Neonatal HSV

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If so please identify here which document/s

Contents

Executive Summary

This guideline provides advice on the diagnosis and management of Neonatal Herpes, a rare and severe infection caused by Herpes simplex virus type 1 and 2 (HSV-1 & -2). The policy consists of two sections: the first section includes diagnostic and treatment algorithms aimed to guide paediatricians. The second section consists of background information to boost the general knowledge about Herpes Simplex Virus, Neonatal Herpes and Genital Herpes in pregnancy.

1

1.1 Introduction

Neonatal Herpes (NH) is a disease caused by Herpes simplex virus (HSV) type 1 and 2. It is a rare and severe disease associated with significant morbidity and mortality. It is normally vertically transmitted at the time of delivery, when HSV replicates in the birth canal. Most mothers are asymptomatic with no past history of Genital Herpes (GH). The diagnosis of NH is challenging because the disease is rare and often non-specific in its presentation. Early diagnosis is critical for to guide the prompt initiation of antiviral treatment.

1.2 Scope

This policy applies to diagnosis and treatment of Neonatal Herpes. The policy is aimed at all paediatricians across Wessex. It may also be used to provide advice to general practitioners, obstetricians and midwives.

1.3 Purpose

This policy ensures that all neonates with possible HSV infection are appropriately risk assessed and receive appropriate diagnostic investigations and antiviral treatment in a consistent and timely manner

1.4 Acronyms

Acronyms	**GH**: Genital Herpes	**MTCT**: Mother To Child Transmission	**PROM**: Premature Rupture Of Membrane
	HSV: Herpes simplex virus	**NH**: Neonatal Herpes	**SEM**: Skin Eye & Mucosal disease
ACV: Aciclovir	**IUGR**: Intrauterine Growth Retardation	**PCR**: Polymerase Chain Reaction	**TDS**: Ter Die Sumendum (taken 3 times/day)
CS: Caesarean Section	**LP**: Lumbar Puncture	**ROM**: Rupture Of Membrane	**VTM**: Viral Transport Medium

2 Roles and Responsibilities

2a. Microbiology/virology laboratory (inc PHE regional diagnostic centre)

- To provide the diagnosis of Neonatal HSV infection and to liaise with Paediatricians to advise on appropriate sample type.

2c Hospital Paediatricians

- To manage neonates with Neonatal Herpes in need of antiviral treatment by following the directive of this policy, to ensure that patients received appropriate treatment in a timely manner.

3 Implementation

This policy will be disseminated to all clinicians who look after newborn infants, including Infection specialists.

4 Process for Monitoring Compliance/Effectiveness

Compliance with these guidelines will not be routinely reviewed unless a concern is identified. This may be through incidents, complaints, claims or performance issues.

5 Arrangements for Review of the Policy

This guideline will be reviewed every three years, or earlier, in case of major advances in the diagnosis and clinical management of this disease.

