

Herpes Simplex Virus Infection During Pregnancy

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KEYWORDS

- Genital herpes • Pregnancy • Antiviral therapy • Prevention • Neonatal herpes
- Serologic screening

KEY POINTS

- Genital herpes is common, with 22% of pregnant women seropositive for herpes simplex virus (HSV)-2.
- An increasing number of genital herpes infections are due to oral-labial transmission of HSV-1.
- Women with a primary infection of HSV-1 or HSV-2 at the time of delivery have a 57% risk of neonatal herpes infection.
- Neonatal herpes is rare, occurring in less than 1 in 3000 live births, but has high mortality and poor neurologic outcome for disseminated disease.
- Antiviral prophylaxis is recommended to suppress recurrent herpes infection in women from 36 weeks until delivery.
- Cesarean section should be performed if an active primary or recurrent herpes outbreak is suspected at delivery, to prevent neonatal transmission.
- There is an unclear role of routine serologic screening for HSV-1 and HSV-2 during pregnancy.

BACKGROUND

The herpesviruses are double-stranded DNA viruses that include several clinically important viruses during pregnancy: herpes simplex virus (HSV), varicella zoster virus, and cytomegalovirus. Herpesviruses encode most of the enzymes required for

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replication and, can establish latency by replicating in slowly or nondividing cells such as neurons. Herpes simplex virus types 1 (HSV-1) and 2 (HSV-2) glycoproteins mediate cellular infection, and glycoprotein G on the viral envelope provides the antigenic specificity that allows for detection of distinct antibodies for HSV-1 and HSV-2. HSV is transmitted via direct mucosal contact, and results in replication in the dermis and epidermis. The primary infection may include painful vesicles or ulcers in the genital tract, fever, lymphadenopathy, dysuria or other nonspecific genitourinary symptoms, or may lack symptoms entirely. Eventually the virus infects the sensory ganglia and persists in a latent form. Reactivation of viral replication may occur periodically for life. Recurrent infections may have a more mild presentation, ulcerative lesions, subtle genitourinary symptoms, asymptomatic lesions, or viral shedding without clinically apparent lesions.

PREVALENCE OF GENITAL HERPES

Genital herpes is one of the most common sexually transmitted diseases. HSV-1 causes gingivostomatitis and keratoconjunctivitis, whereas both HSV-1 and HSV-2 can cause genital herpes. The National Health and Nutrition Examination Survey (NHANES) serologic data from 1988 to 2004 estimated that 22% of pregnant women were seropositive for HSV-2, 63% for HSV-1, and 13% for both HSV-1 and HSV-2¹; this was the first time that the prevalence of HSV-2 had decreased since the inception of NHANES in 1976. Of the women seronegative for HSV-2 during pregnancy, 10% will have an HSV-2 seropositive partner, putting them at risk for acquisition during pregnancy.²

The most recent NHANES data from 2005 to 2010 continue to show a decline in the seroprevalence of HSV-1 (53.9%) and HSV-2 (15.7%) in adults aged 14 to 49 years.³ HSV-1 continues to be more common in women (33.2%) and minority populations such as Mexicans (58.3%) and non-Hispanic blacks (39.6%).³ From the 2007-2010 NHANES data, 20.3% of women versus 10.6% in men have HSV-2. Non-Hispanic black women have the highest rates of HSV-2 (49.9%).⁴ There is no clear explanation for the racial disparity in HSV-2 infection, which has persisted over time.

The declining seroprevalence of HSV-1 with fewer infections in childhood in developed countries and the increase in oral-labial sexual contact has resulted in an increase in HSV-1 genital infections in young women and adolescents, which accounts for up to 80% of new genital herpes infections in college students.⁵ The declining seroprevalence of HSV-1 and HSV-2 increases the risk of primary HSV infection among seronegative pregnant women, the primary risk factor for neonatal herpes transmission.

