CDC
STD Prevention

Ready-to-Use

STD Curriculum for Clinical Educators

Genital Herpes Simplex Virus (HSV) Module

Target Audience - Faculty in clinical education programs, including those programs that train advanced practice nurses, physician assistants, and physicians

Contents - The following resources are provided in this module:

- **Faculty Notes** (Microsoft Word and Adobe Acrobat formats) - Includes notes that correspond to the slide presentation, a case study with discussion points, and test questions with answers
- **Slide Presentation** (Microsoft PowerPoint and Adobe Acrobat formats)
- **Student Handouts**
  - **Case Study** (Microsoft Word format)
  - **Test Questions** (Microsoft Word format)
  - **Slides Handout** (Adobe Acrobat format)
  - **Resources** (Microsoft Word format)

Suggested Time Allowance - The approximate time needed to present this module is 60-90 minutes.

These materials were developed by the Training and Health Communication Branch, Division of STD Prevention, CDC. They are Based on the curriculum developed by the National Network of STD/HIV Prevention Training Centers (NNPTC) which includes recommendations from the 2006 CDC STD Treatment Guidelines

Information on the NNPTC can be Accessed at:
http://depts.washington.edu/nnptc/index.html

The 2006 CDC STD Treatment Guidelines Can be accessed or ordered online at:
http://www.cdc.gov/std/treatment/

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Genital Herpes Simplex Virus (HSV)

[Slide 2]

Learning Objectives

Upon completion of this content, the learner will be able to:

1. Describe the epidemiology of genital HSV infection in the U.S.
2. Describe the pathogenesis of genital HSV.
3. Discuss the clinical manifestations of genital HSV infection.
4. Identify the common laboratory tests used in the diagnosis of genital HSV infection.
5. Describe patient management for genital HSV infection.
6. List public health measures for the prevention of genital HSV infection.
7. Summarize appropriate prevention counseling messages for genital HSV infection.

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Course Outline

I. Epidemiology: Disease in the U.S.
II. Pathogenesis
III. Clinical manifestations
IV. Diagnosis
V. Patient management
VI. Prevention

[Slide 4]

I. Epidemiology

[Slides 5-6]

A. Background and burden of disease
   1. Genital herpes is a chronic, life-long viral infection.
   2. Two serotypes of herpes simplex virus (HSV) have been identified: HSV-1 and HSV-2.
   3. The majority of cases of recurrent genital herpes in the U.S. are caused by HSV-2, although HSV-1 is becoming a more common cause of first episode genital herpes.
   4. At least 50 million persons in the U.S. have genital HSV infection.
   5. It is estimated that at least 1 million new cases occur each year.
   6. In the general U.S. population, 17% of adults aged 14-49 years have HSV-2 antibodies.
   7. HSV-2 antibodies are not routinely detected until puberty, and then HSV-2 seroprevalence increases with age. HSV-2 seroprevalence is higher in women than men in all age groups and varies by race/ethnicity.
   8. The majority of persons infected with HSV-2 have not been diagnosed with genital herpes (86% in the general U.S. population).

[Slide 7] Seroprevalence slide from NHANES 1999-2004

[Slides 8-9]

B. Transmission
   1. HSV-2 is transmitted sexually (genital to genital, oral to genital, or genital to oral) and perinatally (mother to child). HSV-1 is usually transmitted via a non-sexual route; however, sexual transmission appears to be increasing.
   2. The majority of genital herpes infections are transmitted by persons unaware that they have the infection or who are asymptomatic when transmission occurs.
   3. The risk of sexual transmission is difficult to quantify, but is estimated at >5% per year in studies of monogamous heterosexual couples with discordant HSV serum antibody status.
   4. Efficiency of sexual transmission is greater from men to women than from women to men.
   5. The presence of serum antibody to HSV-1 is not thought to protect against acquisition of HSV-2 infection. However, HSV-1 seropositivity increases the likelihood that an acquired HSV-2 infection will be asymptomatic.
   6. Frequency of occurrences and asymptomatic viral shedding, and thus likelihood of transmission to others, declines with increased duration of infection.
   7. Incubation period after acquisition is 2-12 days (average is 4 days).
   8. Drying and soap and water readily inactivate HSV; therefore, fomite transmission is unlikely.

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C. HSV and HIV infection
   1. Genital HSV-2 infection facilitates acquisition of HIV infection.
      a) Prevalent HSV-2 infection is associated with a 2-3 fold increased risk of acquiring HIV infection.
      b) Incident (new) HSV-2 infection is associated with an even higher risk of acquiring HIV infection.
   2. Genital HSV-2 infection is thought to facilitate transmission of HIV infection from persons who are co-infected with both viruses.

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II. Pathogenesis

[Slides 12-13]

A. Virology
   1. Members of the human herpes viruses (herpetoviridae), which include: HSV-1, HSV-2, VZV, EBV, CMV, HHV-6, HHV-7, HHV-8.
   2. HSV-1 and HSV-2 are double-stranded DNA viruses surrounded by an envelope of lipid glycoprotein.
   3. 50% DNA homology exists between HSV-1 and HSV-2.
   4. All members of this species establish latent infection in specific target cells.
   5. Infection persists despite the host immune response, often resulting in recurrent disease. Re-infection can rarely occur despite immunity.

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B. Pathogenesis
   1. Transmission of HSV usually occurs through close contact with a person who is shedding virus at a peripheral site, mucosal surface, or in genital or oral secretions.
      a) HSV penetrates susceptible mucosal surfaces or abraded cracks in the skin.
      b) After mucosal inoculation (in genital infection), the virus is transported along peripheral nerve axons to the nerve cell bodies' sacral ganglia.
      c) Virus remains latent indefinitely in the paraspinous ganglia.
      d) Reactivation is precipitated by multiple known (e.g., trauma, fever, ultraviolet light, stress, etc.) and unknown factors and induces viral replication.
      e) The re-activated virus migrates centrifugally to mucosal surfaces by way of the peripheral sensory nerves, where it may cause a cutaneous outbreak of herpetic lesions or subclinical viral shedding.
   2. Histopathologic changes include focal necrosis, ballooning degeneration of cells, production of mononucleated giant epithelial cells, and eosinophilic intra-nuclear inclusions called Cowdry type A bodies.
   3. Up to 90% of persons seropositive for HSV-2 antibody have not been diagnosed with genital herpes. However, many have mild or unrecognized disease and probably most, if not all, shed virus from the genital area intermittently.

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III. Clinical Manifestations

[Slides 16-18]

A. Definitions of types of infection
   1. First clinical episode
      a) Primary infection
         1) First infection ever with either HSV-1 or HSV-2
         2) No serum antibody present when symptoms appear
         3) Disease more severe than recurrent disease
         4) Serum antibody may take several weeks to a few months to appear
      b) Non-primary infection
         1) Newly acquired infection with HSV-1 or HSV-2 in an individual previously seropositive to the other virus
         2) Manifestations tend to be milder than primary infection.
         3) Type-specific antibody to the prior infection is present initially. Antibody to new infection may take several weeks to a few months to appear.
      c) First episode, recurrence: 25% of patients with first clinical episode of HSV-2 have had a prior unrecognized primary or non-primary first infection. Type-specific antibody will be present when the patient presents and the severity of the episode is comparable to a recurrence.