6 References

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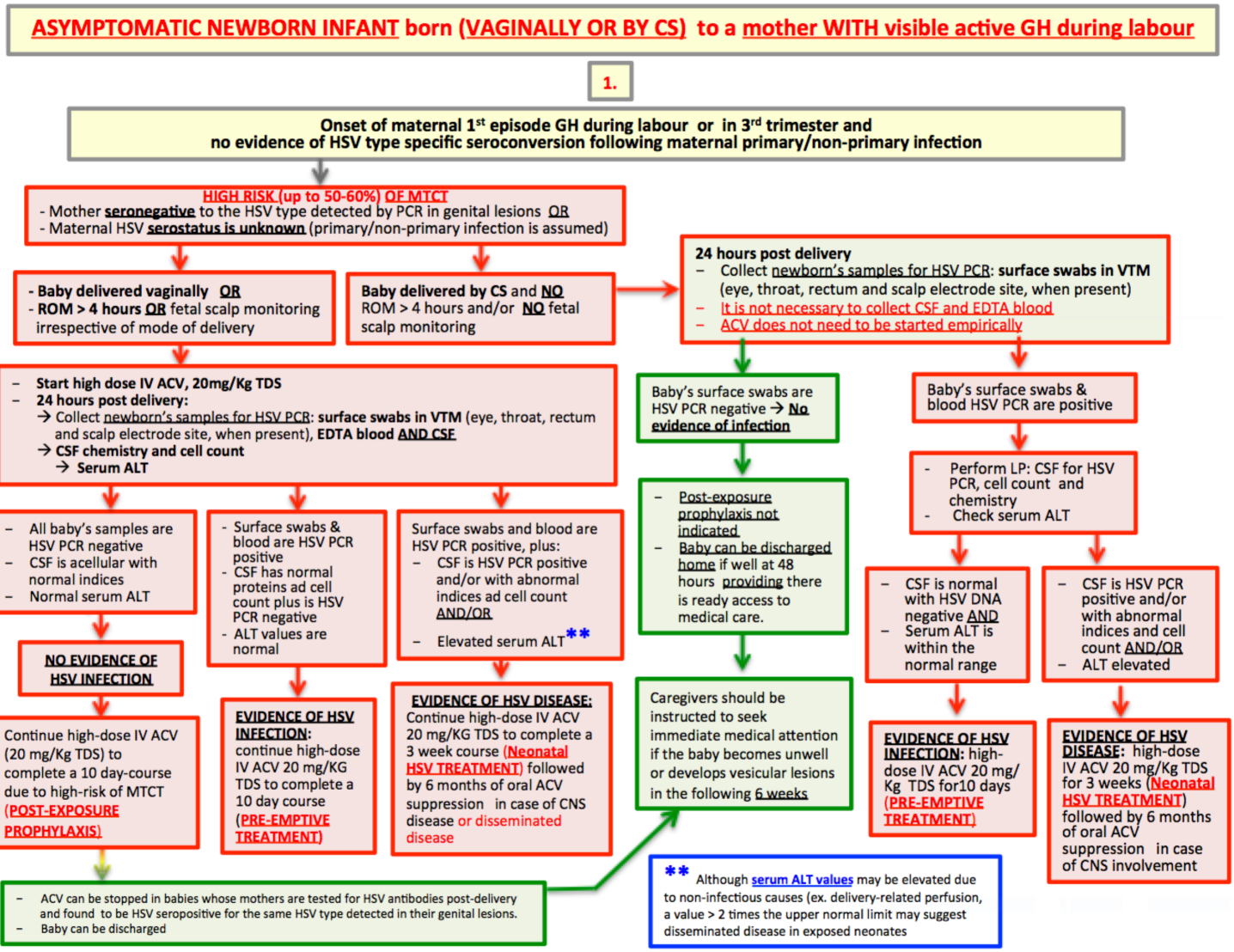
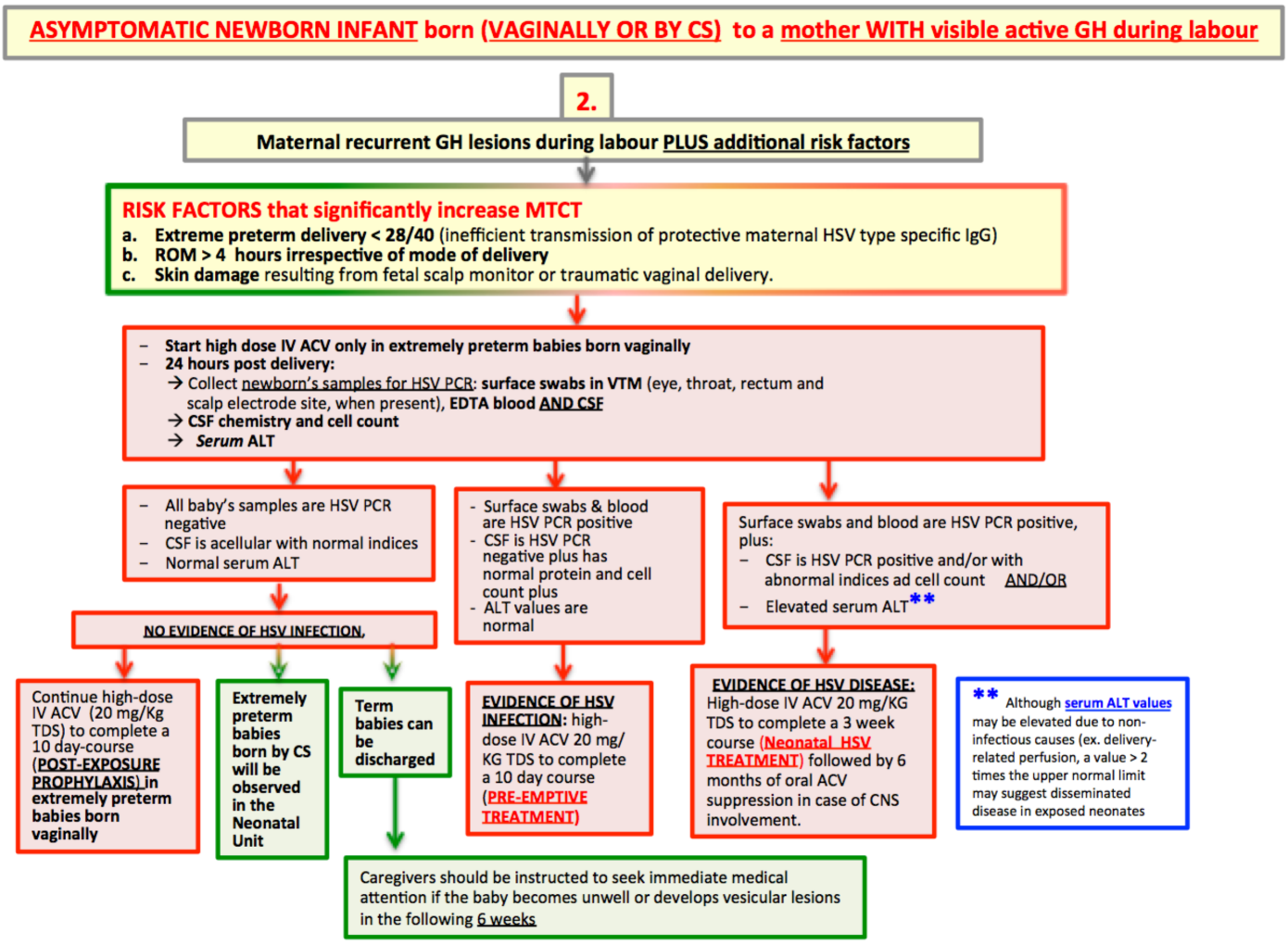
THE NEWBORN INFANT