Poor Correlation Between Symptoms and Infection

Because of the heterogeneous and often asymptomatic nature of primary or recurrent genital herpes infections, up to 90% of persons with serologic evidence of HSV-2 do not report a clinical history of the infection.⁶ Neither a basic nor detailed clinical history correlates with HSV-2 infection by serology.⁷ Signs and symptoms are not able to accurately predict primary herpes infections.⁸ The presence of lesions has a poor correlation with detection of genital tract HSV by culture or polymerase chain reaction (PCR).⁹ These issues create a major diagnostic dilemma for obstetric providers caring for pregnant women who are at risk for primary or recurrent genital herpes infections. While genital herpes is an ongoing cause of maternal morbidity during pregnancy, the real dilemma is how to effectively prevent peripartum herpes transmission. This aspect has been made more complicated by the changing epidemiology of maternal herpes infections (HSV-1 vs HSV-2)¹⁰ and challenges with clinical diagnosis.

SCOPE OF THE PROBLEM: DEVASTATING CONSEQUENCES OF NEONATAL HERPES

Most maternal herpes infections during pregnancy do not result in severe maternal illness, in contrast to the potentially devastating consequences of neonatal herpes infection. Prevention of neonatal exposure to HSV in the maternal genital tract has been the main preventive strategy, as early diagnosis can be difficult, and prompt initiation of antiviral therapy for neonatal HSV does not decrease severe sequelae in many cases. Disseminated neonatal HSV occurs in 25% of cases and has 29% mortality, whereas central nervous system (CNS) disease occurs 30% of the time and is associated with 4% mortality.¹¹ The proportion of cases with skin, eye, or mouth (SEM) disease has increased to 45% in the era of antiviral therapy (Table 1).¹²

Neonatal HSV is acquired during 1 of 3 periods surrounding pregnancy¹¹:

1. Intrauterine (5%)
2. Peripartum (85%)
3. Postnatal (10%)

Intrauterine HSV is a congenital TORCH infection (Toxoplasmosis, Other [syphilis], Rubella, Cytomegalovirus, HSV) and may present as cutaneous manifestations, ophthalmologic findings, and neurologic involvement such as microcephaly, hydranencephaly, or intracranial calcifications. Peripartum acquisition caused by viral exposure in the maternal genitourinary tract at the time of vaginal delivery can result in disseminated, CNS, or SEM infections. Postnatal HSV acquisition is from care providers (including health care workers) with active lesions on the mouth or, rarely, herpetic Whitlow hand lesions.¹³

The American Academy of Pediatrics recently published new management guidelines to standardize the laboratory evaluation and therapy for infants exposed to herpes at the time of delivery.¹⁴ Owing to the late and variable nature of presentation of neonatal herpes, standardizing the approach in infants suspected to have the infection may improve postnatal outcomes (Box 1).

Difficult to Determine: What Is the Incidence of Neonatal Herpes Simplex Virus?

As neonatal HSV is not a reportable illness in most states, surveillance, monitoring the effectiveness of prevention strategies, and establishing evidence-based practice guidelines has been hampered. Many clinicians and investigators have lobbied to

Disease	Frequency (%)	Time (d)	Presentation	Mortality (%)	Normal Development (%) ^a
Disseminated	25	10–12	Viral sepsis, respiratory failure, hepatic failure, coagulopathy, ± rash	29	83
CNS	30	16–19	Seizures, lethargy, feeding failure, temperature instability, ± rash	4	31
SEM	45	10–12	80% have a vesicular rash	—	100

Abbreviations: CNS, central nervous system; SEM, skin, eye, or mouth.

^a At 1 year without antiviral suppression.

Adapted from Pinninti SG, Kimberlin DW. Neonatal herpes simplex virus infections. *Pediatr Clin North Am* 2013;60:354; with permission.