2. Recurrent symptomatic infection
   a) Antibody is present when symptoms appear, although the patient may not be aware of previous episodes.
   b) Disease is usually mild and short in duration.
3. Asymptomatic infection
   a) Serum antibody is present
   b) No known history of clinical outbreaks
   c) Up to two-thirds of patients with identified "asymptomatic" HSV-2 infection may actually have unrecognized symptomatic infection.
   d) Patients should be informed about clinical signs and symptoms of genital herpes, as this may help them recognize symptomatic infection.

Infection Type	Lesions/ Symptoms	Type-specific antibody at time of presentation	
		HSV-1	HSV-2
First episode Primary (Type 1 or 2)	+/Severe, bilateral	-	-
First episode Non-primary Type 2	+/Moderate	+	-
First episode Recurrence Type 2	+/Mild	+/-	+
Symptomatic Recurrence Type 2	+/Mild, unilateral	+/-	+
Asymptomatic Infection Type 2	-	+/-	+

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B. Clinical manifestations
   1. Primary (initial) infection without treatment: characterized by the occurrence of numerous bilateral painful genital lesions. These lesions are more severe, last longer, and have higher titers of virus than recurrent infections.
      a) Typical lesion progression: papules → vesicles → pustules → ulcers → crusts → healed; though patients may present at any stage and lesions may be atypical (e.g., fissures).
      b) Often associated with systemic symptoms, including fever, headache, malaise, myalgia; may cause urinary retention in women.
      c) Illness lasts 2-4 weeks. Painful genital lesions that are numerous and bilateral last an average of 11-12 days; full re-epithelialization takes an average of 17-20 days.
      d) Systemic symptoms peak within 3-4 days of onset of lesions and gradually recede over the next 3-4 days.

e) Local symptoms are predominantly pain, itching, dysuria, vaginal or urethral discharge, and tender inguinal adenopathy (80%).
f) Median duration of viral shedding detected by culture (from the onset of lesions to the last positive culture) is approximately 12 days, and correlates well with the mean time from the onset of vesicles to crusting.
g) Inguinal adenopathy peaks in week 2-3 and is often the last finding to resolve. Nodes are firm, nonfluctuant, and tender to palpation. Suppuration is rare.
h) HSV cervicitis occurs in 70-90% of primary HSV-2 infections and about 70% of primary HSV-1 infections. It may involve the exo- or endocervix and may be symptomatic or asymptomatic. The cervix will appear abnormal in most cases, with ulcerative lesions, erythema, or friability. Clinical differentiation from gonococcal or chlamydial cervicitis may be difficult, although cervical ulceration suggests HSV.
i) Herpes proctitis may be characterized by pain, discharge, tenesmus, constipation with or without symptoms of autonomic dysfunction and severe ulceration on anoscopy.
j) Urethral involvement
    1) Men with first-episode HSV have a positive urethral culture in 33% of cases. Urethritis and/or meatitis may be part of the clinical syndrome and may cause a clear mucoid discharge.
    2) Over 80% of women with primary HSV report dysuria, both external and internal. HSV has been isolated from approximately 5% of women with the dysuria-frequency syndrome.

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2. Recurrent infection without treatment
    a) Prodromal symptoms (localized tingling, irritation) are common and begin 12-24 hours before lesions and sometimes occur without lesions ("false prodrome").
    b) Duration of episodes is shorter than in primary infection: painful genital lesions last 4-6 days; average duration of viral shedding is 4 days.
    c) Lesions tend to be unilateral and much less extensive than with primary infection.
    d) Symptoms tend to be milder and less severe. Usually there are no systemic symptoms.
    e) Atypical presentations can occur, such as small linear ulcerations.
    f) Rate of cervical virus shedding during recurrences is 15-20%.
    g) Up to 90% of patients with symptomatic first episode HSV-2 infection will have a recurrence in the first 12 months of infection.
    h) The median recurrence rate is 4.5 per year in the first year of HSV-2 infection, but is highly variable.
    i) HSV-2 has been found to recur slightly more frequently in men than in women; median 5 recurrences/year compared with 4/year in the first year.
    j) A prolonged primary episode > 30 days predicts more frequent recurrences.

k) HSV-1 primary infection is much less likely to recur than HSV-2 primary infection (median of 1.3 recurrences/year in the first year).
l) The frequency of symptomatic recurrences gradually decreases over time; the frequency of recurrences decreases more quickly for HSV-1 than for HSV-2 infections.

[Slide 22]
Image: Herpes: Primary Lesion

[Slide 23]
Image: Herpes: Multiple ulcers

[Slide 24]
Image: Herpes: Recurrent Lesions

[Slide 25]
Image; Herpes: Periurethal Lesions

[Slide 26]
Image: Herpes: Cervicitis

[Slide 27]
Image: Herpes on the buttock

[Slide 28]
Image: Oral Herpes: Soft palate

[Slides 29-30]

3. Asymptomatic viral shedding
   a) Asymptomatic viral shedding has been documented in the majority of HSV-2 seropositive persons studied.
   b) In one study, the rate of subclinical shedding in patients with no reported history of genital herpes was similar to that in patients with such a history.
   c) Most HSV-2 is transmitted during asymptomatic shedding.
   d) Using more sensitive techniques (e.g., PCR) and more frequent sampling, shedding is found more frequently (up to 20-25% of days).
   e) Rates of asymptomatic shedding are greater with HSV-2 than with HSV-1.
   f) Rates of asymptomatic shedding are highest with newly acquired infections (<2 years) and gradually decrease over time.
   g) Asymptomatic shedding episodes are of briefer duration than shedding during clinical recurrences.
   h) Presence of serum antibody to HSV-1 seems to decrease rates of asymptomatic shedding with HSV-2.
   i) Most common sites of asymptomatic shedding are the vulva and perianal areas in women and penile skin and perianal area in men.

j) Antiviral suppressive therapy dramatically reduces, but does not eradicate shedding.

