Preventing Herpes Simplex Virus in the Newborn

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KEYWORDS

• HSV • Genital herpes • Acyclovir • PCR • Antiviral therapy

KEY POINTS

- Herpes simplex virus (HSV) infection in the newborn is an uncommon disease with devastating consequences.
- Early diagnosis and parenteral antiviral therapy followed by long-term oral suppressive therapy have improved the prognosis of newborns with HSV infection.
- Vaccine development and interventions to decrease neonatal transmission remain a challenge.

VIRAL STRUCTURE

Herpes simplex viruses (HSV-1 and HSV-2) are large, enveloped virions with a double-stranded DNA core. There is considerable cross-reactivity between most HSV-1 and HSV-2 glycoproteins, which mediate attachment to and penetration into cells and evoke host immune responses. However, antibody responses to glycoprotein G allow for serologic distinction between HSV-1 and HSV-2.

MATERNAL GENITAL INFECTIONS DURING PREGNANCY

Terminology pertaining to herpes infections is outlined in **Box 1**. Genital herpes infections are caused by either HSV-1 or HSV-2, and most infections are asymptomatic.

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Box 1
Terminology pertaining to herpes simplex virus infections

- Acquisition of HSV-1 or HSV-2 without prior exposure to either virus and hence no preformed antibodies is referred to as a *first-episode primary infection*.
- Acquisition of HSV-2 in an individual with prior HSV-1 antibodies and vice versa is referred to as a *first-episode nonprimary infection*.
- *Reactivation* refers to isolation of HSV-1 in a person who already has HSV-1 antibodies, or the isolation of HSV-2 in a person who already has HSV-2 antibodies.
- Presence of lesions characteristic of genital herpes with detectable HSV-1 or HSV-2 from the lesions by culture or PCR is referred to as *symptomatic shedding*.
- Detection of HSV-1 or HSV-2 from genital mucosa by culture or PCR in the absence of genital lesions is referred to as *subclinical shedding*.

HSV-2 seroprevalence among pregnant women is estimated to be 20% to 30%, with approximately 10% of HSV-2 seronegative women living with a seropositive partner and hence at risk for acquisition of genital herpes during pregnancy.[1,2] Among discordant couples, women seronegative for both HSV-1 and HSV-2 have an estimated 3.7% chance for seroconversion, while the risk for women already seropositive for HSV-1 to seroconvert to HSV-2 is estimated to be 1.7%.[3] Similar to nonpregnant women, two-thirds of women who acquire genital HSV infection during pregnancy are either asymptomatic or have nonspecific symptoms. Among women with a history of genital herpes acquired before pregnancy, 75% will have at least one recurrence during pregnancy, and 14% will have prodromal symptoms or lesions at the time of delivery.[4,5] For peripartum neonatal transmission, women must be shedding the virus symptomatically or asymptomatically around the time of delivery. It has been shown that 0.2% to 0.39%[6] of all pregnant women shed HSV in the genital tract around the time of delivery irrespective of prior history of HSV, and this incidence of shedding increases to 0.77% to 1.4% among women with prior history of recurrent genital herpes.[7,8]

The risk of transmission of HSV to the neonate remains significantly higher with primary maternal infections acquired closer to the time of delivery compared with recurrent infections (50%–60% with primary infections vs <3% for recurrent infections), most likely due to lack of transplacentally acquired antibodies in the neonate of women with primary infection as well as exposure in the birth canal of those women to larger quantities of virus for longer durations of time.[9]

HERPES SIMPLEX VIRUS IN THE NEWBORN

HSV infection of the neonate is uncommon, with an estimated rate of 1 in 3200 deliveries.[10] Approximately 1500 cases of neonatal HSV disease occur annually in the United States.[11]

Risk Factors for Transmission of Herpes Simplex Virus to the Newborn

The risk of neonatal acquisition of HSV is significantly higher with first episode primary and first episode nonprimary maternal infections when compared with recurrent genital infections (**Box 2**).[10] The risk of neonatal transmission in a large study was identified as 57% with first-episode primary infection, compared with 25% with first-episode nonprimary infection and 2% with recurrent genital HSV infections.[10] Other