GUIDELINE

Herpes Simplex Virus (HSV): management of neonatal HSV and neonates born to HSV positive women

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

Contents

Aim

To provide guidance on the management of neonates born to HSV positive women or with signs of HSV disease.

Risk

Neonatal HSV disease is severe with high risk of mortality and long-term sequelae.

Background

Herpes Simplex Viruses (HSV) is a common infection which may be transmitted between people who are asymptomatic or symptomatic with primary or recurrent infections. Infection can occur with HSV-1 and HSV-2.

In neonates HSV-2 has previously caused more infections than HSV-1. More recently the proportion of neonatal infections due to HSV-1 has increased and thought to be due to increasing rates of genital HSV-1 infections. HSV infection in newborns has an incidence of 1:3000 to 1:20000 depending on the geographical location. The overall global rate of neonatal HSV is estimated to be 10 per 100,000 live births, with a best estimate of 14,000 cases annually.

Refer to the WNHS – Herpes Simplex in Pregnancy for information on antenatal management, antibody testing and delivery of HSV positive women.

Transmission

More than 75% of infants with HSV infection have been born to women with no history or clinical findings suggestive of active HSV infection during pregnancy.

- Neonatal HSV is most commonly transmitted perinatally by passage through an infected genital tract or through an ascending infection. HSV can transmit through intact membranes.
- Neonatal HSV can be acquired in-utero (5%), in the peripartum period (85%), or in the postnatal period (10%).
- Rarely HSV is acquired through postnatal transmission from a parent or caregiver with oro-labial HSV or herpetic whitlow.
- Congenital HSV infection is very rare.

Risk factors for HSV transmission to neonate

1. Type of maternal infection - first-episode primary (57%), first-episode non-primary (25%), recurrent (<2%)
2. Maternal HSV serology status
3. Mode of delivery (vaginal > C-section)
4. Duration of rupture of membranes
5. Disruption of cutaneous barrier (foetal scalp electrodes/instrumentation)
6. HSV serotype (HSV-1 > HSV-2)

Distinguishing between primary and recurrent HSV infection in women by history and examination may be impossible. Maternal type specific serology may be useful.

Classification	HSV-1 and HSV-2 PCR from genital lesion	HSV-1 and HSV-2 Serology
First episode (Primary)	Positive either virus	Both negative
First episode (Non-primary)	Positive HSV-1	Positive HSV-2 and negative HSV-1
	Positive HSV-2	Positive HSV-1 and negative HSV-2
Recurrent	Positive HSV-1	Positive HSV-1
	Positive HSV-2	Positive HSV-2

Clinical Manifestations

Most cases present within 60 days of life. In newborns, HSV can manifest as:

- **SEM disease** (≈45%): Disease localised to **S**kin, **E**ye and **M**ucous membranes. 80% of infants present with vesicular rash and usually present at 10–12 days of life.
- **Central nervous system disease** (≈30%): Neonates usually present at 16–19 days of life, although can present within the first month of life. CNS disease presents with lethargy, irritability, tremors, poor feeding, temperature instability, full anterior fontanelle, and seizures.
- **Disseminated disease** (≈25%): Can involve multiple organ systems including liver, lungs, CNS, heart, adrenal glands, bone marrow, kidneys, gastrointestinal tract and SEM. Disseminated disease presents with viral sepsis and may be indistinguishable from sepsis of another cause. It should be considered especially if neonate presents with respiratory/hepatic failure with disseminated intravascular coagulation (DIC). Disseminated disease presents early and usually around day 10-12 of life.
- **Congenital (in utero) HSV** (rare): triad of skin (active herpes, scarring, pigmentation), CNS (microcephaly, intracranial calcifications), eye (chorioretinitis, optic atrophy, microphthalmia)

It is important to consider HSV infection in the differential diagnosis of all acutely unwell neonates, especially if there is a sepsis-like presentation. In up to 40% of newborns with HSV, there are no skin lesions. In the absence of skin lesions diagnosis may be delayed.