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C. Complications of genital infection
   1. Aseptic meningitis
      a) More common in primary than in recurrent infection
      b) More common with HSV-2 than HSV-1
      c) More common in women than in men (36% of women versus 11% of men with primary HSV-2 infection)
      d) May be severe, requiring hospitalization or parenteral narcotics
      e) There are generally no neurologic sequelae, however recent data suggest that benign recurrent meningitis (Mollaret's meningitis) is usually caused by HSV-2.
   2. Other complications (rare)
      a) Stomatitis and pharyngitis
      b) Radicular pain, sacral paresthesias
      c) Transverse myelitis
      d) Autonomic dysfunction: hyperesthesias, neurogenic bladder, constipation, and impotence
      e) Disseminated (viremic) infection--occasional in patients with atopic eczema, pregnant women, impaired CMI, neonates. Can be a cause of fulminant hepatitis in immunosuppressed patients.
      f) Ocular involvement (more common with HSV-1)
      g) Herpetic whitlow (more common with HSV-1)

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IV. Diagnosis

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A. Diagnosis
   1. Clinical diagnosis is insensitive and nonspecific; therefore, the clinical diagnosis of genital herpes should be confirmed by laboratory testing..
   2. The typical painful multiple vesicular or ulcerative lesions are absent in many infected persons. Up to 50% of symptomatic first-episode cases are caused by HSV-1 in some populations, but recurrences and subclinical shedding are much less frequent for genital HSV-1 infection than genital HSV-2 infection, therefore HSV serotype influences prognosis and counseling.
   3. There are 2 main types of lab tests used for confirmatory diagnosis:
      a) Virologic tests
      b) Type-specific serologic tests
   4. Both virologic and type-specific serologic tests for HSV should be available in clinical settings that provide care for patients with STDs or those at risk for STDs.

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B. Virologic tests
   1. Viral culture
      a) Isolation of HSV in cell culture is the preferred test if genital ulcers or other mucocutaneous lesions are present.
      b) Highly specific (>99%) but sensitivity depends on stage of lesion and proper collection technique (e.g., Dacron swab to obtain specimen from ulcer base) and declines rapidly as lesions begin to heal.
      c) Viral recovery for early vesicles--90%, ulcers--70%, and crusted lesions--30%. Culture is more often positive in primary infection (80%–90%) as contrasted with recurrences (30%).
      d) Time limitations: most cultures will be positive within 24-72 hours, but are generally held for 5-7 days. The enzyme-linked virus-inducible ELVIS HSV system is a 24-hour culture system but it is less sensitive than traditional culture
      e) Stable in viral transport media for 48-72 hours at 4°C.
      f) Allows for easiest typing; all cultures should be typed to determine if HSV-2 or HSV-1 is the cause of infection.
   2. Polymerase Chain Reaction (PCR) assays
      a) PCR assays for HSV DNA are highly sensitive and specific.
      b) PCR is more sensitive than viral culture and has been used instead of culture in some settings; however PCR tests are not FDA-cleared for testing of genital specimens, are not widely available, and may lack standardization across labs.
      c) PCR may be a reasonable choice for diagnosing genital lesions in laboratories that have well-validated assays.
      d) PCR is the test of choice for detecting HSV in spinal fluid for the diagnosis of HSV infection of the central nervous system (CNS).
   3. Antigen detection (DFA)
      a) Some HSV antigen tests, unlike other virologic tests, do not distinguish HSV-1 from HSV-2.
      b) Fairly sensitive (>85%) in symptomatic shedders
      c) Rapid (2-12 hours)
      d) Highly specific; some DFA tests can differentiate HSV-1 from HSV-2 or VZV using monoclonal antibodies, but false positives can occur.
      e) May be better than culture for healing lesions
   4. Cytology (Tzanck or Pap)
      a) Identifies typical HSV-infected cells (multi-nucleated giant cells and eosinophilic inclusion bodies) in exfoliated cells or biopsies.
      b) Cytologic detection of cellular changes of herpes virus infection is insensitive (50%) and nonspecific and should not be relied on for HSV diagnosis, either for genital lesions (i.e., Tzanck preparation) or for cervical Pap smears.

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C. Serologic tests
   1. Type-specific and nonspecific antibodies to HSV develop during the first several weeks to few months following infection and persist indefinitely.
   2. Presence of HSV-2 antibody indicates anogenital infection.
   3. Presence of HSV-1 does not distinguish anogenital from orolabial infection.
   4. The older serological tests (CF, IFA, EIA) did not distinguish between HSV-1 and HSV-2 antibody.
   5. New serological tests based on HSV type-specific antigens glycoprotein G1 (HSV-1) and glycoprotein G2 (HSV-2) have been developed and are now commercially available for type-specific testing.
      a) Currently the FDA-cleared glycoprotein G (gG)-based type-specific assays include the laboratory-based assays HerpeSelect™ -1 ELISA IgG or HerpeSelect™ -2 ELISA IgG and HerpeSelect™ 1 and 2 Immunoblot IgG (Focus Technology, Inc, Herndon, VA) and HSV-2 ELISA (Trinity Biotech USA, Berkeley Heights, NJ)
      b) Two other assays, Biokit HSV-2 and SureVue HSV-2 (Biokit HAS, Lexington, MA and Fisher Scientific, Pittsburgh, PA, respectively), are point-of-care tests that provide results for HSV-2 antibodies from capillary blood or serum during a clinic visit.
      c) The sensitivities of these tests for detection of HSV-2 antibody vary from 80% to 98% and false-negative results may occur, especially early after infection.
      d) The specificities of these assays are $\geq$ 96%; false-positive results can occur, especially in patients with low likelihood of HSV infection. Therefore, repeat or confirmatory testing may be indicated in some settings.
   6. The Western blot assay has been used as the gold standard technique for HSV antibody detection and can differentiate between type 1 and 2 antibodies. However, such tests have not been developed commercially due to high cost and labor intensity.
   7. Serologic tests for HSV based on IgM are not reliable, for diagnosis of genital lesions or neonatal herpes, and should not be used.
   8. Type-specific serologic assays might be useful in the following scenarios:
      a) Recurrent or atypical genital symptoms with negative HSV cultures.
      b) A clinical diagnosis of genital herpes without laboratory confirmation
      c) A sex partner with genital herpes
      d) 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. Cost-benefit analyses have not been performed comparing the costs of the tests vs. the savings resulting from preventing further cases.
   9. While serologic assays from HSV-2 should be available for persons who request them, screening for HSV-1 or HSV-2 infection in the general population is not indicated.

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D. Evaluation of a genital ulcer
    1. A diagnosis based only on the patient's medical history and physical examination frequently is inaccurate.
    2. All patients with genital ulcers should be evaluated with a serologic test for syphilis in addition to a diagnostic evaluation for genital herpes. In settings where chancroid is prevalent, a test for *Haemophilus ducreyi* should also be performed.
    3. Specific tests for evaluation of genital ulcers include: 1) syphilis serology and either darkfield examination or direct immunofluorescence test for *T. pallidum*; 2) culture or antigen test for HSV; and 3) culture for *H. ducreyi*. No FDA-cleared PCR test for these organisms is available in the U.S.; however, such testing can be performed by clinical laboratories that have developed their own tests and conducted a Clinical Laboratory Improvement Amendment (CLIA) verification study.
    4. Health-care providers frequently must treat patients before test results are available, because early treatment decreases the possibility of ongoing transmission and because successful treatment of genital herpes depends on prompt initiation of therapy.

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V. Patient Management

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A. Principles of management of genital herpes
    1. Counseling about the natural history of genital herpes, sexual and perinatal transmission, and methods to reduce transmission is integral to clinical management.
    2. Antiviral chemotherapy offers clinical benefits to most symptomatic patients and is the mainstay of management.
        a) Partially controls symptoms and signs of herpes episodes when used to treat first clinical and recurrent episodes, or when used as daily suppressive therapy.
        b) Does not eradicate latent virus and does not affect risk, frequency, or severity of recurrences after drug is discontinued.

