



CLINICAL GUIDELINE

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

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

This document should be read in conjunction with this [DISCLAIMER](#)

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 causes 75% of infections and HSV-1 25%. HSV infection in newborns has an incidence of 1:3000 to 1:20000 depending on the geographical location. There is concern that with the increasing incidence of HSV-2 infection, numbers of newborn HSV infection will increase. 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 Women and Newborns Health Service guideline – [Herpes Simplex in Pregnancy](#) for information on antenatal management, antibody testing and delivery of HSV positive women.

Transmission

- 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.
- 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 (fetal scalp electrodes and other instrumentation)
 6. HSV serotype (HSV-1 > HSV-2)

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

- **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.**
- Congenital HSV infection may also occur, but is very rare.

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- Rarely HSV is acquired through postnatal transmission from a parent or caregiver with oro-labial HSV or herpetic whitlow.
- Neonatal HSV can be acquired in-utero (5%), in the peripartum period (85%), or in the postnatal period (10%).

Clinical Manifestations

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

- **SEM disease** (≈45%): Disease localised to skin, eye and mucous 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 fontanel 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.

It is important to consider HSV infection in the differential diagnosis of all acutely unwell neonates, especially if there is a sepsis-like presentation and a maternal history of HSV.

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

- Serology is of limited value, as IgG is of maternal origin.
- Surface swabs (transport in viral medium) for immunofluorescence, HSV culture and HSV PCR:
- Skin vesicles if present.
- Umbilical stump.
- Mouth or nasopharynx.
- Eyes (conjunctival swabs).
- Rectum (rectal swab).
- Urine.
- Tracheal aspirate (if ventilated).
- HSV PCR from blood. This requires 0.5 mL EDTA blood.
- Lumbar puncture for HSV PCR: indicated in all cases, where clinically stable.
- Other tests: FBC, Coagulation screen, Liver function tests.
- Chest X-ray if respiratory symptoms.

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Treatment

Aciclovir should be given whilst awaiting the results of laboratory investigations. See [Aciclovir](#) for dosing. **There is no place for oral Acyclovir in neonatal treatment of acute HSV.**

Contact precautions: either in single room or isolette for the duration of IV therapy unless advised earlier by Infection Control/Clinical Microbiologist. Refer to Infection Prevention Manual – [Standard and Transmission Based Precautions](#). These neonates continue to excrete HSV for some days. A review of all the latest culture/PCR results should be done before taking of isolation.

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

Long Term Oral Suppressive Therapy after Acute Treatment

Long term oral suppressive therapy is currently recommended; as better neurodevelopmental outcome and fewer cutaneous recurrences have been reported. Discuss with a Clinical Microbiologist regarding duration of therapy; 6 months is recommended. Monitor for adverse effects.

Follow Up

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

Management of Infant with Presentation Compatible with HSV

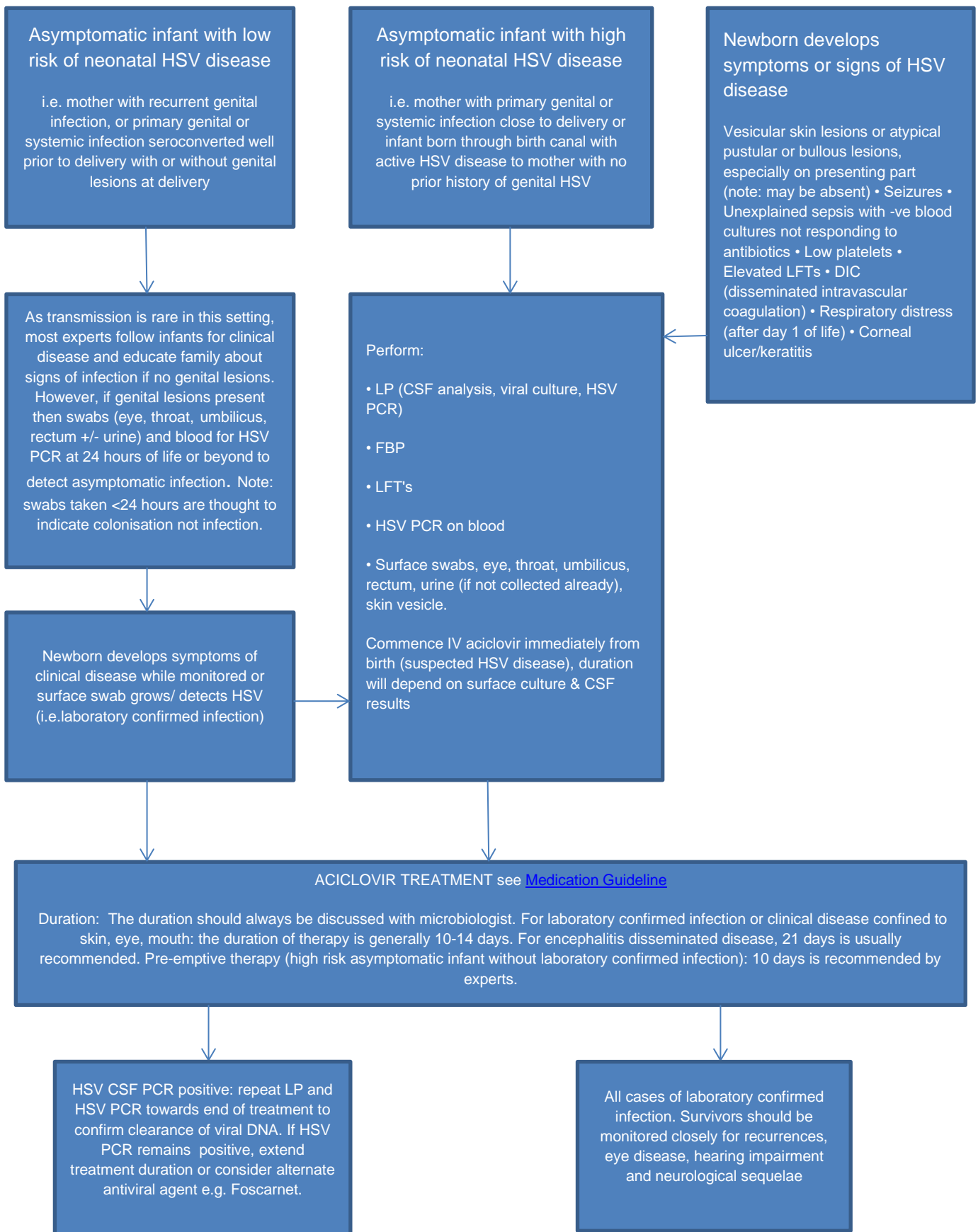
Obtain virological specimens as detailed above, including CSF, and commence treatment with IV Aciclovir (high dose), see NCCU Medication Protocol [Aciclovir](#).