Box 1**Obstetric provider's role in management of infants born to women with genital lesions at delivery, based on American Academy of Pediatrics 2013 guidelines**

For women with genital lesions at delivery, assess maternal viral status:

- Send viral culture and polymerase chain reaction with typing for HSV from genital lesions at delivery
- Order maternal serum HSV-1 and HSV-2 immunoglobulin G serologic studies
- Determine status of maternal infection at delivery (primary vs recurrent)

Data from Kimberlin DW, Baley J. Guidance on management of asymptomatic neonates born to women with active genital herpes lesions. *Pediatrics* 2013;131:383–6.

make neonatal HSV a reportable illness to further our understanding of the modern natural history of this disease and improve clinical care.^{15,16}

Efforts at neonatal herpes prevention have been complicated by the high maternal prevalence of HSV-1 and HSV-2 in addition to the low incidence of neonatal disease. The incidence of neonatal herpes is challenging to define, and has been estimated to be 1 in 3200 live births.¹⁷ With 4 million deliveries annually, there are 1500 cases of neonatal herpes infection.¹¹ Using State of California discharge databases, Morris and colleagues¹⁸ reported an incidence of 12.1 per 100,000. Whitley and colleagues¹⁹ found an incidence of 60 per 100,000 in a managed care population in the Mid-Atlantic and Northeast states. This study used current procedural terminology codes for pregnancy delivery and the International Classification of Diseases, 9th edition (ICD-9) codes, with the caveat that there was no definitive ICD-9 code for neonatal herpes. In Washington state, a prospective study of nearly 40,000 women showed an incidence of neonatal HSV of 30.8 per 100,000,¹⁷ similar to NHANES data, which projected a rate of 33 per 100,000.¹

MATERNAL HERPES SIMPLEX VIRUS INFECTIONS

Maternal genital herpes infections are heterogeneous and may include primary infection or recurrent infections, asymptomatic lesions or viral shedding without lesions, or serologic evidence of herpes infection without evidence of active disease by clinical or laboratory criteria. Maternal infections are defined as:

1. Primary infection: HSV-1 or HSV-2 is detected from genital lesions without serologic evidence of prior infection
2. Nonprimary infection: HSV-1 is detected from genital lesions in an individual with HSV-2 antibodies, or vice versa
3. Recurrent infection: HSV-1 or HSV-2 is isolated in women with serologic evidence of infection to that type of HSV

Maternal acquisition of HSV-1 or HSV-2 near the time of delivery accounts for 60% to 80% of neonatal HSV infection.^{20,21} In a large prospective study,²² 94 of 7046 pregnant women became seropositive for HSV and only 34 (36%) had symptoms consistent with a herpes infection. In this study, 30% of the infections occurred in the first trimester, 30% in the second, and 40% in the third. Women who were initially seronegative for both HSV-1 and HSV-2 had a 3.7% chance of seroconversion for either virus. Women with HSV-1 had a 1.7% chance of acquiring HSV-2. Women with HSV-2 had a zero chance of acquiring HSV-1. This study did not account for the herpes serostatus of the partner. In a subsequent couples study where 47% of male partners consented

to have serologic samples drawn, the rate of seroconversion for susceptible pregnant women was 3.5% for HSV-1 and 20% for HSV-2.²³ Duration of partnership less than 1 year was strongly associated with HSV-2 acquisition (odds ratio 7.8, 95% confidence interval 2.3–25.7).²³

As most HSV infections in pregnancy are asymptomatic, studies have shown that up to 80% of women who have an HSV-infected infant did not have clinical evidence of HSV at delivery and did not have a history, or a partner with history, of genital HSV.^{24–26} Historically most efforts at maternal treatment, prophylaxis, and neonatal HSV prevention have focused on women with a history of symptomatic HSV infections. Among women with HSV-2, 75% will have at least 1 recurrence during pregnancy and 14% will have prodromal symptoms or genital tract lesions at delivery.^{27,28} Of interest, women with HSV-1 are at low risk for recurrence in the genital tract,^{29,30} but when HSV-1 recurrence does occur the neonate has an increased risk of neonatal infection in comparison with HSV-2.^{17,19}

Rare presentations of HSV during pregnancy may include fulminant HSV hepatitis that has been reported but is rare. HSV hepatitis can be confused with severe pre-eclampsia or HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count), as transaminitis, liver dysfunction, and abdominal pain may be present in both illnesses.³¹ Severe or disseminated maternal herpes infections may present as maternal viral sepsis, pneumonitis, or encephalitis.