BACKGROUND INFORMATION ABOUT GH AND NH

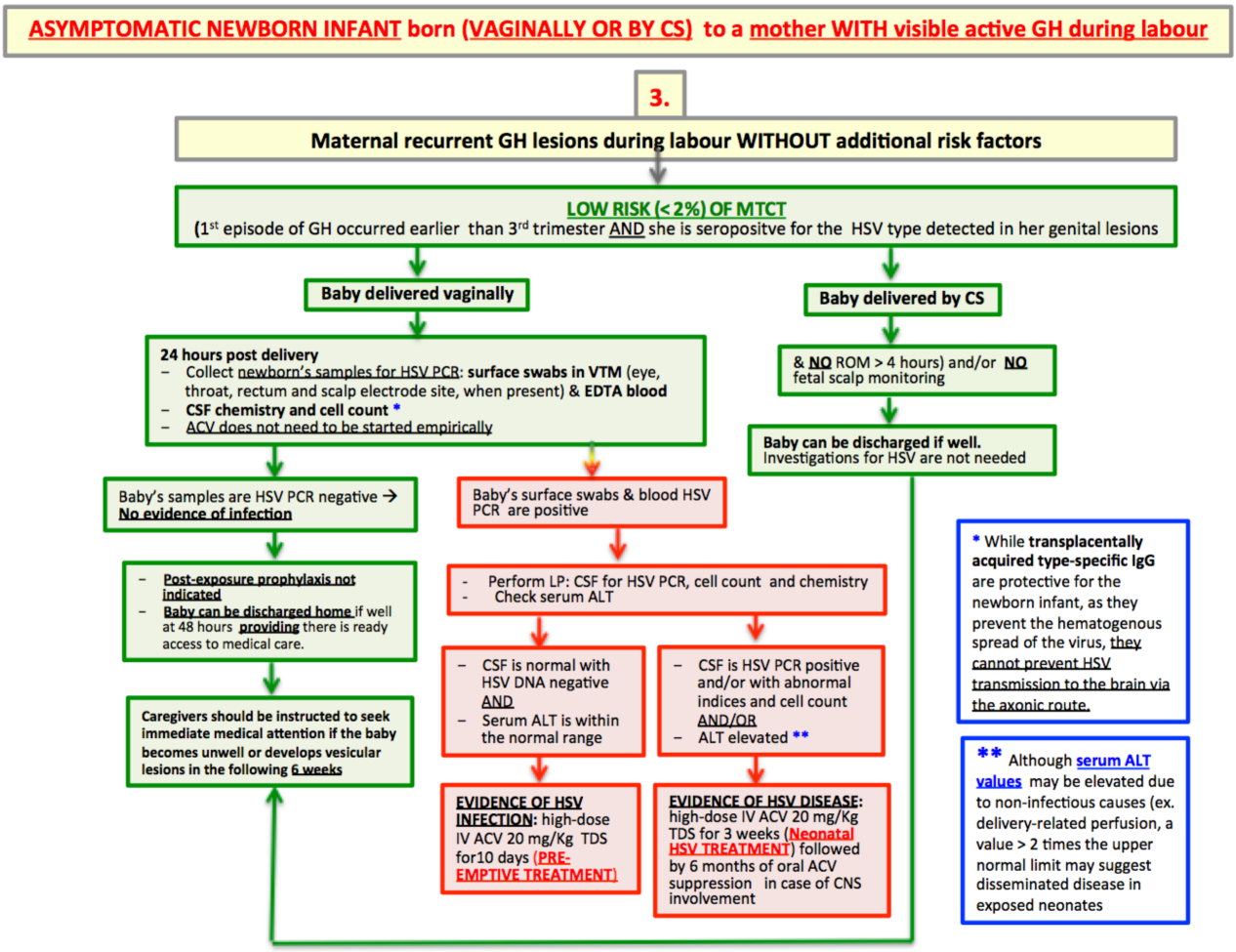
APPENDIX A1


ASYMPTOMATIC NEWBORN INFANT born (VAGINALLY OR BY CS) to a mother WITH visible active GH during labour
1.
Onset of maternal 1st episode GH during labour or in 3rd trimester and no evidence of HSV type specific seroconversion following maternal primary/non-primary infection
HIGH RISK (up to 50-60%) OF MTCT
- Mother seronegative to the HSV type detected by PCR in genital lesions OR
- Maternal HSV serostatus is unknown (primary/non-primary infection is assumed)
- Baby delivered vaginally OR
- ROM > 4 hours OR fetal scalp monitoring irrespective of mode of delivery
Baby delivered by CS and NO ROM > 4 hours and/or NO fetal scalp monitoring
24 hours post delivery
– Collect newborn's samples for HSV PCR: surface swabs in VTM (eye, throat, rectum and scalp electrode site, when present)
– It is not necessary to collect CSF and EDTA blood
– ACV does not need to be started empirically
– Start high dose IV ACV, 20mg/Kg TDS
– 24 hours post delivery:
→ Collect newborn's samples for HSV PCR: surface swabs in VTM (eye, throat, rectum and scalp electrode site, when present), EDTA blood AND CSF
→ CSF chemistry and cell count
→ Serum ALT
Baby's surface swabs are HSV PCR negative → No evidence of infection
Baby's surface swabs & blood HSV PCR are positive
– All baby's samples are HSV PCR negative
– CSF is acellular with normal indices
– Normal serum ALT
- Surface swabs & blood are HSV PCR positive
- CSF has normal proteins ad cell count plus is HSV PCR negative
- ALT values are normal
Surface swabs and blood are HSV PCR positive, plus:
– CSF is HSV PCR positive and/or with abnormal indices ad cell count AND/OR
– Elevated serum ALT**
– Post-exposure prophylaxis not indicated
– Baby can be discharged home if well at 48 hours providing there is ready access to medical care.
- Perform LP: CSF for HSV PCR, cell count and chemistry
- Check serum ALT
– CSF is normal with HSV DNA negative AND
– Serum ALT is within the normal range
– CSF is HSV PCR positive and/or with abnormal indices and cell count AND/OR
– ALT elevated
NO EVIDENCE OF HSV INFECTION
EVIDENCE OF HSV INFECTION: continue high-dose IV ACV 20 mg/KG TDS to complete a 10 day course (PRE-EMPTIVE TREATMENT)
EVIDENCE OF HSV DISEASE: Continue high-dose IV ACV 20 mg/KG TDS to complete a 3 week course (Neonatal HSV TREATMENT) followed by 6 months of oral ACV suppression in case of CNS disease or disseminated disease
Caregivers should be instructed to seek immediate medical attention if the baby becomes unwell or develops vesicular lesions in the following 6 weeks
EVIDENCE OF HSV INFECTION: high-dose IV ACV 20 mg/Kg TDS for10 days (PRE-EMPTIVE TREATMENT)