Contact precautions: either in single room or isolette for the duration of IV antiviral therapy. Isolation may need to be prolonged beyond this period pending results of virological investigations. Refer to Infection Prevention Manual – [Standard and Transmission Based Precautions](#).

Length of treatment will be determined by extent of disease. Suggested duration of treatment for confirmed neonatal HSV infection is 14 days for infants with SEM disease and 21 days for CNS and disseminated disease. If there are CSF abnormalities, repeat CSF examination towards the end of the treatment should be performed. Neonates with positive HSV on repeat CSF need further anti-viral treatment and have poor prognosis. Consultation with Clinical Microbiologist is advised.

HSV INFECTIONS IN PREGNANCY: NEONATAL MANAGEMENT

(Australasian Society for Infectious diseases 2014)




Related CAHS internal policies, procedures and guidelines
<ul style="list-style-type: none">• Standard and Transmission Based Precautions• Aciclovir

References and related external legislation, policies, and guidelines
WNHS: Infection Prevention Manual <ul style="list-style-type: none">• Neonatal Viral Infections• Transmission Based Precautions
<ol style="list-style-type: none">1. Enkin, M., Keirse, M., Neilsen, J et al. (2000). A guide to effective care in pregnancy and childbirth. Melbourne: Oxford University Press.2. Kimberlin DW,et al National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections. <i>Pediatrics</i>. 2001 Aug;108(2):230-3. Kimberlin D. Herpes Simplex Virus, Meningitis and Encephalitis in Neonates. <i>Herpes</i>. 2004 Jun;11 Suppl 2:65A-76A4. Kimberlin DW. Neonatal herpes simplex infection. <i>Clin Microbiol Rev</i>. 2004 Jan;17(1):1-13.5. Maayan-Metzger, A., Mazkareth, R., & Kuint, J. (2003). Fever in healthy asymptomatic newborns during the first few days of life. <i>Arch Dis Child</i>, 88, F312-4.6. Red Book 2003 Report of the Committee on Infectious Diseases 26th ed. Elk Grove Village, IL: American Academy of Pediatrics;2003: 336-340. www.cdc.gov/hepatitis7. Seidel, HM. Rosentein, BJ. Pathak, A. (2001). Primary Care of the Newborn. St. Lois, Mosby8. Wiswell, T.E., Baumgart, S., Gannon, C.M., Spritzer, A.R. (1995). No lumbar puncture in the evaluation for early neonatal sepsis: will meningitis be missed? <i>Pediatrics</i>, 95, 803-6.9. Sullender W.M., Yasukawa L.L., Schwartz M., et. al.: Type-specific antibodies to herpes simplex virus type 2 (HSV-2) glycoprotein G in pregnant women, infants exposed to maternal HSV-2 infection at delivery, and infants with neonatal herpes.J Infect Dis 1988; 157: pp. 164-171.10. Pinninti.S, Kimberlin.D. Neonatal herpes simplex virus infections. <i>Seminars in Perinatology</i> 2018; 48:168-175.11. Looker K.J., Magaret A.S., May M.T., et al: First estimates of the global and regional incidence of neonatal herpes infection. <i>Lancet Glob Health</i> 2017; 5: pp. e300-e309.12. Kimberlin DW, WhitleyRJ, WanW,etal. Oral acyclovir suppression and neurodevelopment after neonatal herpes. <i>N EnglJMed</i>. 2011;365:1284–1292.13. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and caesarean delivery on transmission rates of herpes simplex virus from mother to infant. <i>J Am Med Assoc</i>. 2003;289:203–209.14. Kimberlin DW, Jacobs RF, Powell DA, et al. Safety and efficacy of high-dose acyclovir in the management of neonatal herpes simplex virus infections. <i>Pediatr</i> 2001;108(2);230-8.15. Kimberlin DW, Lin CY, Jacobs RF, et al. Natural history of neonatal herpes simplex virus infections in the acyclovir era. <i>Pediatrics</i> 2001;108(2):223-9.16. Palasanthiran P, Starr M, Jones C, Giles M. Management of perinatal infections. Australasian Society for Infectious disease 2014.

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