LRI Children's Hospital

UHL Children's Hospital Neonatal Sepsis Guideline

Staff relevant to:	This guideline is relevant to all medical and nursing staff employed by UHL, including bank, agency and locum staff.
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Written by:	E Artley
Trust Ref:	D5/2022

Contents

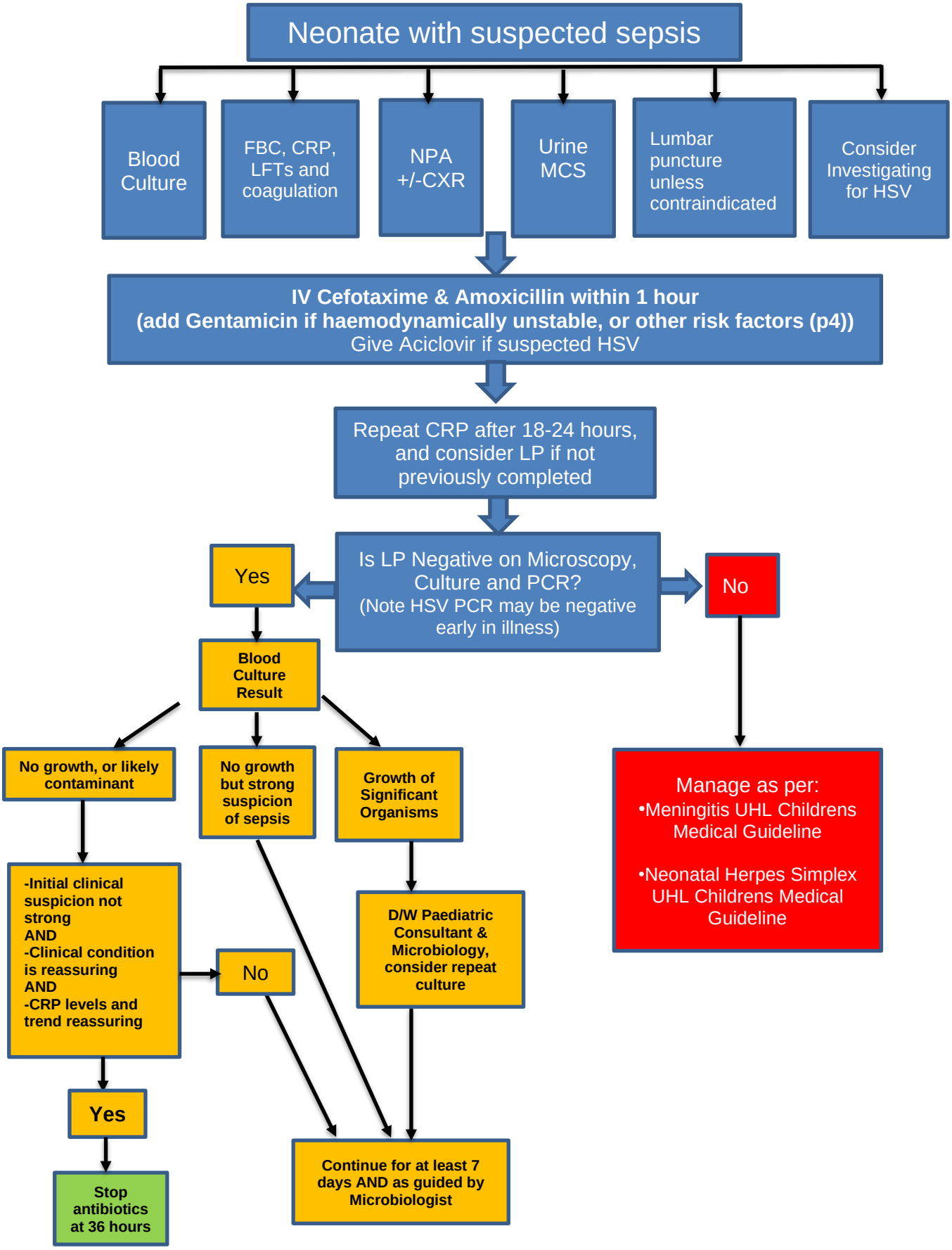
1. Introduction and Who Guideline applies to

- This guideline is relevant to all medical and nursing staff employed by UHL, including bank, agency and locum staff.
- **NB – a 'neonate' is any term baby presenting at <28 days old, a preterm infant is considered a 'neonate' until 44/40 corrected gestational age**
- This guideline applies to all neonates presenting to UHL as acute admissions or as existing inpatients, including the Paediatric Emergency Department (PED)
- This guideline does NOT apply to neonates within the UHL Maternity Services (Labour Ward, Neonatal Units, Post Natal Ward)
- **If babies have been transferred to the Children's Hospital direct from the Neonatal unit, please follow the NNU guideline**