EVIDENCE OF HSV DISEASE: high-dose IV ACV 20 mg/Kg TDS for 3 weeks (Neonatal HSV TREATMENT) followed by 6 months of oral ACV suppression in case of CNS involvement
Continue high-dose IV ACV (20 mg/Kg TDS) to complete a 10 day-course due to high-risk of MTCT (POST-EXPOSURE PROPHYLAXIS)
– ACV can be stopped in babies whose mothers are tested for HSV antibodies post-delivery and found to be HSV seropositive for the same HSV type detected in their genital lesions.
– Baby can be discharged
** Although serum ALT values may be elevated due to non-infectious causes (ex. delivery-related perfusion, a value > 2 times the upper normal limit may suggest disseminated disease in exposed neonates

APPENDIX A2


ASYMPTOMATIC NEWBORN INFANT born (VAGINALLY OR BY CS) to a mother WITH visible active GH during labour
2.
Maternal recurrent GH lesions during labour PLUS additional risk factors
RISK FACTORS that significantly increase MTCT
a. Extreme preterm delivery < 28/40 (inefficient transmission of protective maternal HSV type specific IgG)
b. ROM > 4 hours irrespective of mode of delivery
c. Skin damage resulting from fetal scalp monitor or traumatic vaginal delivery.
– Start high dose IV ACV only in extremely preterm babies born vaginally
– 24 hours post delivery:
→ Collect newborn's samples for HSV PCR: surface swabs in VTM (eye, throat, rectum and scalp electrode site, when present), EDTA blood AND CSF
→ CSF chemistry and cell count
→ Serum ALT
– All baby's samples are HSV PCR negative
– CSF is acellular with normal indices
– Normal serum ALT
- Surface swabs & blood are HSV PCR positive
- CSF is HSV PCR negative plus has normal protein and cell count plus
- ALT values are normal
Surface swabs and blood are HSV PCR positive, plus:
– CSF is HSV PCR positive and/or with abnormal indices ad cell count AND/OR
– Elevated serum ALT**
NO EVIDENCE OF HSV INFECTION,
Continue high-dose IV ACV (20 mg/Kg TDS) to complete a 10 day-course (POST-EXPOSURE PROPHYLAXIS) in extremely preterm babies born vaginally
Extremely preterm babies born by CS will be observed in the Neonatal Unit
Term babies can be discharged
EVIDENCE OF HSV INFECTION: high-dose IV ACV 20 mg/ KG TDS to complete a 10 day course (PRE-EMPTIVE TREATMENT)
EVIDENCE OF HSV DISEASE: High-dose IV ACV 20 mg/KG TDS to complete a 3 week course (Neonatal HSV TREATMENT) followed by 6 months of oral ACV suppression in case of CNS involvement.
** Although serum ALT values may be elevated due to non-infectious causes (ex. delivery-related perfusion, a value > 2 times the upper normal limit may suggest disseminated disease in exposed neonates
Caregivers should be instructed to seek immediate medical attention if the baby becomes unwell or develops vesicular lesions in the following 6 weeks