RISK FACTORS FOR VERTICAL TRANSMISSION

In a large prospective study, women with recurrent genital herpes had a low risk of neonatal HSV infection (2%) in comparison with nonprimary infection (25%) or primary infection (57%).¹⁷ Although these rates of neonatal HSV transmission, especially with primary infection, seem staggeringly high, the absolute number of infants with neonatal HSV in this study was small. Of the 58,000 pregnant women included in this prospective cohort, 40,023 had HSV genital cultures obtained within 48 hours of delivery and 31,663 had HSV serologic testing. Of women with both cultures and serologies available, there were 202 who had HSV present in the genital tract at delivery (0.5%) while only 10 neonates had HSV (5% of HSV exposed neonates).

Maternal antibody status has a significant effect on rates of neonatal HSV disease (Table 2). The explanation for this is multifactorial:

1. Women who are seronegative for both HSV-1 and HSV-2 are at risk for acquiring either form of genital herpes proximal to delivery.
2. The lack of maternal antibodies to provide passive transplacental immunity also increases the likelihood of neonatal HSV disease.

Table 2 Effect of maternal antibody status on neonatal HSV transmission	
Maternal HSV Status	Rate/100,000 Live Births (95% CI)
HSV seronegative	54 (19.8–118)
HSV-1 seropositive only	26 (9.3–56)
HSV-2 seropositive only	35 (4.2–126)
HSV-1 and HSV-2 seropositive	12 (0.3–70)

Abbreviation: CI, confidence interval.

Data from Brown ZA, Wald A, Morrow RA, et al. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *JAMA* 2003;289:207.

3. HSV-2 seropositive women are most likely to have recurrent HSV (lesions or shedding) at delivery but are also at lowest likelihood to have HSV transmission in comparison with women with primary or nonprimary infection.

A subsequent study of women in Seattle, Washington, Stanford, California and Stockholm, Sweden showed increased risk for neonatal HSV infection (odds ratio 19.2) for HSV-1 versus HSV-2,³² which is concerning given the increased importance of both genital HSV-1 and neonatal HSV-1 infections. To date, targeting prevention strategies on women with recurrent HSV-2 by maternal history has inadequately addressed the populations at greatest risk and does not address the complex pathophysiology involved in neonatal HSV infection.

The relative contribution of each risk factor for neonatal HSV transmission is listed in **Table 3**. Invasive procedures such as placement of a fetal scalp electrode have been shown to increase the risk of vertical HSV transmission. According to the American Congress of Obstetricians and Gynecologists (ACOG), a fetal scalp electrode may be placed if there is a strong clinical indication in a patient with history of HSV but no active lesions.³³ Other procedures such as transcervical chorionic villous sampling may be delayed if active cervical HSV is suspected. Amniocentesis, transabdominal chorionic villous sampling, and percutaneous umbilical blood sampling are not associated with HSV transmission.

The data for duration of membrane rupture are limited³⁴; however, for women with labor or rupture of membranes, ACOG recommends proceeding with a term delivery by cesarean section without delay if genital HSV lesions or prodromal symptoms are present in a woman with recurrent HSV.³³ In women with preterm premature rupture of membranes (PPROM), there are insufficient data regarding timing of delivery, weighing the risks of HSV and prematurity.³³ One small study of women (N = 29) with recurrent HSV lesions and PPRM expectantly managed from 25 to 31 weeks did not show any cases of neonatal herpes transmission.³⁵ Management of primary HSV infection and PPRM may have to be individualized based on clinical factors, including gestational age.³⁶

Additional risk factors for neonatal herpes include parental age. Women at greatest risk for a having a neonate with HSV are younger than 25 years and have young partners (<20 years old).³⁷

Risk Factor	aOR (95% CI)
Presence of HSV in maternal genital tract	346 (125–956)
Type of infection (primary vs recurrent)	59 (6.7–525) ^a
Type of HSV (HSV-1 vs HSV-2)	35 (3.6–335) ^a
Maternal antibody status	see Table 2
Delivery mode (cesarean vs vaginal delivery)	0.14 (0.14–1.26) ^a
Duration of membrane rupture	N/A
Integrity of cutaneous barrier (fetal scalp electrode or instrumentation)	3.5 (0.6–19) ^a

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; N/A, no data available.

