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HERPES SIMPLEX VIRUS (HSV) INFECTIONS DURING PREGNANCY

A. Background

1. Among 14- to 49-year-old females, the prevalence of HSV-2 infection is 15.9%. Approximately 10% of women who are HSV-2 seronegative have partners who are seropositive and are at risk for transmission of HSV-2 during the pregnancy.
2. Vertical transmission to the newborn is accompanied by devastating consequences. Neonatal HSV infections can be classified as disseminated disease (25%); central nervous system disease (30%); and disease limited to the skin, eyes, or mouth (45%). Mortality has decreased substantially over the past 2 decades but is still 30% for disseminated disease and 4% for central nervous system disease.
3. The neonatal risk is greatest in women who acquire HSV for the first time during the pregnancy, as compared to women with longstanding HSV whose infection is reactivated during the pregnancy (risk 25-50% vs. <1%).
4. Newly acquired HSV infection accounts for 80% of neonatal cases and is usually the associated with asymptomatic cervical viral shedding.
5. Up to 50-80% of new genital infections in women, and 30-50% of neonatal infections, may be caused by HSV-1, so the former distinction between HSV-1 and HSV-2 has become less meaningful at present; either viral type may be associated with severe neonatal disease.

B. Diagnosis

1. A diagnosis of genital HSV infection based on physical examination unfortunately has a sensitivity of only 40% and a false positive rate of 20% but is what must most commonly be relied upon in clinical decision making.
2. Viral culture for HSV, once considered the 'gold standard', is limited by stage of the lesion at the time of specimen collection (vesicle>ulcer>crusted lesion), and by viral inoculum (80% positive for primary lesions, 40% positive for recurrent lesions). It is a 'send out' test with a 1-2 wk turnaround time and provides HSV typing if specified.
3. Polymerase chain reaction techniques (PCR) have superior sensitivity compared to culture. ANMC Laboratory offers HSV Type 1 and Type 2 virologic PCR. It is a 'send out' test with a 1-2 wk turnaround time.
4. ANMC Laboratory offers HSV 1 and 2 specific IgG antibody sero-testing with reflex. If patient result falls between 0.91 (Equivocal) and 5.00 (Low Positive) Index values, the specimen will reflex to 163006 HSV-2 Supplemental test per CDC guidelines. It is a 'send out' test with a 1-2 wk turnaround time.

5. There is no current evidence that screening asymptomatic patients is cost-effective, and such a strategy is not recommended by American College of Obstetricians and Gynecologist, (ACOG), the Center for Disease Control and Prevention (CDC), or the US Preventative Services Task Force (USPSTF).
6. Differentiation of primary HSV infection from a non-primary first episode during pregnancy (secondary or recurrent infection) can only be made by positive viral detection and a negative serologic test result.
7. Diagnosis of a primary infection is based on the combination of positive viral detection and negative serologic test results or evidence of seroconversion.
8. A nonprimary first-episode infection is confirmed when one viral type is detected in lesions from individuals with evidence of antibodies to the other viral type in the serum.

Clinical designation of genital herpes simplex virus infection (HSV)

Direct viral test result*	Type-specific serologic status¶		Classification of genital HSV infection
	HSV-1 antibodies	HSV-2 antibodies	
HSV-1 detected	–	–	Primary HSV-1 infection
	–	+	Nonprimary first episode HSV-1 infectionΔ
	+	– or +	Recurrent HSV-1 infection
HSV-2 detected	–	–	Primary HSV-2 infection
	+	–	Nonprimary first episode HSV-2 infection
	– or +	+	Recurrent HSV-2 infection

* Testing of the ulcerative lesion with culture, polymerase chain reaction, or direct fluorescent antibody.
¶ Performed at the time of initial presentation with the ulcerative lesion.
Δ Nonprimary first episode genital HSV-1 infection is rare.