APPENDIX A3


ASYMPTOMATIC NEWBORN INFANT born (VAGINALLY OR BY CS) to a mother WITH visible active GH during labour
3.
Maternal recurrent GH lesions during labour WITHOUT additional risk factors
LOW RISK (< 2%) OF MTCT
(1st episode of GH occurred earlier than 3rd trimester AND she is seropositve for the HSV type detected in her genital lesions
Baby delivered vaginally
Baby delivered by CS
24 hours post delivery
– Collect newborn's samples for HSV PCR: surface swabs in VTM (eye, throat, rectum and scalp electrode site, when present) & EDTA blood
– CSF chemistry and cell count *
– ACV does not need to be started empirically
& NO ROM > 4 hours) and/or NO fetal scalp monitoring
Baby can be discharged if well.
Investigations for HSV are not needed
Baby's samples are HSV PCR negative → No evidence of infection
Baby's surface swabs & blood HSV PCR are positive
– Post-exposure prophylaxis not indicated
– Baby can be discharged home if well at 48 hours providing there is ready access to medical care.
- Perform LP: CSF for HSV PCR, cell count and chemistry
- Check serum ALT
Caregivers should be instructed to seek immediate medical attention if the baby becomes unwell or develops vesicular lesions in the following 6 weeks
– CSF is normal with HSV DNA negative AND
– Serum ALT is within the normal range
– CSF is HSV PCR positive and/or with abnormal indices and cell count AND/OR
– ALT elevated **
EVIDENCE OF HSV INFECTION: high-dose IV ACV 20 mg/Kg TDS for10 days (PRE-EMPTIVE TREATMENT)
EVIDENCE OF HSV DISEASE: high-dose IV ACV 20 mg/Kg TDS for 3 weeks (Neonatal HSV TREATMENT) followed by 6 months of oral ACV suppression in case of CNS involvement
* While transplacentally acquired type-specific IgG are protective for the newborn infant, as they prevent the hematogenous spread of the virus, they cannot prevent HSV transmission to the brain via the axonic route.
** Although serum ALT values may be elevated due to non-infectious causes (ex. delivery-related perfusion, a value > 2 times the upper normal limit may suggest disseminated disease in exposed neonates

APPENDIX B

The asymptomatic NEWBORN INFANT born to a mother WITH history of GH but NO active lesions in labour (mother may be on ACV suppressive treatment)

- Infant born at term: should be observed for signs of NH, but does not require ACV treatment.
- If first clinical episode of maternal GH is **in the third trimester**, **or at any time in case of extreme premature birth (<28 weeks)**, maternal HSV type-specific serology and surface swabs in the neonate should be considered.
- Note that maternal suppressive ACV treatment during pregnancy does not completely eliminate HSV asymptomatic shedding and MTCT of HSV infection.
- Parents and caregivers should be educated about the signs and symptoms of NH.

APPENDIX C

The SICK NEWBORN BABY with clinical presentation compatible with NH or Congenital HSV disease from birth to the 6th week of life

CLINICAL PRESENTATIONS: although most infected infants present within the first 2 weeks of life, onset of disease symptoms and signs may occur during the first 24 hours and has been described beyond 30 days. The absence of fever is common at the time of presentation of neonatal HSV disease.

- Note that **up to 40% of patients do not have skin vesicles** at presentation, nor they develop them during the course of the disease.
- Note that **maternal suppressive ACV treatment during pregnancy does not completely eliminate HSV asymptomatic shedding and MTCT of HSV infection**. Therefore, NH should be considered in the differential diagnosis in symptomatic newborns born to mothers who received suppressive treatment with ACV or valacyclovir.

1. **SKIN, EYE AND MUCOSAL DISEASE OR SEM DISEASE** (average onset at 5-10 days): at presentation there are skin and/or mucosal vesicles/ulcers. Skin lesions may appear in areas of trauma (ex. site of foetal scalp electrodes) and may not be frankly vesicular. Conjunctivitis and keratoconjunctivitis are typical findings. Fever and poor feeding may be present. SEM disease may progress to CNS and disseminated disease if untreated.

2. DISSEMINATED DISEASE (average onset at 5-10 days, but may occur in the first few days of life. Normally follows primary HSV infection in the mother): **sepsis-like picture** with respiratory and hepatic failure (HSV pneumonitis and hepatitis), adrenal glands involvement, severe coagulopathy (**DIC**) and **marked elevation of ALT**. There may be CNS involvement (65%). SEM lesions develop in 60% of children, at presentation or during the course of the illness.

3. CNS DISEASE (average onset between 1-2 weeks; normally follows recurrent maternal infection): CNS involvement (temperature instability, focal/generalised seizures, lethargy, irritability, tremors, poor feeding and bulging fontanels, which can progress to hypotension, apnea and shock) ± skin/mucosal lesions (present in about 60-70%). Morbidity of CNS disease is higher with HSV-2 than with HSV-1.

4. CONGENITAL HSV DISEASE. Unlikely to be missed due to the extent of involvement of affected babies. Clinical presentation at birth may vary and can include **a wide variety of skin lesions** (grouped vesicles, bullae, zoster-like lesions, skin erosions and denudation, aplasia cutis, erythematous patches and hypo-pigmented / hyper-pigmented scarring), **eye disease** (chorioretinitis or microphthalmia), **CNS involvement** (microcephaly or hydranencepahly, seizures and intra-cerebral calcifications) , **hepatosplenomegaly**, **prematurity** (60%) and **IUGR** (25%). Skin lesions/scarring alone are uncommon (7%).