^a Odds ratios were adjusted for first episode versus reactivation HSV.

Data from Brown ZA, Wald A, Morrow RA, et al. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. *JAMA* 2003;289:206.

DIAGNOSIS OF GENITAL HERPES

There are several methods available for direct HSV testing. PCR testing of a lesion, cerebrospinal fluid, or tissue/fluid is rapid, highly sensitive, and identifies type-specific lesions, but may have limited availability or excessive cost. Culture is the historical gold standard, and can differentiate HSV type into vesicles, pustules, and ulcers, but has lower sensitivity and is less useful in detecting asymptomatic shedding. Women with symptoms concerning for HSV should have viral identification by PCR/culture and HSV serologic testing to determine whether the infection is primary or recurrent.

Type-specific antibodies will develop within a few weeks of initial infection, and persist indefinitely. Historically, early type-specific serologic tests could not accurately discriminate between HSV-1 and HSV-2 antibodies. Newer glycoprotein G (gG)-based assays allow for type-specific testing and can be requested by the ordering obstetric provider. The sensitivity of the gG assay for HSV-2 antibody is 80% to 98%, with specificity of greater than 96%.³⁸ Repeat or confirmatory testing may be indicated, especially with recent HSV acquisition. Immunoglobulin M tests are not recommended, as they are not type-specific and may be positive with recurrent HSV-2 lesions.

Although not widely in use, point-of-care and rapid tests have been developed from serum or capillary blood for HSV antibodies and HSV PCR.³⁹ Avidity testing may provide additional information in women with concern for primary genital herpes. HSV-1 and HSV-2 antibody avidity increases over time after herpes virus acquisition. Low antibody avidity has been associated with the risk of HSV transmission to the neonate,⁴⁰ but this testing is not widely available.

TREATMENT OF HERPES SIMPLEX VIRUS EPISODES IN PREGNANCY

There are 3 Food and Drug Administration category B antiviral medications for the treatment of herpes: acyclovir, famciclovir, and valacyclovir. Acyclovir is a nucleoside analogue that inhibits the viral thymidine kinase and DNA replication in infected cells. It has low bioavailability and requires frequent dosing. Valacyclovir is a prodrug that is rapidly metabolized to acyclovir with improved bioavailability, and requires less frequent dosing. There are minimal data on the use of famciclovir in pregnancy, but there is no documented fetal or embryonic teratogenicity from these medications. Neutropenia may be a side effect of neonatal treatment with acyclovir, but this has not been reported with maternal prophylactic therapy.¹²

Treatment regimens for HSV in pregnancy are listed in [Table 4](#). The frequent dosing of acyclovir may limit compliance. Both acyclovir and valacyclovir are now generically

Indication	Acyclovir	Valacyclovir
Primary or first-episode	400 mg PO TID for 7–10 d	1 g PO BID for 7–10 d
Symptomatic recurrent episode	400 mg PO TID for 5 d 800 mg PO BID for 5 d	500 mg PO BID for 3 d 1 g PO daily for 5 d
Prophylaxis or suppression	400 mg PO TID from 36 wk until delivery	500 mg PO BID from 36 wk until delivery

Abbreviations: BID, twice daily; PO, by mouth; TID, 3 times daily.