Diagnostic Tests

PCR is the primary means for direct detection of HSV. However, in very small number of neonates it may be negative in early disease - if strong clinical suspicion discuss case with Clinical Microbiologist or Paediatric Infectious Diseases Physician. For further details on testing see Pathwest Test Directory and on specimen collection requirements see Sepsis: Neonatal

Refer to Microbiological Diagnostic Testing for Infections in Neonates (previously TORCH) for testing recommendations in key neonatal infections.

Immunofluorescence and HSV culture are not routinely available.

Neonatal HSV serology is not useful in diagnosis of neonatal HSV as IgG is of maternal origin. HSV IgM testing is not recommended or available at PathWest.

TESTING TO BE PERFORMED URGENTLY:		
Test	**Site/sample**	**Container/collection requirements**
HSV PCR	Surface swabs; eyes, throat, umbilical, rectal, skin vesicle	[a]Dry swab
HSV PCR	Blood	EDTA (purple top) – 0.5mL Dedicated sample preferred.
HSV PCR **MCS, protein, glucose**	CSF (if no contraindications)	3 Sterile CSF specimen containers. Preferred volume 10 drops(0.5mL)/tube in term neonate.
Bloods (other)	FBP, coagulation screen, liver function tests	
TESTS THAT CAN BE CONSIDERED:		
HSV PCR	Urine (if urine MCS performed)	[b]Sterile container
CXR	If respiratory symptoms present	

PCR minimum volume is 220ul, 0.5mL recommended in case of repeats. If performing additional testing (e.g. CSF MCS, protein, glucose) on same sample larger volume required. Separate EDTA tube required for PCR and FBP.

a – e.g. Dry rayon tip or flocked swab with or without viral transport media (VTM). (DO NOT USE swab for bacterial MCS with charcoal transport media). Also see CAHS CPM Nasopharyngeal And Throat Swab Collection and Wound swab collection (for more details on swab selection).

b - e.g. 50ml yellow top container

Treatment

IV Aciclovir is the primary treatment and should be given while awaiting the results of laboratory investigations. See Aciclovir for dosing. **There is no place for oral Aciclovir in neonatal treatment of acute HSV**.

One year mortality has reduced to 29% for disseminated disease and 14% for CNS disease with introduction of high dose aciclovir therapy, while neurological complications among survivors at 12 months of age are 25% and 70% in disseminated and CNS disease respectively.

Management of Infant with Presentation Compatible with HSV

Obtain virological specimens as detailed above, including CSF, and commence treatment with IV Aciclovir (high dose), see Neonatal Medication Protocol Aciclovir.

Length of treatment will be determined by extent of disease. Suggested duration of treatment for confirmed neonatal HSV infection is 10-14 days for infants with SEM disease and 21 days for CNS and disseminated disease. Some experts advise to repeat LP and CSF HSV PCR towards end of treatment to confirm clearance of viral DNA. Not all experts advise this routinely as the value of an end of therapy HSV CSF PCR test after 21 days of aciclovir with clinical response has not been demonstrated. If performed and the HSV PCR remains positive discuss with Clinical Microbiologist or Paediatric Infectious Diseases Physician.

Management of Asymptomatic Infant born to mother with active HSV

Risk stratification is required based on risk of transmission, maternal history and testing (see Transmission above and Herpes Simplex in Pregnancy). This dictates investigations and need for empirical treatment. See Appendix 1 Management of Asymptomatic Neonate born to mother with active genital herpes at delivery for guidance.

Long Term Oral Suppressive Therapy after Acute Treatment

Long term oral suppressive therapy is currently recommended following CNS and disseminated disease as better neurodevelopmental outcome and fewer cutaneous recurrences have been reported. Discuss with Paediatric Infectious Diseases Physician regarding duration of therapy. Monitor for adverse effects. Some experts also recommend oral aciclovir to suppress troublesome cutaneous recurrences in those without CNS involvement. This is not routinely recommended as it has not been shown to alter neurological outcome. Discuss with Paediatric Infectious Diseases Physician prior to prescribing. See Aciclovir Monograph – Paediatric for dosing.