APPENDIX D

Laboratory Diagnosis of NH and testing algorithm

The following investigations should be performed for all clinical presentations of NH:

1. HSV PCR (same day result for samples submitted by 10 am during routine working hours Mondays to Saturdays)

- **Swabs from skin and/or mucosal lesions (when present). Swabs must be in Viral transport medium (VTM)** that can be requested by phoning UHS Serology.
- **Throat, eye and rectal swabs in Viral Transport Medium (VTM)**
- **EDTA blood:** all clinical disease categories can have detectable DNAemia.
- **CSF:** please note that HSV DNA can be detected in CSF for up to 7 days after ACV has been commenced. In the early stages of disease a negative HSV PCR in CSF does not rule out CNS disease as the HSV viral load may be very low.

2. CSF cell count, protein and glucose.

3. Serum ALT and clotting

For viral PCRs select on Equest: "Neonatal sepsis, viral investigations (NEO CODE)" to request HSV, enterovirus and adenovirus PCRs on the following specimens: throat, eye and rectal swabs in VTM, CSF and EDTA blood. Please phone the laboratory if parechovirus PCR is required (currently not included in the UHS in-house panel).
Turnaround time for HSV PCR is 8-48 hours, depending on the time and the day of the week samples are submitted.
"TORCH screen" (see specific test codes on Equest) should be also considered in septic neonates. This request code includes Rubella IgM, CMV IgM and Toxoplasma IgM on clotted blood plus CMV PCR on urine.

For any query Virology extension numbers are: Serology Laboratory 6342, Molecular Laboratory 8760, Consultant Virologist 5101.

Testing algorithm

Laboratory investigations for HSV infection should be performed:

1. In **ALL** neonates with **skin vesicles** even if the lesions suggest bacterial infection (much more common than HSV neonatal infection) and independently of their clinical conditions: testing should be performed even if the neonate is systemically well.

2. In **ALL** neonates with **CNS disease:** despite the rarity of neonatal HSV encephalitis, it is established clinical practice to test CSF for HSV PCR when CNS infection is suspected on clinical ground. However, it is worth stressing that, in case of query neonatal HSV encephalitis, it is NECESSARY to collect not only CSF but also EDTA blood and surface swabs, as listed above.

3. Selecting HSV testing in **septic neonates** is more complex, as bacterial and fungal causes are much more common and, in addition, other viruses such as enteroviruses, parechoviruses and adenoviruses can present similarly (with enteroviruses causing neonatal sepsis, or meningitis, more commonly than HSV). As a consequence, whilst septic neonates are always tested for bacterial and fungal infections and treated empirically with antibiotics, consideration for HSV testing may arise only later, due to lack of response to antibiotic or antifungal treatments; at this stage it may be too late to secure a good clinical outcome.
Whilst routine empirical ACV in any neonates with query sepsis is not warranted, HSV testing should be considered, especially in neonates who are haemodynamically unstable, requiring fluid boluses, or with deranged LFTs / clotting. Of course, in order to be helpful in the management of NH, a disease that often progresses rapidly, the turnaround time for the test result should be short (i.e. hours). Please arrange urgent testing by directly contacting the laboratory on ext. 6342/8760/5101.

APPENDIX E

TREATMENT OF NEONATAL HERPES

1. **POST-EXPOSURE PROPHYLAXIS WITH IV ACV 20 MG/KG THREE TIMES PER DAY (TDS)**
Asymptomatic high-risk neonates exposed to HSV at birth: complete a 10 day-course.

2. **TREATMENT OF CONFIRMED NH WITH IV ACV 20 MG/KG THREE TIMES PER DAY (TDS)**
Always monitor FBC twice weekly while on ACV therapy

A. **HSV INFECTION** (Pre-emptive treatment): 10 day-course.
B. **SEM disease**: 2 weeks
C. **Disseminated disease**: 3 weeks
D. **CNS disease or disseminated disease with CNS involvement**: 3 weeks. Repeat LP at day 21 and continue high-dose IV ACV for a further week if HSV DNA is still detectable. A further LP should be performed on a weekly basis until the CSF is negative for HSV DNA. At this point treatment can be stopped

3. **EMPIRICAL ACICLOVIR TREATMENT WITH IV ACV 20 MG/KG THREE TIMES PER DAY (TDS)**
NH is a severe disease often non-specific in its presentation. While the implementation of empirical antiviral treatment may be justified by the fact that delayed receipt of ACV treatment is associated with higher morbidity and mortality, NH remains a rare disease. Therefore, empirical ACV in any neonates with query sepsis is not warranted. EMPIRICAL IV ACV TREATMENT should be considered when the neonate is significantly unwell at admission, or deteriorates quickly (hours) and whenever risk factors for NH have been identified. In particular:

a. Infants aged < 6 weeks (more commonly < 2 weeks) presenting with vesicles (skin)/ulcers (mouth, eye), conjunctivitis
b. respiratory distress, lethargy, septic picture (haemodynamic instability requiring fluid resuscitation, **marked deranged serum ALT** and clotting), and/or abnormal CSF indices, signs of CNS disease (including seizures).
c. The index of suspicion should be higher in presence of maternal history of GH, PROM, invasive procedures during labour and intra-partum (scalp electrodes), prematurity, caregivers with exposed HSV lesions (ex. cold sore, herpetic whitlow).