Related UHL Documents:

- Sepsis UHL Childrens Hospital Guideline Trust Ref B31/2016
- Neonatal Herpes Simplex UHL Childrens Medical Guideline Trust ref:C1/2014
- Meningitis UHL Childrens Medical Guideline Trust ref:C22/2014
- Antibiotic Guideline for Early-Onset and Late-Onset Neonatal Infection Trust Ref C38/2015
- Fluid Electrolyte Management UHL Childrens Hospital Guideline Trust ref:C6/2015
- Ophthalmia Neonatorum (neonatal conjunctivitis) UHL Childrens Hospital Guideline Trust Ref D2/2021
- Lumbar Puncture UHL Childrens Hospital Guideline Trust ref: C82/2007
- Central Line Infection UHL Childrens Hospital Guideline Trust ref: C12/2019

Investigations and Antibiotics flow chart


Neonate with suspected sepsis
Blood Culture
FBC, CRP, LFTs and coagulation
NPA +/-CXR
Urine MCS
Lumbar puncture unless contraindicated
Consider Investigating for HSV
IV Cefotaxime & Amoxicillin within 1 hour
(add Gentamicin if haemodynamically unstable, or other risk factors (p4))
Give Aciclovir if suspected HSV
Repeat CRP after 18-24 hours, and consider LP if not previously completed
Is LP Negative on Microscopy, Culture and PCR?
(Note HSV PCR may be negative early in illness)
Yes
No
Blood Culture Result
No growth, or likely contaminant
No growth but strong suspicion of sepsis
Growth of Significant Organisms
Manage as per:
•Meningitis UHL Childrens Medical Guideline
•Neonatal Herpes Simplex UHL Childrens Medical Guideline
-Initial clinical suspicion not strong
AND
-Clinical condition is reassuring
AND
-CRP levels and trend reassuring
No
D/W Paediatric Consultant & Microbiology, consider repeat culture
Yes
Stop antibiotics at 36 hours
Continue for at least 7 days AND as guided by Microbiologist

Sepsis < 1 Month age
Dosing and Administration information 1/2

Version 3
UHL AWG 2022
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Authors: JT, DH, TA, RR

Amoxicillin

Dose	Frequency	Administration
50mg/kg/dose IV	**12 hourly (under 7 days old)** **8 hourly (over 7 days old)**	250mg vial add 4.8ml water for injection (50mg/ml) **IVI over 30 minutes** Flush with 0.9% sodium chloride

** Consider 100mg/kg/dose for Listeria meningitis

CefoTAXime

Dose	Frequency	Administration
50mg/kg/dose IV	**12 hourly (under 7 days old)** **8 hrly (7 to 20 days old)** **6 hrly (over 20 days old)**	500mg vial add 1.8ml water for injection (250mg/ml) **IV bolus over 3 - 5 minutes** Flush with 0.9% sodium chloride

*** Ceftriaxone may be used as an alternative to cefotaxime once clinical recovery is evident, but ceftriaxone should **not** be used in premature babies or in babies with jaundice, acidosis or hypoalbuminaemia.

*** Always prescribe 1st dose in once only/stat section on front of prescription chart**

Page 1 of 2 for Sepsis < 1 Month age recommendations

Sepsis < 1 Month age

Dosing and Administration information 2/2

Version 3
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Gentamicin

ONLY for the following indications:

1. Haemodynamic instability
   - E.g., Raised lactate / inotrope requirement / > 40 ml/kg fluid resuscitation / ICU care
2. Concern / high risk for multi-drug resistant organisms
   - Risk factors: Frequent hospitalisations / Previous NICU or ICU admission / Previous treatment for NEC / Recent foreign travel/hospitalisation
   - Previous known multi-resistant gram-negative organisms – to discuss with microbiology if empiric treatment needs to be adjusted esp. if cefotaxime and/or gentamicin resistant

Post Conceptional age	Dose	Frequency	Administration
< 34 weeks CGA	Use NNU dosing		Slow bolus (over 3 - 5 minutes) Plan to measure levels pre & post third dose
≥ 34 to < 38 weeks CGA	5 mg/kg	36 hourly	
≥ 38 weeks CGA, up to 7 days old	5 mg/kg	36 hourly	
≥ 38 weeks CGA. 7 – 28 days old	5 mg/kg	24 hourly	