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B. Antiviral therapy for HSV
    1. HSV systemic antiviral chemotherapy includes three oral medications:
        a) Acyclovir (ACV)
        b) Valacyclovir (Valine ester of acyclovir)--high oral bioavailability
        c) Famciclovir (Penciclovir prodrug)--high oral bioavailability
    2. Topical antiviral treatment is of minimal clinical benefit and is not recommended.

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C. Management of first clinical episode of genital herpes
    1. Many patients with first episode herpes present with mild clinical manifestations but later develop severe or prolonged symptoms. Therefore, patients with initial genital herpes should receive antiviral therapy.
    2. Antiviral therapy has dramatic effect in initial HSV infection, especially if symptoms <7 days and no history of oral HSV.

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    3. CDC-recommended regimens for the treatment of first clinical episode
        a) Acyclovir 400 mg orally 3 times a day for 7-10 days or
        b) Acyclovir 200 mg orally 5 times a day for 7-10 days, or
        c) Famciclovir 250 mg orally 3 times a day for 7-10 days, or
        d) Valacyclovir 1 g orally twice a day for 7-10 days.
    4. Treatment may be extended if healing is incomplete after 10 days of therapy.
    5. Higher dosages of acyclovir (e.g., 400 mg orally 5 times a day) have been used in treatment studies of first-episode herpes proctitis. However, no comparative studies have been conducted, and whether HSV proctitis requires higher doses of antiviral drugs than used for genital herpes is unknown.
    6. Factors to weigh when considering treatment: severity of symptoms, immune status, pregnancy, history of complications, and cost.

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D. Recurrent episodes of genital herpes
    1. Most patients with symptomatic primary genital HSV-2 infection experience recurrent outbreaks.
    2. Recurrences are less frequent after initial HSV-1 infection.
    3. Antiviral therapy for recurrent genital herpes can be administered either continuously as suppressive therapy, to reduce the frequency of occurrences, or episodically, to ameliorate or shorten the duration of lesions.
    4. Treatment options should be discussed with ALL patients.

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    5. Suppressive therapy
        a) Suppressive therapy reduces the frequency of genital herpes recurrences by 70%-80% among patients who have frequent recurrences (> 6 recurrences per year), and many patients report no symptomatic outbreaks.
        b) Treatment is also effective in patients with less frequent recurrences.
        c) Safety and efficacy have been documented among patients receiving daily therapy with acyclovir for as long as 6 years and with valacyclovir or famciclovir for 1 year.
        d) Quality of life often is improved in patients with frequent recurrences who receive suppressive therapy, compared with episodic therapy.

e) The frequency of recurrent outbreaks diminishes over time in many patients, and the patient's psychological adjustment to the disease may change. Periodically during suppressive treatment (e.g., once a year), discontinuation of therapy should be discussed with the patient to reassess the need for continued suppressive therapy.
f) Daily treatment with valacyclovir 500 mg daily decreases the rate of HSV-2 transmission in discordant, heterosexual couples in which the source partner has a history of genital HSV-2 infection. Such couples should be encouraged to consider suppressive antiviral therapy as part of a strategy to prevent transmission, in addition to consistent condom use and avoidance of sexual activity during recurrences.
g) Suppressive antiviral therapy probably reduces transmission when used by persons who have multiple partners (including MSM) and by those who are HSV-2 seropositive without a history of genital herpes.

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6. CDC-recommended regimens for suppressive therapy for recurrent infection
   a) Acyclovir 400 mg orally twice a day, or
   b) Famciclovir 250 mg orally twice a day, or
   c) Valacyclovir 500 mg orally once a day, or
   d) Valacyclovir 1 g orally once a day.
7. 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).
8. Several studies have compared valacyclovir or famciclovir with acyclovir. The results of these studies suggest that valacyclovir and famciclovir are comparable to acyclovir in clinical outcome.
9. Ease of administration and cost are important considerations for prolonged treatment.

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10. Episodic therapy
    a) Successful episodic treatment requires initiation of therapy within 1 day of lesion onset.
    b) Clinicians should provide the patient with a supply of drug or a prescription and instructions to self-initiate treatment immediately when symptoms begin.

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11. CDC-recommended regimens for episodic therapy for recurrent infection
    a) Acyclovir 400 mg orally 3 times a day for 5 days, or
    b) Acyclovir 800 mg orally twice a day for 5 days, or
    c) Acyclovir 800 mg orally 3 times a day for 2 days; or
    d) Famciclovir 125 mg orally twice a day for 5 days, or
    e) Famciclovir 1000 mg orally twice a day for 1 day

f) Valacyclovir 500 mg orally twice a day for 3 days, or
g) Valacyclovir 1 g orally once a day for 5 days.

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E. Severe disease
   1. IV acyclovir should be provided for patients with severe HSV disease or complications requiring hospitalization (e.g., disseminated infection, pneumonitis, or hepatitis), or complications of the central nervous system (e.g., meningitis or encephalitis).
   2. CDC-recommended regimen
      a) Acyclovir 5-10 mg/kg IV every 8 hours for 2-7 days or until clinical improvement, followed by oral antiviral therapy to complete at least 10 days total therapy.

F. Allergic and other adverse reactions to acyclovir, valacyclovir, and famciclovir are rare. Desensitization to acyclovir is described in Henry RE, et al. Successful oral acyclovir desensitization. Ann Allergy 1993; 70:386-8.

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G. Herpes in HIV Infected Persons
   1. Immunocompromised patients may have prolonged or severe episodes of genital, perianal, or oral herpes.
   2. Herpes lesions are common in HIV-infected patients and may be persistent, severe, painful, and atypical.
   3. Genital ulcers increase the risk of HIV transmission and acquisition.
   4. AIDS case definition applies if lesions persist >1 month in recurrent disease.
   5. HSV shedding is increased in HIV-infected persons. While antiretroviral therapy reduces the severity and frequency of symptomatic genital herpes, frequent subclinical shedding still occurs.
   6. Suppressive or episodic therapy with oral antiviral agents is effective in decreasing the clinical manifestations of HSV among HIV-positive persons.
   7. HIV-infected persons are likely to be more contagious for HSV; the extent to which suppressive antiviral therapy will decrease HSV transmission from this population is unknown.
   8. Some specialists suggest that HSV type-specific serologies be offered to HIV-positive persons during their initial evaluation, and that suppressive antiviral therapy be considered in those who have HSV-2 infections.
   9. Suppressive antiviral therapy with acyclovir and valacyclovir has been shown to decrease plasma HIV viral load and genital and rectal HIV shedding; it is currently unknown whether suppressive antiviral therapy can affect acquisition or transmission of HIV.

