Neonatal Herpes Simplex Infection

Revision Dates

Case Definition	August 2011
Reporting Requirements	December 2018
Remainder of the Guideline (i.e., Etiology to References sections inclusive)	June 2005

Case Definition

Confirmed Case

Laboratory confirmation of infection with or without clinical illness[(A)] in a neonate:

- Virus isolation from an appropriate clinical specimen (CSF, skin or other tissue)

OR

- Detection of viral nucleic acids in CSF using molecular diagnostic techniques, when available.

Probable Case

Clinical illness[(A)] in a neonate born to a female with primary or active HSV infection during pregnancy:

- Presence of anti-HSV IgM antibodies in mother's serum

OR

- Evidence of seroconversion in mother (i.e., fourfold or greater increase in anti-HSV IgG titre) by any standard serologic assay

OR

- Isolation of virus by culture or detection of viral antigen by DFA from active lesions.

[(A)] Clinical illness can be of 3 different syndromes: skin, visceral, and central nervous system infections. Dermatologic manifestations are often a late manifestation, or might not occur at all.

Reporting Requirements

1. **Physicians, Health Practitioners and Others**
   Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

2. **Laboratories**
   All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the:
   - Chief Medical Officer of Health (CMOH) (or designate), and
   - MOH (or designate) of the zone.

3. **Alberta Health Services and First Nations Inuit Health Branch**
   - The MOH (or designate) of the zone where the case currently resides shall forward the Perinatally Acquired Notifiable Disease Enhanced Report form for all confirmed and probable cases to the CMOH (or designate) within four weeks of notification.
   - For out-of-province and out of country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
     - name,
     - date of birth,
     - out-of-province health care number,
     - out-of-province address and phone number,
     - positive laboratory report, and
     - other relevant clinical / epidemiological information.

Etiology

Herpes simplex virus (HSV) types 1 and 2 are the agents responsible for causing disease. HSV-2 causes 75% of neonatal HSV infections.

Clinical Presentation

Herpes simplex in the newborn is a serious viral infection. It affects major organs (brain, liver, lungs) often causing permanent damage or death (1). The infection can be divided into three clinical presentations:

- Disseminated infection involving multiple organs occurs in approximately 25% of cases. Onset is usually in the first week of life and is often fatal.
- Localized central nervous system (CNS) infection occurs in approximately 35% of cases. Onset is usually between the second and third week of life and is often fatal.
- Infection limited to the skin, eyes or mouth occurs in approximately 40% of cases. In many cases the skin lesions do not develop or they appear late. Skin lesions assist in the diagnosis. In their absence, the diagnosis of HSV infection is difficult.

The risk to the newborn depends on two factors: the first is the stage of pregnancy at which the mother sheds the HSV; and the second is whether the infection is primary or secondary. Only excretion at the time of delivery is dangerous to the newborn. Intrauterine infections are rare. Primary infection in the mother increases the risk of transmission of infection to the newborn.

Symptoms appear most often in the first two weeks of life but may not appear until the fourth week. Approximately 50% of infants initially develop a vesicular skin rash. More serious symptoms begin in 7-10 days if treatment is not started. Other symptoms include variable temperature, convulsions, drowsiness, poor muscle tone, dyspnea, liver inflammation and poor feeding. Asymptomatic infection is not thought to occur in neonates.

Relapses may occur after the cessation of therapy. There may be evidence of recurrent disease and neurological sequelae. Sequelae are most likely to occur among infants who were diagnosed with CNS or disseminated disease. Recurrent skin lesions are frequent in infants with neonatal HSV. This may be associated with CNS sequelae if they occur during the first six months of life.

Diagnosis

The diagnosis of neonatal HSV infection made through the isolation of the virus from the oropharynx, nasopharynx, stool, blood buffy coat, urine, CSF, fluid from skin lesions or other tissues. Virus isolation by culture remains the definitive diagnostic method for neonatal HSV infection. Diagnosis is difficult especially in the absence of skin lesions, however, if skin lesions are present, rapid diagnostic techniques are of value (direct immunofluorescence for virus-infected cells and enzyme immunoassays for the presence of HSV antigens).

Newborns exposed (mother has active lesions at the time of delivery) to HSV infection during labour and vaginal delivery should have HSV cultures performed 48 hours after birth. In some cases weekly surveillance cultures for 4-6 weeks may be recommended to detect active viral replication. Newborns whose mothers have active herpetic lesions at the time of delivery and are born by cesarean section should be carefully observed and cultured 48 hours after birth.

Epidemiology

Reservoir

Humans are the reservoir. Pregnant women with active genital lesions (especially primary lesions) are the most common source of infection for the fetus or newborn.

Transmission (1)

Maternal infection is generally classified as primary (newly acquired) or recurrent. Newly acquired infections include a first episode primary in which the mother is seronegative for HSV types 1 and 2 at the onset of the infection or a first episode nonprimary in which the mother has antibodies to one virus type and a new infection with the other virus type. A recurrent infection occurs when the mother has pre-existing antibodies to the same virus type as isolated from the mother's genital tract. Infants who are born to mothers with a first episode primary genital infection at the time of delivery are at the greatest risk of acquiring HSV. Transmission rates are 50% or greater. In infants born to mothers who have a first episode nonprimary infection, the transmission rate is approximately 30%. The lowest risk for neonatal transmission occurs when the mother has an active infection prior to becoming pregnant or in the early stages of pregnancy. HSV infection occurs in less than 2% of these infants.