C. Management

1. Primary HSV infection: All primary HSV outbreaks during pregnancy should be treated at presentation to reduce the severity of the symptoms, shorten the duration of the outbreak, and reduce the duration of viral shedding.
2. The following regimens are recommended:

    a. Acyclovir 400 mg po 3x daily x 7-10 days -OR-
    b. Valacyclovir 1000 mg po 2x daily x 7-10 days

3. Topical therapy with acyclovir cream is ineffectual, but many women may have severe symptoms with fever and urinary retention and require local symptomatic treatment, oral analgesics, and/or urinary drainage until the lesions crust over and the pain is relieved.
4. Women with complications that require hospitalization should receive:

    Acyclovir 5-10 mg/kg IV q8h x 2-7 days, followed by 10 days of oral therapy
5. Primary outbreaks that occur in the third trimester: continuing antiviral therapy until delivery may be considered.

6. Recurrent HSV infections:
    A. Episodic treatment of recurrences: The following treatment regimens are recommended:

        a. Acyclovir 400 mg po 3x daily x 5 days -OR-
        b. Valacyclovir 1000 mg po 2x daily x 5 day

    B. Suppressive therapy for recurrent HSV: Women who have had active genital recurrences will benefit from suppressive treatment at 36 weeks as it can reduce the frequency of recurrences by 75%, reduce the incidence of cesarean delivery by 40%, and reduce the rate of shedding (as determined by PCR) by 90%. Nevertheless, the current evidence has not clearly demonstrated that suppressive treatment near term is able to decrease the incidence of neonatal infection.

        The suggested regimen is:

        a. Acyclovir 400 mg po 3x daily from 36 weeks gestation
        b. Valacyclovir 500 mg po 2x daily from 36 weeks gestation

        Other:
        c. Consistent condom use and abstinence during acute episodes should be encouraged, but likewise has not been demonstrated to prevent neonatal infection.
        d. Acyclovir has not been demonstrated to be teratogenic and is considered safe in all trimesters. The drug only becomes active in viral infected cells. It has been associated with transient neonatal leukopenia in up to 20% of the infants of mothers taking the drug, but no long-term adverse effects have been observed.

e. Valacyclovir has better bioavailability compared to acyclovir and is metabolized to acyclovir in vivo.
f. Women at risk are begun on suppressive therapy at 36 weeks gestation, not earlier in the pregnancy.

7. Intrapartum Care

a. Cesarean delivery is indicated for women with active genital HSV lesions or significant prodromal symptoms (vulvodynia) at the time of active labor. Nevertheless, neonatal infection may occur in 1.2% of women delivered abdominally, and cesarean is not able to prevent all vertical transmission.
b. For women with a primary or nonprimary first-episode genital HSV infection in the third trimester, especially the last 6 weeks (RCOG October 2014), cesarean delivery may be offered due to the possibility of prolonged viral shedding. This is a shared decision - as cesarean delivery effect on rates of transmission in this setting is not clear, nor is a decreased rate of neonatal infection. Continuing antiviral therapy may be attractive to women who prioritize having a vaginal delivery, since antiviral therapy reduces the risk of lesions at the time of delivery.
c. There is no evidence that there is a duration of ruptured membranes beyond which cesarean delivery is not beneficial or not recommended in women with active HSV infection.
d. Women with preterm premature rupture of membranes prior to 34 weeks who have active disease do not present a contraindication to antenatal corticosteroid therapy for fetal lung maturation. Treatment with an antiviral agent may also be offered.
e. In women with a history of HSV and no active lesions who are undergoing a trial of labor, there is no evidence to alter usual obstetric management, including the use of invasive fetal monitoring and operative vaginal delivery when indicated.
f. Women with recurrent HSV *nongenital* lesions (e.g., on the face, buttocks or thigh) do not require cesarean delivery, but the lesions should be isolated with an occlusive dressing.
g. Breastfeeding is not contraindicated in women with active genital lesions, but good handwashing is advised before handling the infant.

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