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   10. CDC-recommended regimens for suppressive therapy for HIV-infected persons
      a) Acyclovir 400-800 mg orally twice to 3 times a day, or
      b) Famciclovir 500 mg orally twice a day, or

c) Valacyclovir 500 mg orally twice a day.

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11. CDC-recommended regimens for episodic therapy for HIV-infected persons
    a) Acyclovir 400 mg orally 3 times a day for 5-10 days, or
    b) Famiciclovir 500 mg orally twice a day for 5-10 days, or
    c) Valacyclovir 1 g twice a day for 5-10 days.
12. Acyclovir, valacyclovir, and famciclovir are safe for use in immunocompromised patients in doses recommended for treatment of genital herpes. For severe cases, initiating therapy with acyclovir 5-10 mg/kg IV every 8 hours may be necessary.
13. If lesions persist or recur in a patient receiving antiviral treatment, HSV resistance should be suspected and a viral isolate obtained for sensitivity testing. Such patients should be managed in consultation with a specialist, and alternative therapy should be administered. All acyclovir-resistant strains are resistant to valacyclovir and most are resistant to famciclovir. (Refer to the CDC 2006 STD Treatment Guidelines for treatment alternatives http://www.cdc.gov/STD/treatment/).

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H. Genital herpes in pregnancy
    1. The majority of mothers of infants who acquire neonatal herpes lack histories of clinically evident genital herpes.
    2. Risk for transmission to neonate from infected mother is high (30%-50%) in women who acquire genital herpes near time of delivery and low (<1%) in women with histories of recurrent herpes or who acquire genital HSV during the first half of pregnancy. However, because recurrent genital herpes is much more common than initial HSV infection during pregnancy, the proportion of neonatal HSV infections acquired from mothers with recurrent herpes is substantial.
    3. Prevention of neonatal herpes depends on avoiding acquisition of HSV during late pregnancy and avoiding exposure of infant to herpetic lesions during delivery.
    4. Women without known genital herpes should be counseled to avoid intercourse during 3rd trimester with partners known or suspected of having genital herpes.
    5. Women without known orolabial herpes should be counseled to avoid receptive oral sex during 3rd trimester with partners known or suspected of having orolabial herpes.
    6. Some specialists believe that type-specific serologic tests are useful to identify pregnant women at risk for HSV infection and to guide counseling regarding the risk for acquiring genital herpes during pregnancy. Such testing should be offered to women without genital herpes whose sex partner has HSV infection.
    7. The results of viral cultures during pregnancy in women with or without visible herpetic lesions do not predict viral shedding at the time of delivery, and

therefore routine viral cultures of pregnant women with recurrent genital herpes are not recommended.

8. The effectiveness of antiviral therapy to decrease the risk for HSV transmission to pregnant women has not been studied.
9. All pregnant women should be asked whether they have a history of genital herpes.
10. At onset of labor:
    a) All women should be questioned carefully about symptoms of genital herpes, including prodromal symptoms.
    b) All women should be examined carefully for herpetic lesions.
11. Women without symptoms or signs of genital herpes or its prodrome can deliver vaginally.
12. Most specialists recommend that women with recurrent genital herpetic lesions at onset of labor deliver by cesarean section to prevent neonatal herpes. However, abdominal delivery does not completely eliminate the risk for HSV transmission to the infant.
13. Risk factors for HSV transmission to the infant include: new infection, primary infection, lack of type-specific antibodies, and use of scalp electrodes.
14. Safety of systemic acyclovir, valacyclovir, and famciclovir therapy in pregnant women has not been definitively established. Available data do not indicate increased risk for major birth defects compared with the general population in women treated with acyclovir during the first trimester. These findings provide some assurance to women who have had prenatal exposure to acyclovir. The experience with prenatal exposure to valacyclovir and famciclovir is too limited to provide useful information on pregnancy outcomes.
15. Acyclovir may be administered orally to pregnant women with first episode genital herpes or severe recurrent herpes and should be administered IV to pregnant women with severe HSV infection.
16. Acyclovir treatment late in pregnancy reduces the frequency of cesarean sections among women who have recurrent genital herpes by diminishing the frequency of recurrences at term, and many specialists recommend such treatment.
17. No data support the use of antiviral therapy among HSV seropositive women without a history of clinical genital herpes.
18. The risk for herpes is high in infants of women who acquire genital HSV during late pregnancy; such women should be managed in consultation with an infectious diseases specialist. Some experts recommend acyclovir therapy in this circumstance, some recommend routine cesarean section to reduce the risk of neonatal herpes, others recommend both.

I. Neonatal Herpes
    1. Infants exposed to HSV during birth, as documented by maternal virologic testing or presumed by observation of maternal lesions, should be followed carefully in consultation with a specialist.

2. Some specialists recommend that such infants undergo surveillance cultures of mucosal surfaces to detect HSV infection before development of clinical signs of neonatal herpes.
3. Some specialists also recommend the use of acyclovir for infants born to women who acquired HSV near term because the risk of neonatal herpes is high for these infants.
4. All infants who have neonatal herpes should be promptly evaluated and treated with systemic acyclovir.
5. The recommended regimen for infants treated for known or suspected neonatal herpes is acyclovir 20 mg/kg body weight IV every 8 hours for 21 days for disseminated and CNS disease or for 14 days for disease limited to the skin and mucous membranes.

J. Therapy of acyclovir-resistant HSV infections
   1. All acyclovir-resistant strains are resistant to valacyclovir and most are resistant to famciclovir.
   2. The therapy of choice in acyclovir-resistant HSV infections is intravenous sodium phosphonoformate (Foscarnet).
   3. Foscarnet injections once or twice weekly may be necessary to suppress recurrent episodes of acyclovir-resistant HSV in immunosuppressed patients.
   4. Topical cidofovir gel 1% applied to lesions might be effective. This preparation is not commercially available and must be compounded by a pharmacy.

K. Adjunctive therapy
   1. Pain relief--usually necessary only in primary disease. Painful urination can be alleviated by urinating in warm bath.
   2. Topical measures: drying or analgesia--of unproven benefit, but some patients report relief.
   3. Sitz baths

[Slide 58]

VI. Patient Counseling and Education

[Slide 59]

A. Patient Counseling and Education
   1. Counseling has two main goals:
      a) To help patients cope with the infection, and
      b) To prevent sexual and perinatal transmission.
   2. Although initial counseling can be provided at first visit, many patients benefit from learning about the chronic aspects of the disease after the acute illness subsides.
   3. Numerous resources are available to assist patients and clinicians in counseling (see the Resources list at the end of this module for more information).
   4. HSV-infected persons may express anxiety about genital herpes that does not reflect the actual clinical severity of their disease.

5. Common concerns about genital herpes include the severity of initial clinical manifestations, recurrent episodes, sexual relationships and transmission to sex partners, and ability to bear healthy children.
6. The misconception that HSV causes cancer should be dispelled, because HSV-2 is not a primary etiologic agent in cervical cancer.
7. The psychological effect of a serologic diagnosis of HSV-2 infection in a person with asymptomatic or unrecognized genital herpes appears small and transient.