Follow Up

Infants with neonatal HSV infection should be followed up and evaluated for recurrent disease and neurological sequelae.

Infection Prevention and Control

Contact precautions: a single room or isolette should be used for all neonates with confirmed HSV and with skin lesions typical of HSV awaiting test results. Precautions to remain in place until lesions are dry and crusted or as advised by Infection Control. Refer to Infection Prevention Manual – Standard and Transmission Based Precautions and Transmissible Diseases Index.

Related CAHS internal policies, procedures and guidelines

Neonatology Microbiological Diagnostic Testing for Infections in Neonates (previously TORCH)

Neonatal medication protocol: Aciclovir

CAHS ChAMP Monographs: Aciclovir

CAHS: Infection Prevention Manual:

- Standard and Transmission Based Precautions
- Transmissible Diseases Index

WNHS: Infection Prevention Manual: Standard and Transmission-Based Precautions

WNHS Herpes Simplex in Pregnancy

References and related external legislation, policies, and guidelines

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Appendix 1: Management of Asymptomatic Neonate born to mother with active genital herpes at delivery[a] Adapted from Australasian Society for Infectious diseases 2022

Asymptomatic infant with VERY LOW RISK of HSV exposure and disease (< 2% in Australia)[b]
– Mother with active recurrent genital HSV at delivery, or
– Mother who has first clinical episode genital HSV and who has now developed HSV type specific IgG prior to delivery.

- The predictive value of surface swabs has not been shown in settings where the incidence of neonatal herpes is low, like in Australia.
- The consensus view in Australia, NZ and the UK (in contrast to the US) is that collection of surface swabs from well babies born to mothers with recurrent genital herpes is not indicated.[c]
- All families should monitor the baby closely for symptoms and signs of HSV disease.[d]

Newborn develops symptoms and signs of clinical disease while monitored. Investigate for HSV disease.

Asymptomatic infant with POSSIBLE HIGH RISK of exposure and HSV disease (~25-57%)
– Mother with first episode genital or systemic infection close to delivery, or
– Infant born to mother with active genital herpes and no known past history of genital HSV, or
– Preterm infant born to mother with active genital herpes, or
– Infant born to immunocompromised mother with active genital herpes

Perform:
- LP (CSF analysis, HSV PCR)
- FBP, LFTs, Coagulation studies
- HSV PCR on blood
- Surface swabs HSV PCR- eye, throat, umbilicus, rectum, skin vesicle
- +/- urine HSV PCR

Commence IV aciclovir immediately. See duration below.

ACICLOVIR treatment duration
- Laboratory confirmed infection or clinical disease confined to skin, eye, mouth: 10-14 days
- Encephalitis, disseminated disease: 21 days
- Neonates with high risk of exposure but with negative testing should be discussed prior to cessation as some experts suggest pre-emptive therapy.
- **Duration should be discussed with Clinical Microbiologist or Paediatric ID Physician**

CSF HSV PCR positive:
- Some experts advise repeat CSF HSV PCR at end of treatment
- Not all experts advise this routinely as the value of an end of therapy HSV CSF PCR test after 21 days of aciclovir with clinical response has not been demonstrated.
- If performed and the HSV PCR remains positive discuss with Clinical Microbiologist or Paediatric ID Physician

See additional recommendations for long term suppressive therapy and follow up above.

Comments
a. This algorithm is for use in settings where the prevalence of genital herpes and neonatal HSV disease is low. It does not refer to asymptomatic infants born to mothers with a history of genital herpes but no active lesions
b. Data available to guide risk is primarily for HSV-2
c. Experts from the US, where the prevalence of genital and neonatal HSV disease is higher, recommend surface swabs on well infants after possible exposure to HSV
d. Monitor for skin, eye, mouth disease, lethargy/irritability, poor feeding
e. Caesarean section with intact membranes significantly reduces but does not eliminate risk of neonatal HSV
f. If risk stratification uncertain discuss case with Clinical Microbiologist or Paediatric ID Physician.