Empirical treatment SHOULD BE COUPLED WITH URGENT HSV TESTING → stop IV ACV if the specimens are HSV PCR negative.
It is worth reiterating the fact that empirical ACV is routinely started when HSV encephalitis is in the differential diagnosis. This occurs at any age group, including neonates. Deciding whether empirical ACV is indicated in neonates presenting with query sepsis is more challenging. In our experience at Southampton, these babies present very early in life (1st week), are very sick at admission, deteriorate quickly and have grossly deranged ALT values at admission or within a few hours post admission (hepatotropism of HSV).

4. **HSV SUPPRESSIVE TREATMENT IN INFANTS SURVIVING NH WITH CNS INVOLVEMENT WITH ORAL ACV 300 mg per m^2 TDS for 6 months**

- Infants surviving neonatal HSV disease with CNS involvement have improved neurodevelopmental outcomes when they receive oral ACV suppressive therapy after the completion of the IV treatment. There are no controlled data that suggest that oral suppressive therapy administered for longer than 6 months or with higher doses of ACV is beneficial.
- As suppressive ACV for 6 months also helps to prevent skin recurrences, its implementation is also recommended following disseminated and SEM disease, as the recurrence risk does seem to be reasonably common. However, ACV suppressive treatment following disseminated (with no CNS involvement) and SEM disease has to be balanced against potential side effects of ACV. This should be a point of discussion with the family.
- Dosage should be weight adjusted monthly.
- Neutrophil count should be obtained every 2 weeks for the 1st month and monthly thereafter. Although most cases of neutropenia are transient, consider dose reduction to 50% and GCSF administration.
- Discontinue ACV if neutrophil count remains < 500 despite dose reduction and GCSF.

APPENDIX F

VIROLOGICAL AND CLINICAL CLASSIFICATION OF GENITAL HERPES (GH)

VIROLOGICAL

1. **PRIMARY INFECTION:** 1st infection with HSV-1 (more often acquired orally) or HSV-2 in the absence of both HSV-1 and HSV-2 type specific antibodies.
2. **NON-PRIMARY INFECTION:** newly acquired HSV-1 or HSV-2 infection in individual previously seropositve to the other viral type.
3. **REACTIVATION**: after infection HSV becomes latent in sensory ganglia; reactivation of GH is the detection of same type of virus from genital lesions.

CLINICAL

1. **FIRST CLINICAL EPISODE**: it may represent **a) primary infection**, **b) non-primary infection** or **c) reactivation after a previous asymptomatic infection**. It is not possible to clinically distinguish between a),b) and c).
2. **RECURRENT CLINICAL EPISODE:** due to reactivation of HSV; normally less severe and of shorter duration compared to 1st clinical episode. It is the most common form of GH during pregnancy. Recurrence rates vary greatly, but are more frequent, and with a shorter time to first recurrence, after more severe primary infection. HSV-2 infections recurs more frequently compared to HSV-1.
3. **ASYMPTOMATIC INFECTION:** detection of HSV-1 or -2 DNA in the absence of genital lesions or evidence of antibody to HSV-2 (predominantly a genital strain) in a person with no previous history and no signs or symptoms of HSV infection. Asymptomatic infection can be **primary**, **non-primary** or **recurrent**

CLINICAL CLASSIFICATION OF NEONATAL HERPES (NH)

Peri-partum and post-natal acquisition

a. **HSV INFECTION (17%):** HSV DNA is detected in **surface swabs** (rectal, oro-pharynx, eye) **+/- in blood**, in the absence of any signs of disease, including skin lesions. Serum ALT values and CSF (cell count, chemistry) are normal. CSF HSV PCR is negative. Neonatal HSV infection is normally missed, as asymptomatic infants are not normally tested.

b. **HSV DISEASE (83%):** the virus produces clinical signs of illness.
   - **b1. Skin, eye and mucosal (Skin, Eye & Mouth or SEM) disease** (45% of NH)**:** as HSV infection, but with skin or mucosal HSV lesions (vesicles, ulcers, keratoconjunctivitis) +/- fever and poor feeding
   - **b2. CNS disease** (30% of NH): presence of HSV DNA in CSF, and/or raised CSF indices, are sufficient to define HSV CNS disease.
   - **b3. Disseminated disease** (25% of NH): raised serum ALT values 2 times upper normal limits (HSV hepatitis), sepsis-like picture with multiple organ involvement (notably the liver and the lungs) +/- coagulation disorders, in babies with HSV DNA detected in surface swabs, blood, +/- CSF. The presence of HSV DNA in blood, per se, does not indicate disseminated disease, as all clinical categories of HSV-1 infection and disease can have detectable DNAemia.

In-utero acquisition **(congenital infection):** the neonates are symptomatic at birth or within the first 48 hours of life.