[Slide 60]

B. Patient counseling and education should include:
   1. Natural history of the infection
   2. Treatment options
   3. Transmission and prevention issues
   4. Neonatal HSV prevention issues

[Slide 61]

C. Natural history of the infection
   1. Recurrent episodes are likely following a symptomatic first episode
      a) HSV-2 infections have more frequent recurrences than HSV-1 infections
      b) The frequency of outbreaks generally decreases over time
   2. Asymptomatic viral shedding occurs, and HSV can be transmitted to a sex partner during asymptomatic periods
      a) Asymptomatic shedding is more frequent in genital HSV-2 infection than genital HSV-1 infection.
      b) Asymptomatic shedding is most frequent during the first 12 months after acquiring HSV-2.
   3. Stressful events may trigger recurrences
   4. Prodromal symptoms may precede outbreaks

[Slide 62]

D. Treatment options
   1. Suppressive therapy is available and is effective in preventing symptomatic recurrent episodes.
   2. Episodic therapy sometimes is useful in shortening the duration of recurrent episodes if started within 1 day of lesion onset.
   3. When and how to take antiviral medications
   4. Recognition of prodromal symptoms to know when to begin episodic therapy
   5. Strategies for relief of painful urination such as urinating in a tub and the use of topical analgesics

[Slide 63]

E. Transmission and Prevention
   1. HSV can be transmitted when lesions are not present and most cases are transmitted during asymptomatic periods.
   2. Encourage all persons with genital herpes infection to:

a) Inform current sex partners about diagnosis of genital herpes.
b) Inform future partners before initiating a sexual relationship.

3. Abstain from sexual activity with uninfected partners when lesions or prodromal symptoms are present.
4. Correct and consistent use of latex condoms might reduce the risk of genital herpes transmission.
5. Daily treatment with valacyclovir 500 mg decreases the rate of HSV-2 transmission in discordant, heterosexual couples in which the source partner has a history of genital HSV-2 infection. Such couples should be encouraged to consider suppressive antiviral therapy as part of a strategy to prevent transmission, in addition to consistent condom use and avoidance of sexual activity during recurrences.
6. Suppressive antiviral therapy probably reduces transmission when used by persons who have multiple partners (including MSM) and by those who are HSV-2 seropositive without a history of genital herpes.

[Slide 64]

F. Neonatal herpes prevention
   1. Risk of neonatal HSV infection should be explained to all patients, including men.
   2. Advise pregnant women and women of child-bearing age to inform their prenatal and neonatal care providers that they have genital herpes.
   3. Advise pregnant women who are not infected with HSV-2 to avoid intercourse during the third trimester with men who have genital herpes.
   4. Advise pregnant women who are not infected with HSV-1 to avoid genital exposure to HSV-1 during the third trimester (e.g., oral sex with a partner with oral herpes and vaginal intercourse with a partner with genital HSV-1 infection).

[Slide 65]

G. Counseling for asymptomatic persons
   1. Give asymptomatic persons diagnosed with HSV-2 infection by type-specific serologic testing the same counseling messages as persons with symptomatic infection.
   2. Teach about the common manifestations of genital herpes, as many will become aware of them with time.
   3. Antiviral therapy is not recommended for persons without clinical manifestations of infection.
   4. Type-specific serological testing of asymptomatic partners can determine whether risk of HSV acquisition exists.

[Slide 66]

VII. Partner Management

A. Counseling of infected persons and their sex partners is critical to management of genital herpes. Sex partners are likely to benefit from evaluation and counseling.

B. Symptomatic sex partners should be evaluated and treated in the same manner as patients who have genital lesions.
C. Asymptomatic sex partners of patients who have genital herpes should be asked about any history of genital lesions, counseled to recognize symptoms of herpes, and offered type-specific serologic testing for HSV infection.
    1. Sex partners of infected persons should be advised that they might be infected even if they have no symptoms.
    2. Type-specific serologic testing of asymptomatic partners of persons with genital herpes can determine whether risk of HSV acquisition exists.

CASE STUDY

[Slide 68]
Roberta Patterson is a 26-year-old woman who presents for her first prenatal visit. She is concerned for her baby because of her husband Franklin's history of genital herpes. She states that she is 6 weeks pregnant.

History

- Roberta has never had symptoms of vaginal or oral herpes.
- She was diagnosed and treated for chlamydia seven years ago (age 19); no other STD diagnoses reported.
- Her 26-year-old husband had his first episode of genital herpes during his last year of high school; no other STD diagnoses reported.
- Her husband (and sex partner for the last 16 months) has not had HSV lesions visible since she's been sexually active with him, and reports having had no prodromal symptoms or symptoms of active disease.
- She has had no sex partners other than her husband for the last 16 months.

[Slide 69]
Physical Exam

- Vital signs: blood pressure 112/68, pulse 58, respiration 13, temperature 38.5° C
- Cooperative, good historian
- Chest, heart, musculoskeletal, and abdominal exams within normal limits
- Uterus consistent with a 6-week pregnancy
- Normal vaginal exam without signs of lesions or discharge
- No lymphadenopathy

[Slide 70]
1. Which HSV general education messages should be discussed with Roberta?

Correct responses include the following:

- Genital herpes is a chronic, life-long viral infection.
- HSV-2 causes the majority of genital herpes cases in the U.S.
- Genital herpes is very common: at least 50 million people in the U.S. have genital HSV infection.
- Most persons infected with HSV-2 are undiagnosed: up to 90% of persons seropositive for HSV-2 antibody have no clinical history of anogenital herpes outbreaks.
- Most sexual transmission occurs while the source case is asymptomatic.

2. Given that Roberta's husband Franklin has a history of genital herpes, would it be appropriate to test Roberta for genital herpes using a type-specific serologic test?

Yes, it would be appropriate to use a type-specific serologic test to test Roberta for genital herpes, given that she is pregnant and her husband has a history of genital herpes. Some specialists believe type-specific serologic tests are useful to identify

pregnant women at risk for HSV infection and to guide counseling with regard to the risk of acquiring genital herpes during pregnancy. Because the greatest risk for neonatal herpes occurs when a woman acquires genital herpes for the first time in late pregnancy, such testing and counseling may be especially important when a woman's sex partner has HSV infection but she is not known to be infected.

3. What other STD screening should be considered for Roberta?

Because of the potential for neonatal infection, CDC recommends screening all pregnant women for syphilis, chlamydia, gonorrhea, hepatitis B, and HIV.

[Slide 71]
Roberta's Laboratory Results

- HSV gG-based type-specific serologies: HSV-1 negative; HSV-2 positive
- DNA probe for *Chlamydia trachomatis*: negative
- Culture for *Neisseria gonorrhoeae*: negative
- RPR: nonreactive
- HIV antibody test: negative
- Pregnancy test: positive

4. What would you tell Roberta about her HSV infection, based on clinical manifestations and test results?

Roberta most likely has an asymptomatic or unrecognized genital herpes infection. She does have evidence of exposure to HSV-2, but reports no symptoms or previous clinical episodes.