Data from ACOG Committee on Practice Bulletins. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists. No. 82 June 2007. Management of herpes in pregnancy. *Obstet Gynecol* 2007;109:1492.

manufactured, but the local cost may still be higher for valacyclovir for women without insurance. These factors could influence practitioners' prescribing habits and patient compliance. For rare disseminated or severe HSV disease requiring hospitalization because of CNS manifestations, pneumonitis, or hepatitis, intravenous acyclovir, 5 to 10 mg/kg every 8 hours for 2 to 7 days followed by prolonged oral therapy, is indicated.

Both acyclovir and valacyclovir are safe during breastfeeding. Genital herpes is not a contraindication to breastfeeding. If a woman has vesicular or ulcerative lesions on the breast, areola, and nipple, a swab should be performed for HSV PCR and type-specific culture. HSV mastitis is a rare contraindication to breastfeeding, and women should avoid breastfeeding on the affected breast while active lesions are present.

PREVENTION: HOW DO WE REDUCE THE RISK OF NEONATAL HERPES SIMPLEX VIRUS?

There are several nonmodifiable risk factors for neonatal HSV, including maternal genital herpes history before pregnancy. To minimize the rare but potentially catastrophic occurrence of neonatal herpes infection, several evidence-based interventions must be considered:

1. Viral suppression
2. Physical examination/cesarean section at time of labor
3. Postnatal assessment and treatment of neonates
4. Serologic screening of pregnant women

Maternal Viral Suppression

The 2008 Cochrane review⁴¹ of antiviral prophylaxis during pregnancy evaluated 7 randomized controlled trials (N = 1249), and included 5 studies of acyclovir^{28,42–45} and 2 studies of valacyclovir.^{27,46} There were no cases of neonatal herpes in the treatment or placebo groups in these studies. Although the meta-analysis could not comment on a reduction in neonatal HSV disease, it demonstrated a reduction in genital tract HSV at the time of delivery, symptomatic recurrence at delivery, and cesarean section for genital herpes (Table 5). In addition, several cost-effectiveness studies have shown that antiviral suppression with acyclovir is cost-effective for women with recurrent genital herpes over a wide range of assumptions.^{47–49}

Role of Cesarean Section with Acute or Suspected Herpes Simplex Virus Lesion

Cesarean section is effective at decreasing HSV transmission.¹⁷ For women with active genital lesions or prodromal symptoms on admission in labor, ACOG and the Society of

Table 5
Cochrane meta-analysis of antiviral prophylaxis during pregnancy

Outcome	Effect of Antiviral Prophylaxis
Symptomatic recurrence of genital at delivery	RR 0.28 (95% CI 0.18–43)
HSV detected in the genital tract at delivery (asymptomatic shedding)	RR 0.14 (95% CI 0.05–0.39)
Cesarean delivery for genital herpes	RR 0.30 (95% CI 0.2–0.45)

Abbreviations: CI, confidence interval; RR, risk ratio.

Data from Hollier LM, Wendel GD. Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. *Cochrane Database Syst Rev* 2008;1:CD004946.

Obstetricians and Gynaecologists of Canada recommend cesarean section to reduce the risk of neonatal HSV.^{33,50} European guidelines further recommend cesarean section for women who have a primary infection within 6 weeks of delivery.⁵¹ Unfortunately, cesarean delivery does not completely decrease vertical transmission, as neonatal herpes can occur with cesarean delivery before membrane rupture. Women with history of recurrent herpes should have a careful examination of the cervix, vagina, and vulva on admission in labor. If active genital disease is not suspected during labor based on examination and history, vaginal delivery is reasonable. Although the presence of nongenital herpes lesions can indicate an increase in genital herpes shedding,⁵² cesarean delivery is also not recommended for nongenital lesions because of the low risk of transmission, and an occlusive dressing can be used during labor.³³

Neonatal Screening and Treatment of Infants Exposed to Herpes Simplex Virus

In 2013, the American Academy of Pediatrics published guidelines for management of the newborn exposed to genital herpes at delivery.¹⁴ These recommendations take into consideration the changing epidemiology of genital herpes infections and many of the risk factors that contribute to neonatal HSV disease, including HSV type and primary versus recurrent infection. The guidelines are only applicable at institutions with PCR availability, and require a multidisciplinary involvement by laboratory medicine, pediatrics, and obstetrics providers to apply laboratory results to the newborn treatment algorithm (see **Box 1**).