Transmission occurs most commonly via passage through the infected birth canal and less commonly in utero, or in the postpartum period. The risk of infection to an infant born vaginally to a mother with recurrent infection is much lower than a newly acquired infection, occurring in less than 5% of cases. More than three quarters of infants who become infected with HSV are born to women with no history or clinical suggestion of active HSV infection in pregnancy. Postnatal transfer from a parent or caregiver occurs rarely.

Incubation Period

The incubation period varies from 2-12 days. In newborns, the infection may be present at birth or may occur as late as four weeks postpartum.

Period of Communicability

Infected newborns are infectious for the duration of the illness.

Host Susceptibility

Humans are universally susceptible to HSV infection. For newborns this may be reduced in the presence of maternal antibody.

Occurrence

General (1)

Neonatal HSV infection occurs worldwide. It is estimated that the incidence infection ranges from 1/3,000-20,000 live births. The United Kingdom reports a rate of 2/100,000 live births. A rate of 20-50/100,000 live births is reported in the United States where 75% of neonatal infections are caused by HSV-2 and 25% by HSV-1. The prevalence HSV infection is greatest in low socioeconomic groups and in individuals with multiple sex partners.

Canada (1, 2)

The Canadian Paediatric Surveillance Program reports 43 confirmed cases of neonatal HSV infection (and an additional five under investigation) from October 2000 to December 2002. The rate of infection during this period was 5.8/100,000 live births. Ninety-eight percent of the infants received acyclovir. Over one third of the infections were disseminated cases with an overall case fatality rate of 16%. Seven infants died within 24 days of birth. HSV-1 accounted for 62% of cases and 38% were HSV-2. The majority of fatal cases were reported as HSV-2. Approximately 80% of the infants were delivered vaginally. Ontario and Quebec reported 65% of the cases, 7% were reported from the Maritimes and the remaining 28% were from the Western provinces. The mean age of the mother at the time of delivery was 26 years of age.

More than three quarters of the women were Caucasians. A significant number of women were not aware of a history of genital HSV infection prior to delivery.

Alberta (3)
Neonatal HSV infection is rare in Alberta. From 1998 to 2002, a total of six cases were reported; one case in 1999, three cases in 2001 and two cases in 2002. The outcome of these cases is unknown

Key Investigation

Single Case/Household Cluster

- History of HSV infection in the mother.
- Clinical assessment of the mother for primary or recurrent genital herpes infection, especially late in pregnancy or close to the time of delivery.
- History of HSV infection in a caregiver.

Control

Management of a Case (2)

- In addition to routine practices, neonates with HSV infection should be isolated while in hospital and managed with contact precautions.
- Newborns whose mothers had active lesions at the time of delivery should be carefully observed and have HSV cultures performed 48 hours after birth following both vaginal delivery and cesarean section.
- In-hospital observation time may be increased. This may depend on the ability of the family to observe the infant at home and the availability of follow-up care and clinical assessment.
- If the newborn is monitored at home, educate the parents to observe carefully for any rash or other symptoms.

Treatment of a Case

- Treatment should be administered in consultation with a pediatric specialist to all neonates with HSV infection irrespective of presenting clinical findings.
- Intravenous acyclovir for 14-21 days is the treatment of choice for symptomatic neonatal HSV infection or in infants whose mothers have proven or presumed primary infection (2).
- The duration of treatment will depend on the gestational age and renal function of the newborn.

Management of Contacts

- No public health interventions are required for contacts.

Preventive Measures

- Educate members of the public on the use of condoms. Use of latex condoms may decrease the risk of acquiring genital herpes infection during pregnancy.
- Educate members of the public about the risk of transmission with oral sex.
- Prenatal evaluation of pregnant women regarding past or current signs or symptoms consistent with HSV infection.
- Prenatal evaluation of pregnant women regarding past or current signs or symptoms consistent with HSV infection in their partner.
- Oral acyclovir given in the late third trimester should be considered for high-risk women with gestational HSV infection. This may prevent recurrent genital HSV infection thus preventing the need for a cesarean section and reducing the risk of neonatal transmission of the HSV (2).

- Use of a scalp electrode on an infant during labour is not recommended in women suspected of having HSV infection (4).
- If active lesions are present at the onset of labour, cesarean section may be performed although this practice and recommendation varies. Cesarean section does not eliminate but reduces the risk of HSV infection in newborns by 86% (3, 4).
- Pregnant women with recurrent genital herpes should undergo specialist evaluation for consideration of suppressive antiviral therapy.
- Counsel pregnant women with a previous HSV infection about the risk of recurrence and that transmission may occur to the baby even if they are asymptomatic. (A Singh, personal communication, December 2003)
- Pregnant women with a previous HSV infection should inform their healthcare provider that they have a history of herpes. (A Singh, personal communication, December 2003)

References

(1) Wong T. *Neonatal herpes simplex virus infection (October 2000 to September 2003)*. Canadian Paediatric Society. Canadian Paediatric Surveillance Program. CPSP 2002 Results. http://www.cps.ca/english/CPSP/About/2002Results.pdf

(2) Allen U. *Current management of herpes simplex infection in pregnant women and their newborn infants: What's hot and what's not*. Can J Infect Dis 2003;14-4.

(3) Alberta Health and Wellness, Disease Control and Prevention. *Congenital infections in Alberta 1998 – 2002*. Communicable Disease Reporting System. May 2003.

(4) Brown Z, Wald A et al. *Effects of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant*. JAMA 2003;289(2):203-9.