Refer to prescription chart for further information

Aciclovir

Indicated for Concerns for Herpes Simplex Virus (HSV) infection

- Risk factors: Maternal HSV or cold sores / peri partum fever or PROM / Scalp electrode monitoring / History of contact / Cutaneous vesicles and/or mucosal ulcers / Seizures – particularly focal seizures / Elevated transaminases

Dose	Frequency	Administration
20mg/kg/dose IV	**8 hourly**	250mg vial add 25ml water for injection (25mg/ml) **IVI over 60 minutes** Flush with 0.9% sodium chloride

*** Always prescribe 1st dose in once only/stat section on front of prescription chart**

Page 2 of 2 for Sepsis < 1 Month age recommendations

2. Guideline Standards and Procedures

- **Sepsis** is a life threatening illness caused by the body's response to infection.
- Neonates can present critically unwell for a range of different reasons (see fig 1), but sepsis is still the most common cause.
- Causative pathogens for sepsis in neonates are different from those for older children. As well as bacterial causes, consider the risk of viral (especially HSV) and fungal infection.
- The use of antibiotics in the treatment of suspected neonatal sepsis will result in the treatment of neonates without bacterial infection. It is important to review the continued need for antibiotics and whether treatment tailoring is required.

2.1 Diagnosis

Fig 1 Other Differential Diagnoses to consider in a critically unwell neonate

Other Differential Diagnoses to consider in a critically unwell neonate
• Cardiac abnormalities • Endocrine crisis • Electrolyte imbalance • Trauma – accidental or non-accidental

Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs without delay. These are risk factors (see fig 2) and clinical indicators (see fig 3) to note – **sepsis can be present without risk factors.**

Fig 2 History & Risk Factors of possible neonatal sepsis

History & Risk Factors of possible neonatal sepsis
• Sibling of multiple pregnancy treated for sepsis • Preterm or ex-preterm infant born < 37 weeks gestation • Prolonged rupture of membranes (>24 hours) • Maternal infection/fever post-partum • Previous NNU admission

Fig 3 Clinical indicators of possible neonatal sepsis

Clinical indicators of possible neonatal sepsis	
Behaviour	Parents or care-giver concern for change in behaviour Appears ill to a healthcare professional Does not wake, or if roused does not stay awake Weak high-pitched or continuous cry
Respiratory	Raised respiratory rate ≥ 60/min Grunting Apnoea Oxygen saturation <90% in air or increased oxygen requirement over baseline
Circulation and hydration	Persistent tachycardia: HR ≥160/min Persistent bradycardia: HR <100/min
Skin	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin
Other	Temperature ≥38˚C unexplained by environmental factors Temperature <36˚C unexplained by environmental factors Alterations in feeding pattern Abdominal distension Seizures Bulging fontanelle Conjunctivitis*

*Neonates presenting with conjunctivitis or **Ophthalmia Neonatorum** may or may not have systemic disease, please refer to our hospital guideline for therapy:

Ophthalmia Neonatorum (neonatal conjunctivitis) UHL Childrens Hospital Guideline Trust Ref D2/2021

Intravenous antibiotic therapy should be started as soon as possible and always **within the first hour** of the decision to treat, after appropriate cultures and investigations have been taken – **this should not delay treatment.**

2.2 Investigations for suspected neonatal sepsis

Before administering the first dose of antibiotics include:-

- **Blood Culture**
- **Full blood count (FBC)**, **C-reactive protein (CRP**) (repeat 18-24 hours), **Liver Function Tests (LFTs)** and **Coagulation**
- **Lumbar puncture** unless contraindicated (see Lumbar Puncture guideline) this is important in diagnosing meningitis, encephalitis or HSV infection. Contact the microbiology technician to arrange urgent investigation – see Appendix A for microscopy ranges
- **Urine culture** – catheter sample or SPA

The following can be performed after antibiotic administration: -

- **NPA**
- **CXR** only if clinical signs suggestive of pneumonia
- **EDTA blood HSV PCR** if there is a strong clinical suspicion of HSV as well as
- **Skin & mucous swabs for HSV PCR**

Please refer to **Flow Chart on page 2** for further guidance for investigation timeline

2.3 Antibiotics & Antivirals for Suspected Neonatal Sepsis

Neonates presenting from the community a given a double antibiotic regimen as follows:

1. **Cefotaxime** – a third generation cephalosporin to cover common community acquired bacteria such as Neisseria meningitidis, Streptococcus pneumoniae, Escherichia coli, Staphylococcus aureus and Haemophilus influenzae
2. **Amoxicillin** – to cover against Listeria

Gentamicin – is considered good cover for neonatal period gram negative bacteria – it is to be added in event of haemodynamic instability, or in event of concerns of multi drug resistant gram negative organism sepsis, consider in particular for the following risk factors:

- Haemodynamic instability (particularly if needing inotropes/ICU care)
- Frequent hospitalisations
- Previous NICU/ICU stay – (consider possible CVL infection - D/W microbiology)
- Recent foreign travel/hospitalisation
- Previous known multi resistant gram negative organisms – to discuss with microbiology if empiric treatment need to be adjusted esp cefotaxime and/or gent resistant.