Role of Serologic Screening

Over the decades many research groups have advocated for routine prenatal serologic testing to identify all women at risk for HSV infection at delivery.^{2,53,54} This approach could benefit both society and individuals by decreasing neonatal HSV, cesarean sections for genital HSV at the time of delivery, and genital herpes acquisition or recurrence. Pregnant women and obstetric providers may be amenable to the practice of routine screening for HSV during pregnancy.⁵⁵ The acceptability of partner testing ranges from 47% to 78%.^{23,56}

A decision analysis by Tita and colleagues⁵⁷ regarding antenatal herpes screening cited the lack of an effective intervention to prevent maternal acquisition of new infection in late pregnancy, and reviewed the cost-effectiveness of various approaches to serologic screening. Routine serologic screening for HSV during pregnancy, with or without antiviral prophylaxis to serodiscordant male partners, has been shown to have total cost estimates ranging from US\$150,000 to \$4,000,000 depending on the assumptions used.^{58–62} Education, counseling, and treatment of seropositive partners can prevent near-term acquisition of HSV infection in susceptible women under study conditions.⁶³ Pregnant women in serodiscordant relationships for HSV-2 were less likely to engage in unprotected genital sex acts, but there was no change in sexual behavior for HSV-1 serodiscordant couples.⁶⁴ These strategies depend on willingness of partners to be tested, which can be limited because of personal and economic consequences. Without this information, recommending abstinence or education regarding sexual practices will likely have minimal impact. At this time neither ACOG nor the Centers for Disease Control and Prevention supports routine screening for HSV in previously undiagnosed pregnant women.^{33,38}

RECOMMENDATIONS

At present there are insufficient data to recommend the strategy of routine serologic screening for all pregnant women as a means to decrease neonatal HSV disease.

There is unlikely to be a prospective study large enough to detect a difference in this rare outcome in the general population.

A second strategy would include screening rapid HSV genital PCR for women admitted in labor followed by serologic screening to identify women with a primary infection. This scenario would address 3 of the most important risk factors for neonatal HSV transmission: HSV in the genital tract at delivery, HSV-1 or HSV-2, and primary versus nonprimary or recurrent infections. Unfortunately neither the technology nor infrastructure is currently available for this strategy, and further study is needed. Similar to group B *Streptococcus* and human immunodeficiency virus (HIV) infections during pregnancy, identification of women at greatest risk of vertical HSV transmission has considerable merit as long as there is an appropriate intervention such as cesarean delivery or antiviral prophylaxis. The major concern of this approach is that it would result in an increase in cesarean deliveries without the ability to measure an impact on this rare neonatal infection.

The third strategy is to continue the current practice of focusing efforts on prophylaxis for women with a history of recurrent genital herpes who are at lowest likelihood to transmit the infection. This approach is suboptimal, as it does not address the changing epidemiology of HSV genital infections with greater numbers of HSV-1 infections in addition to the declining seroprevalence of both HSV-1 and HSV-2, placing a greater number of women at risk for primary infections during pregnancy.

Vaccination as a method to prevent genital herpes infections may be the best option to limit the risk of neonatal transmission. Development of effective immunizations for both HSV-1 and HSV-2 could be targeted to adolescents and young adults before sexual activity and pregnancy. There is no effective vaccine for HSV-2, but recent results have shown a modest 58% efficacy against HSV-1 genital disease.⁶⁵

There is a complicated relationship between HSV-2 and HIV-1 coinfection with increased rates of HIV horizontal transmission among HSV-2-infected individuals but, thus far, no improvement with HSV-2 antiviral suppression.⁶⁶ In pregnancy, HSV-2 has not been consistently shown to increase perinatal HIV transmission.^{67,68} Additional work needs to be done to further characterize the relationship between concomitant HSV and HIV infections and the role of HSV in the perinatal transmission of HIV.

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