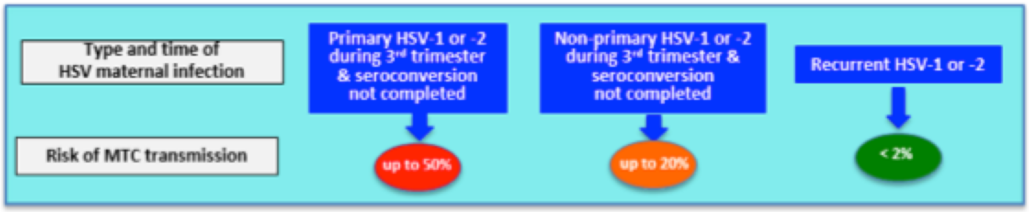
APPENDIX G

TIMING AND ROUTES OF HSV INFECTION IN NEONATES

- **85%** of neonatal infections occur **peri-partum (perinatally)**, via direct contact with infected birth canal secretions during birth. Between 0.2 & 0.4 % of all pregnant women shed HSV in the genital tract around the time of delivery, irrespective of prior HSV history. The incidence increases to 0.8 - 1.4% in women with history of recurrent GH.
- **10%** of neonates acquire HSV infection **after birth** (almost always HSV-1), usually from non-genital lesions (ex. cold sore, herpetic whitlow) from mum or other caregivers and family members.
- **5%** acquire HSV infection **in-utero**, transplacentally or via the ascending route (described even in the absence of rupture of membranes).

RISKS FACTORS FOR MOTHER-TO-CHILD-TRANSMISSION (MTCT) OF HSV.

a) type of maternal infection (primary/non-primary higher risk than recurrent)
b) maternal HSV seronegative status or inefficient transplacental transmission of maternal IgG due to prematurity (< 28 weeks gestation)
c) duration of rupture of **membranes (ROM)**
d) loss of integrity of mucocutaneous barriers in fetus/neonate (e.g., use of fetal scalp electrodes)
e) mode of delivery (Caesarean section versus vaginal delivery)



HIGH RISK: mother is HSV antibody negative (primary infection) or antibody positive for the the HSV type that has not been detected in the genital lesions (non-primary infection).
LOW RISK: mother is antibody positive for the same HSV type detected in genital lesions (recurrent infection).

60% - 80% of women who deliver HSV-infected infants have asymptomatic GH at delivery and have neither a past history of GH, nor a sexual partner reporting a history of GH.
Between 0.2 and 0.4 of all pregnant women shed HSV in the genital tract at delivery irrespective of prior history of GH. Incidence increases to 0.8 - 1.4% in women with history of recurrent GH.

APPENDIX H

DIAGNOSTIC TESTS: HSV PCR and HSV-type specific serology.

- **HSV PCR**: very sensitive and specific diagnostic investigation based on the amplification of conserved regions of the HSV DNA; it can be performed on surface swabs, CSF and EDTA blood. Surface swabs from asymptomatic newborns delivered vaginally should be collected 12-24 hours after birth to avoid HSV neonatal skin/mucosal contamination from maternal genital tract secretions (see page 4).
- **HSV type specific serology**: detects serum IgG to the HSV-1 or -2 type specific glycoproteins (glycoproteins G-1 and G-2 respectively; i.e. it can distinguish between HSV-1 and HSV-2 infections), markers of type specific protection.
- The level of cross protection between HSV-1 and -2 from non-type specific antibodies is not significant.
- HSV type specific serology in pregnant women is useful to assess risk of mother to child transmission (MTCT). **Transplacentally acquired type-specific IgG** are protective for the newborn infant, as they prevent the hematogenous spread of the virus. However, they cannot prevent HSV transmission to the brain via the axonic route.
- Time to type-specific seroconversion varies between individuals: 60-80% of individuals newly infected with HSV-2 complete seroconversion in 6-8 weeks; however, 7–27% had not seroconverted by 3 months. Repeat testing at 8–12 weeks is appropriate to confirm or rule out seroconversion. When test performed in neonates, presence of HSV antibodies normally indicates transplacental transfer of maternal antibodies and not neonatal infection. Effective transplacental transfer occurs after the 28th week of pregnancy.
- **HSV type specific serology:** can be performed on **maternal blood (can be performed on stored antenatal booking blood)** to ascertain maternal serostatus and on **neonatal samples** to inform on efficiency of transplacental transfer of maternal antibodies. Turnaround time: 45 minutes from sample receipt during routine laboratory working hours (Mondays to Fridays 9 am to 4.15 pm and Saturday morning 9 am to 11.15 am).

Appendix I

Paediatric Regional Guideline Consultation Documentation:

Trust	Name of person consulted* (print)	Designation of signatory[$]	Signature
Chichester			
Dorchester	Will Verling		
Hampshire Hospitals Foundation Trust	Ayo Kadri Katie Yallop		
Poole	Steve Wadams		
Portsmouth	Amanda Freeman		
Salisbury	Nick Brown		
Southampton	Sanjay Patel		
IOW	Arun Gulati		

* this person agrees they have read the guidelines, consulted with relevant colleagues and members of MDT, managers and patients, young people & their families as appropriate. Any queries raised during consultation and review process should be documented with responses and any changes made to guideline.

[$] this can be electronic for ease