Up to two-thirds of patients with identified "asymptomatic" HSV-2 infection may actually have symptomatic infection that is mild or simply unrecognized as genital herpes. Most patients with asymptomatic or unrecognized genital HSV infections will still shed virus intermittently in the genital tract.

Patients such as Roberta should be taught to recognize signs and symptoms of genital herpes. She should inform her obstetric provider(s) about her HSV-2 infection status and assess whether any signs or symptoms of infection develop at the onset of labor.

The risk for transmission of HSV-2 to a neonate is low (<1%) among women who have acquired HSV-2 infection before the second half of pregnancy. Women without symptoms of genital herpes or its prodrome and without signs of herpetic lesions on careful examination at the onset of labor can deliver vaginally. Most specialists recommend that women with recurrent herpetic lesions at the onset of labor deliver by cesarean section to prevent neonatal herpes.

5. Would routine viral cultures during Roberta's pregnancy be recommended?

No. The results of viral cultures during pregnancy of women with or without visible herpetic lesions do NOT predict viral shedding at the time of delivery, and therefore routine viral cultures of pregnant women with recurrent genital herpes are NOT recommended.

[Slide 72]
Partner Management
Sex partner and exposure information:

Franklin Patterson
First sexual exposure: 16 months ago
Last sexual exposure: 1 month ago
History of genital herpes infection; first episode 8 years ago. No HSV testing or treatment at time of first episode or with subsequent episodes.
No history of other STDs; no sex partners other than Roberta in the past 16 months.

6. Franklin reports genital lesions during Roberta's sixth month of pregnancy. Which laboratory tests should be performed on him?

Correct responses include the following:

HSV viral culture of the lesions. Viral cultures are the preferred HSV test for patients with genital ulcers or other mucocutaneous lesions. HSV PCR testing is a sensitive and specific option in some settings. Tzanck stain of the lesions is insensitive and nonspecific, and should not be relied on for HSV diagnosis. Viral culture is preferred over DFA or EIA antigen detection tests when a patient has a genital lesion.

Darkfield microscopy or DFA-TP on genital lesions and RPR to test for syphilis. Syphilis testing should be considered for any patient presenting with genital lesions since genital lesions are a symptom of primary syphilis.

Testing for *C. trachomatis*, *N. gonorrhoeae*, and HIV. Because patients who have contracted an STD may be at greater risk for exposure to other STDs, it is useful to screen for other STDs, such as chlamydia, gonorrhea, and HIV.

[Slide 73]
Laboratory Results for Franklin
Franklin's laboratory test results are as follows:
HSV cultures: HSV-1 negative; HSV-2 positive
DNA probe for *Chlamydia trachomatis*: negative
Culture for *Neisseria gonorrhoeae*: negative
RPR: nonreactive
DFA: negative for *Treponema pallidum*
HIV antibody test: negative

7. What is an appropriate episodic treatment for Franklin?
Correct responses include the following:

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

Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks.

[Slide 74]
Follow-Up
Roberta had no HSV symptoms during her pregnancy.

Roberta discussed the use of acyclovir treatment in late pregnancy with her certified nurse-midwife, but decided against it because there are no data to support the use of antiviral therapy among HSV seropositive women without a history of clinical genital herpes episodes.

At onset of labor, she reported no prodromal or other HSV symptoms and no lesions were found on examination.

After a 14-hour labor, she vaginally delivered a healthy 7.2 lb baby girl.

[Slide 75]
8. What questions should be asked of ALL women beginning labor (regardless of their history of genital HSV infection)?

All women beginning labor should be questioned about prodromal and other HSV symptoms and should be examined for lesions.

9. If Roberta had genital herpetic lesions at the onset of labor, should she deliver vaginally or abdominally? What is the risk to the infant?

Most specialists recommend that women with genital herpetic lesions at the onset of labor deliver abdominally to reduce the risk of neonatal herpes. However, abdominal delivery does not completely eliminate the risk for HSV transmission to the infant.

[Slide 76]
10. Roberta is asymptomatic at the time of delivery. Is it medically appropriate for her to deliver vaginally?

Yes, women without signs or symptoms of genital herpes or its prodrome can deliver vaginally.

11. If Roberta had acquired genital herpes around the time of delivery, would she be more or less likely to transmit genital herpes to her baby during a vaginal delivery than if she had a history of recurrent genital herpes?

If she had acquired genital herpes around the time of delivery, she would be more likely to transmit it to her baby than if she had a history of recurrent genital herpes. With vaginal delivery, transmission from an infected mother to the neonate occurs in up to 30%-50% of genital herpes infections acquired around the time of delivery and in <1% of recurrent infections.

TEST QUESTIONS

1. Genital herpes is:
    a. A chronic, life-long bacterial infection
    b. A chronic, life-long viral infection
    c. A transient infection caused by a protozoal organism
    d. A transient viral infection

2. The majority of genital and perirectal recurrent herpetic outbreaks in the U.S. are caused by HSV-1.
    a. True
    b. False

3. Which of the following statements is true about the prevalence and incidence of HSV-2?
    a. At least 50 million persons in the U.S. have genital HSV infection.
    b. Most people with HSV-2 infection have not been diagnosed.
    c. In the general U.S. population, 17% of adults aged 14-49 years have HSV-2 antibodies.
    d. All of the above

4. Which of the following statements is true about the transmission of HSV?
    a. The average incubation period is 10 days.
    b. Likelihood of transmission does not change with increased duration of infection.
    c. HSV is readily inactivated by drying and soap and water.
    d. Most sexual transmission occurs while the source contact case is symptomatic.

5. In most cases of sexual transmission of genital HSV, the source case is asymptomatic at the time of transmission.
    a. True
    b. False

6. Sexual transmission of genital herpes is **less efficient** from
    a. Women to men
    b. Men to women
    c. Transmission efficiency is the same from men to women and from women to men.

7. Up to __% of persons seropositive for HSV-2 antibody have no clinical history of anogenital herpes outbreaks.
    a. 50
    b. 75
    c. 90
    d. 95

8. Which of the following statements is true about the pathogenesis of HSV?
    a. Up to 90% of persons seropositive for HSV-2 antibody have a clinical history of anogenital herpes outbreaks.
    b. Most persons who are seropositive for HSV-2 but report no symptoms still shed virus from the genital area intermittently.
    c. HSV-2 is not associated with HIV acquisition or transmission.
    d. All herpes viruses establish active infection in specific target cells.

