourself the best chance of avoiding infection.
2. No precautions: you’ve most likely had it, your girlfriend will shed for 6 months at least, and then she (or others) will shed intermittently when healthy.

So, Your Advice to Him is:

1. Wait 4 weeks
2. No precautions

EBV: Take Home Points

• By age 18, up to 75% of adults have been infected with EBV

• After acute infection, patients shed EBV for at least 6 months and then intermittently 25-75% of the time

• Diagnosis can usually be made by monospot, but serologies (and/or PCR) can provide a definitive diagnosis when needed

• There is no role for antivirals, but can consider steroids for severe complications such as airway obstruction

Thank you!

• Questions?
APPENDIX 1

Oral HSV Drug Regimens

Antivirals for Primary Oral HSV Infection

Table 1. Episode Dosing for Initial Primary Labial Herpes

<table>
<thead>
<tr>
<th>Antiviral Drug</th>
<th>Dosing Schedule</th>
<th>Level of Evidence</th>
<th>FDA Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>800 mg twice a day for 7 d</td>
<td>II-III</td>
<td>No</td>
</tr>
<tr>
<td>Valacyclovir hydrochloride</td>
<td>1 g once a day</td>
<td>II</td>
<td>No</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>500 mg twice a day</td>
<td>II</td>
<td>No</td>
</tr>
</tbody>
</table>

Not known if antiviral ppx can decrease oral HSV-1 shedding or transmission

Episodic Therapy for Recurrent Oral HSV

Table 2. Intermittent Episodic Therapy or Recurrent Labial Herpes

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<thead>
<tr>
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<th>FDA Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>400 mg 5 times a day for 5 d</td>
<td>II</td>
<td>No</td>
</tr>
<tr>
<td>Valacyclovir hydrochloride</td>
<td>2 g twice a day for 1 d</td>
<td>II</td>
<td>Yes</td>
</tr>
<tr>
<td>Famciclovir</td>
<td>Three 500-mg tablets as a single dose</td>
<td>II</td>
<td>Yes</td>
</tr>
<tr>
<td>Topical Therapy</td>
<td>Peniclovir cream, 1%</td>
<td>II</td>
<td>Yes</td>
</tr>
<tr>
<td>Acyclovir cream, 5%</td>
<td>Apply every 2 hours for 4 d</td>
<td>II</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Suppressive Regimens for Oral HSV

Table 5. Chronic Suppressive Therapy for Labial Herpes

<table>
<thead>
<tr>
<th>Antiviral Drug</th>
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**Not known if antiviral ppx can decrease oral HSV-1 shedding or transmission**
APPENDIX 2
Genital Herpes Drug Regimens

First episode of Genital Herpes

Recommended Regimens
Acyclovir 400 mg orally three times a day for 7-10 days
OR
Acyclovir 200 mg orally five times a day for 7-10 days
OR
Famciclovir 250 mg orally three times a day for 7-10 days
OR
Valacyclovir 1 g orally twice a day for 7-10 days

*Treatment can be extended if healing is incomplete after 10 days of therapy.

CDC, STD Treatment Guidelines 2010, MMWR 59 (No. RR-12), Mertz et al, JAMA 1984; 252:1147.

Episodic Rx for Recurrent Genital Herpes

Recommended Regimens
Acyclovir 400 mg orally three times a day for 5 days
OR
Acyclovir 200 mg orally twice a day for 5 days
OR
Acyclovir 100 mg orally three times a day for 2 days
OR
Famciclovir 125 mg orally twice daily for 5 days
OR
Famciclovir 500 mg orally twice daily for 1 day
OR
Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days
Valacyclovir 500 mg orally twice a day for 3 days
OR
Valacyclovir 1 g orally once a day for 5 days

CDC, STD Treatment Guidelines 2010, MMWR 59 (No. RR-12), Strand et al, Sex Transm Infect 2002; 78:435.

Suppressive Therapy for Genital Herpes

Recommended Regimens
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

* Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in patients who have very frequent recurrences (i.e., >10 episodes per year).