

Current management of herpes simplex virus infection in pregnant women and their newborn infants



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SUMMARY

There have been major advances over the past two decades in our knowledge of the epidemiology, pathogenesis and natural history of disease due to herpes simplex virus (HSV). Effective antiviral therapy has also resulted in major advances in the management of neonatal HSV infections. Despite these advances, HSV remains an important cause of morbidity and mortality among neonates. The present statement addresses current issues relating to the prevention, diagnosis and treatment of perinatal HSV infection. The document is a synopsis of the key recommendations, which relate to pregnant women, women in labour, newborn infants and infection control strategies.

RECOMMENDATIONS

Prevention of neonatal HSV infections

Pregnant women

- All pregnant women should be asked about any history of genital HSV infection in themselves or their sexual partner(s). Signs and symptoms of current genital HSV infection should be checked in all patients during their prenatal evaluations (B-II-3).
- Women with primary or first episode infections are known to be at high risk of transmitting HSV to their newborns. Such women may benefit from antiviral treatment of primary or first episode infections and suppressive acyclovir therapy starting at 36 weeks' gestation at a dose of 400 mg three times daily (B-II-3).
- Caesarean delivery should be offered to women who develop primary HSV infection in the third trimester (after 28 weeks), notably in the setting where lesions occur within six weeks of anticipated delivery and adequate maternal seroconversion has not yet occurred (B-II-3). Consultation with experts in infectious diseases is recommended, particularly if there are questions regarding the woman's serostatus.
- There is increasing evidence and consensus to suggest that acyclovir suppressive therapy (400 mg three times daily starting at 36 weeks' gestation) should be offered to pregnant women who experience recurrent genital HSV infections during pregnancy (B-I).

Women in labour

- During labour, all women should be asked about recent symptoms and carefully examined for evidence of genital HSV infection (A-II-3).
- In the presence of HSV lesions in the perineal region, caesarean section is recommended. This mode of delivery may reduce the risk of neonatal HSV infection if performed within 4 h to 6 h of membrane rupture (B-II-3). However, many experts recommend caesarean delivery even if the membranes have been ruptured for longer than 6 h (B-III).
- Caesarean section should be performed immediately on a woman who presents with ruptured membranes and active genital lesions at term (B-II-3). However, the appropriate management of delivery is not established if the membranes are ruptured at a gestational age when the fetal lung is very immature. In such situations, some experts recommend that intravenous acyclovir (15 mg/kg/day in three divided doses, maximum 1200 mg/day) be given to the mother if labour and delivery are delayed (F-III).
- In the absence of genital lesions, a maternal history of genital HSV infection is not an indication for caesarean delivery (D-III).
- Procedures that potentially increase the risk of infection should be avoided when possible in women with active genital HSV infection (D-II-3). Such procedures include early rupture of membranes, fetal scalp monitors and scalp sampling.

Newborn infants

The approach to the management of asymptomatic infants who were exposed to HSV at the time of delivery takes into account whether the mother has proven or presumed primary infection, known recurrent lesions or an unknown current status. Women in the latter category may be regarded as having presumed primary infection.

Infants born by vaginal delivery

- All asymptomatic infants who were exposed to HSV at the time of delivery should have HSV cultures performed 48 h after birth (B-III). In addition, cultures

Table 1
Classification scheme for neonatal herpes simplex virus disease

Type of presentation	Relative frequency
Intrauterine infection	Less than 5%
Postnatal infection	} Approximately 33% each
Disseminated disease	
Skin, eye and mouth disease	
Localized central nervous system disease	

are recommended if the mother had an HSV infection during pregnancy, but with no visible lesions at delivery. Samples for HSV cultures should be taken from urine, stool or rectum, mouth, eyes and nasopharynx. One option is to perform weekly surveillance cultures for four to six weeks in an effort to detect evidence of active viral replication before the frank manifestations of disease (B-III).