9. Which clinical presentation is typical of a primary first episode HSV-2 infection?
    a. No lesions or symptoms, HSV-1 antibodies may or may not be present, HSV-2 antibodies are present
    b. Lesions present, symptoms usually mild, HSV-1 antibodies may or may not be present, HSV-2 antibodies are present
    c. Lesions present, symptoms usually severe, HSV-1 and HSV-2 antibodies are not present
    d. Lesions present, symptoms usually moderate, HSV-1 antibodies are present, HSV-2 antibodies are not present

10. In primary HSV infection without treatment, the median duration of viral shedding detected by culture is:
    a. Approximately 4 days
    b. Approximately 12 days
    c. 5-10 days
    d. 2-4 weeks

11. All of the following are true of asymptomatic viral shedding, EXCEPT:
    a. Asymptomatic shedding occurs in most, if not all, HSV-2 seropositive persons.
    b. Rates of asymptomatic shedding are greater with HSV-1 than HSV-2.
    c. Rates of asymptomatic shedding with HSV-2 are highest in early infection and decrease over time.
    d. The most common sites of asymptomatic shedding are the vulva and the perianal area in women and penile skin and the perianal area in men.

12. Which of the following is true about aseptic meningitis, a complication of genital herpes infection?
    a. It is more common in women than men.
    b. It is more common with HSV-1 than HSV-2 infection.
    c. It is more common in recurrent than primary infection.
    d. It generally has severe neurologic sequelae.

13. Which of the following factors can affect the severity and frequency of clinical manifestations and recurrence rates of genital herpes infection?
    a. Viral type
    b. Immune status of the host
    c. Gender

d. All of the above

14. Which of the following statements describes non-primary first episode HSV infection?
    a. First infection ever with either HSV-1 or HSV-2
    b. Disease is milder than recurrent disease
    c. No serum antibody present when symptoms appear
    d. Newly acquired infection with HSV-1or HSV-2 in an individual previously seropositive to the other virus

15. Primary infection without treatment lasts:
    a. 3-4 days
    b. 5-7 days
    c. 10-12 days
    d. 2-4 weeks

16. Which of the following statements is true about recurrent infection without treatment?
    a. Duration is shorter than primary infection.
    b. HSV-1 infection is much more likely to recur than HSV-2.
    c. There are usually systemic symptoms associated with the recurrent infection.
    d. HSV-2 will recur slightly more frequently and after a shorter period of time in women than in men.

17. Which of the following statements is true about asymptomatic viral shedding?
    a. Most HSV-2 is not transmitted during asymptomatic shedding.
    b. Rates of asymptomatic shedding in HSV-2 seropositive persons do not change over time.
    c. **Presence of serum antibody to HSV-1 seems to decrease rates of asymptomatic shedding with HSV-2.**
    d. Antiviral suppressive therapy completely eradicates shedding.

18. Which of the following tests should not be relied upon for HSV diagnosis?
    a. Type-specific serology
    b. Antigen detection
    c. Tzanck smear
    d. PCR assay

19. Type-specific serologic tests are recommended for all of the following reasons EXCEPT:
    a. To confirm a clinical diagnosis of genital herpes without laboratory confirmation
    b. To aid in diagnosis of recurrent genital symptoms with negative HSV cultures
    c. To screen for HSV-1 or HSV-2 infection in the general population

d. To manage sex partners of persons with genital herpes

20. Which of the following best describes antigen detection (DFA or EIA) testing?
    a. Preferred test for detecting HSV in spinal fluid; highly sensitive and specific; role in diagnosis of genital ulcer disease not well-defined
    b. Rapid and highly specific; fairly sensitive for symptomatic shedders; may be better than culture for healing lesions
    c. Considered the gold standard; preferred test for patients with genital ulcers or other mucocutaneous lesions
    d. Insensitive and nonspecific; should not be relied on for HSV diagnosis

21. Which of the following is true regarding systemic antiviral therapy?
    a. It partially controls symptoms and signs of herpes episodes when used to treat first clinical and recurrent episodes or when used as daily suppressive therapy.
    b. It reduces the frequency of genital herpes recurrences by 40%-50% when used as suppressive therapy for patients who have frequent recurrences.
    c. It should never be provided to patients to self-initiate treatment when symptoms begin.
    d. It is less effective than topical antiviral treatment for management of severe disease.

22. HSV systemic antiviral chemotherapy includes which of the following oral medications?
    a. Acyclovir
    b. Valacyclovir
    c. Famciclovir
    d. All of the above

23. Which of the following is true about episodic treatment of recurrent episodes of HSV disease?
    a. It can ameliorate or shorten the duration of lesions
    b. Patient should self-initiate the medication
    c. Successful treatment requires initiation of therapy within 1 day of lesion onset
    d. All of the above

24. All of the following are true of herpes in pregnancy, EXCEPT:
    a. The risk for transmission from infected mother to neonate is 30%-50% in women who acquire genital herpes near the time of delivery.
    b. The risk for transmission from infected mother to neonate is <1% in women with histories of recurrent genital herpes or who acquire genital HSV during the first half of pregnancy.
    c. Most specialists recommend that women with recurrent genital herpetic lesions at the onset of labor be delivered by cesarean section.

d. Most specialists recommend that women with histories of recurrent genital herpes who have no symptoms or signs of genital herpes or its prodrome at the onset of labor deliver by cesarean section.

25. Asymptomatic sex partners of persons diagnosed with genital herpes should be:
    a. Questioned concerning histories of genital lesions
    b. Informed that they might be infected with HSV even if they have not previously recognized any symptoms
    c. Offered type-specific serologic testing for HSV infection
    d. All of the above

26. Patients with genital herpes should be informed that:
    a. Sexual transmission of HSV can occur during asymptomatic periods.
    b. Stressful events may trigger recurrences.
    c. The frequency of outbreaks generally decreases with increasing duration of the infection.
    d. All of the above

27. Which of the following is true of the relationship between HSV and HIV infection?
    a. Genital ulcers have no effect on the risk of HIV transmission and acquisition.
    b. Lesions caused by HSV are uncommon in HIV-infected persons.
    c. In co-infected persons, suppressive antiherpetic therapy has been shown to decrease plasma HIV viral load and genital and rectal HIV shedding.
    d. All of the above

28. Patient education should include all of the following, EXCEPT:
    a. HSV can be transmitted sexually during asymptomatic periods.
    b. The frequency of outbreaks generally decreases with increasing duration of infection.
    c. Sex partners of infected persons are unlikely to be infected if they do not have symptoms.
    d. Risks of neonatal infection should be explained to women and men.

29. Patients with genital herpes should be advised to:
    a. Abstain from sexual activity with uninfected partners when prodromal symptoms are present.
    b. Inform their obstetric providers of their HSV status, if they are women who are pregnant or of child-bearing age.
    c. Inform future sex partners that they have genital herpes before initiating a sexual relationship.
    d. All of the above

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Websites and Other Resources

1. CDC, Division of STD Prevention: www.cdc.gov/std
2. National Network of STD/HIV Prevention Training Centers: http://depts.washington.edu/nnptc/
3. 2006 CDC STD Treatment Guidelines: http://www.cdc.gov/STD/treatment/
4. CDC-INFO
   1-800-CDC-INFO (800-232-4636)
   TTY: 1-888-232-6348
   In English, en Español
5. CDC National Prevention Information Network (NPIN): www.cdcnpin.org
6. American Social Health Association (ASHA): www.ashastd.org
7. International Herpes Management Forum (IHMF): http://www.ihmf.org/