- There is no firm consensus regarding the antiviral management of asymptomatic infants whose mothers had proven or presumed primary infection. Most experts recommend empirical acyclovir at birth (B-III). Others prefer to wait on the results of HSV cultures or signs or symptoms of infection before initiating therapy. If therapy is being initiated, a cerebrospinal fluid (CSF) sample should be obtained before treatment. Once initiated, the duration of therapy may be guided in part by emerging laboratory results. The expected duration of therapy is 14 to 21 days.
- An infant whose mother has known, recurrent genital lesions should be observed carefully for evidence of infection. Acyclovir therapy is not recommended for the asymptomatic infant (B-III).
- All symptomatic infants should be evaluated for possible HSV infection as part of a complete evaluation for sepsis. Polymerase chain reaction (PCR) testing of the CSF is recommended for all such infants.
- In the above symptomatic infants, samples for HSV culture should be taken from skin lesions, conjunctiva, nasopharynx, mouth, stool or rectum, urine, blood buffy coat and CSF. PCR testing of blood should also be considered (B-III).

In these infants, acyclovir treatment should be started if HSV infection is strongly suspected or if any of the above tests reveal the presence of HSV infection (B-III). This index of suspicion should be maintained for six weeks.

- The length of observation in hospital for infants at increased risk of HSV infection should be individualized, taking into account local resources, adequacy of observation at home and the nature of follow-up care (B-III).

- Given that neonatal HSV infection may occur as late as four to six weeks after delivery, physicians and caregivers should be vigilant, and rashes and symptoms should be appropriately evaluated (B-III).

Infants born by caesarean delivery

- Infants born by caesarean delivery with at least 6 h of membrane rupture whose mothers had herpetic lesions should be observed carefully and cultured as above. Antiviral therapy is not routinely started for such infants who are asymptomatic, but such therapy should be initiated if culture results from the infants are positive for HSV or if HSV infection is strongly suspected on clinical grounds (B-III).

Infection control measures

The infection control measures are summarized in the full statement at <www.cps.ca/english/publications/InfectiousDiseases.htm> according to women in labour and postpartum women with HSV, as well as neonates with HSV infection and those exposed to HSV.

Diagnostic tests for neonatal HSV infection

The Canadian Paediatric Society makes the following recommendations:

- In the evaluation of neonatal HSV infection, samples should be obtained for culture from skin lesions, mouth, nasopharynx, conjunctiva, urine, stool or anorectum, blood buffy coat and CSF. Positive cultures from any of the above sites at more than 48 h after delivery are consistent with viral replication as opposed to colonization after intrapartum exposure (B-III).
- Serological tests should not be relied on because they are generally not helpful in diagnosing acute neonatal HSV infection (E-II-3).
- PCR testing for HSV DNA in the CSF is the recommended diagnostic method of choice for HSV encephalitis (A-II-3).

Treatment and follow-up of neonates with HSV infection

- Intravenous acyclovir is the drug of choice for the treatment of neonatal HSV infection. The dosage of acyclovir is 60 mg/kg/day in three divided doses (B-II-2), with appropriate adjustments for renal impairment as necessary. Adverse events from acyclovir can be minimized by ensuring that the patient is adequately hydrated, with an appropriate urine output.
- The duration of acyclovir treatment for neonatal HSV infection should be 14 days if disease is limited to the skin, eye and mouth, and 21 days if the disease involves the central nervous system or is disseminated (B-III) (Table 1).
- The use of oral acyclovir is contraindicated for the treatment of HSV infections in neonates (E-III).

- The optimal management of post-treatment relapses is unclear. The value of long-term suppressive or intermittent acyclovir therapy for infants with skin, eye and mouth disease is being evaluated, and a definitive recommendation cannot be made at this time.
- In addition to parenteral acyclovir, neonates with ocular involvement due to HSV infection should receive a topical ophthalmic agent, such as trifluridine (B-III).
- Infants with HSV infection should be followed and evaluated for recurrent disease and neurological sequelae. Recurrent skin lesions are frequent in infants with neonatal HSV infection and may be associated with central nervous system sequelae if they occur during the first six months of life (B-III). Consequently, CSF examination and PCR, combined

with intravenous acyclovir therapy, are warranted at the time of recurrence of skin lesions (B-III).

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For more information, refer to the full statement at <www.cps.ca/english/publications/InfectiousDiseases.htm>.

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The recommendations in this statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate. Internet addresses are current at time of publication.