Metronidazole – only if concerns of intra-abdominal sepsis e.g. NEC.

All antimicrobials should be reviewed daily. Microbiology authorisation code is required beyond recommended antibiotic duration.

Table 1: Antibiotic choice and duration for specific organism bacteraemias
(Please see meningitis guideline if meningitis diagnosed, as durations may differ)

Organism	Minimum duration	Antibiotic of choice (if susceptible)
Group B strep bacteraemia	10 days	IV benzylpenicillin
Strep pneumoniae bacteraemia	10 days	IV cefotaxime/ceftriaxone, may be changed to an oral agent when improved
E coli (or other gram negative) bactaeramia without meningitis	10 days	IV cefotaxime/ceftriaxone, may be changed to an oral agent when improved
Listeria bacteraemia/meningitis	14-21 days	IV amoxicillin (+gent for 7 days)
Staph aureus (MSSA) bacteraemia	14 days	IV flucloxacillin, may be changed to oral when improved
MRSA bacteraemia	14 days	IV vancomycin
Haemophilus influenzae bacteraemia	10 days	IV cefotaxime/ceftriaxone, may be changed to an oral agent when improved

Follow guidance on timing of gentamicin assays and dosing provided in the IV monographs and pre-printed charts.

Audiology assessment at 8 months is arranged for infants identified to have high gentamicin levels (pre dose greater than 2mg/l and/or post dose greater than 12mg/l)

Aciclovir is an antiviral medication used primarily in the treatment of Herpes Simplex infections, an important consideration in an acutely unwell neonate.

- **Please ensure blood EDTA for HSV PCR has been taken prior to treatment + skin swab** – if it is safe to do so please ensure CSF for HSV PCR has also been taken

The dosing regimen is explained on pages 3-4**.**

For information on contraindications, cautions, drug interactions and adverse effects refer to the British National Formulary for children or the drug Summary of Product Characteristics.

2.4 Neonatal Herpes Simplex (HSV) infection

Neonatal HSV infection is an important consideration in neonates with suspected sepsis.

ALT levels are elevated with disseminated HSV disease and severe sepsis.

Fig 4 HSV risk factors

HSV risk factors *NB. These may not be present in all cases
Maternal: • Maternal history of current or past HSV infections (including cold sores) • Maternal peri partum fever • History of prolonged rupture of membranes **Neonatal**: • History of contact • Scalp electrode monitoring • Cutaneous vesicles and/or mucosal ulcers • Seizures – particularly focal seizures • Elevated transaminases

Neonatal HSV may be very non-specific and subtle. It can mimic bacterial and viral illness such as enterovirus infection. Always think of HSV infection in neonates with mucocutaneous lesions, CNS abnormalities or sepsis-like picture. If left untreated, mortality rate of disseminated disease and CNS disease are 85% and 50% respectively.

Please refer to our Neonatal HSV guideline for further information. Neonatal Herpes Simplex UHL Childrens Medical Guideline

2.5 Feeding & IV fluids during treatment for Neonatal Sepsis

Neonates are very susceptible to fluctuation in their hydration status; every effort should be made to ensure that enteral feeding is supported as intravenous fluid administration should be the last resort.

In the event of inadequate feeds taken orally via breast or bottle, NG feeds should be the next consideration.

Breastfeeding mothers should be encouraged to express milk for NG feeds if required.

In the event of IV fluid administration, please refer to the Fluid Electrolyte Management UHL Hospital Guideline.

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements

5. Supporting References

NICE NG195 Neonatal infection: antibiotics for prevention and treatment [published: April 2021]

UK Paediatric Antimicrobial Stewardship. Antimicrobial paediatric summary for hospitals. Available: https://uk-pas.co.uk/Antimicrobial-Paediatric-Summary-UKPAS.pdf [issued: February 2022]

6. Key Words

Antibiotics, Antivirals, Lumbar puncture

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Ruth Radcliffe - Consultant Edward Artley – Specialist Trainee	**Executive Lead** Chief Medical Officer
Details of Changes made during review: New guideline	

Appendix A – Normal CSF Values (Mean and Range)

Type of Infant	WBC / mm3	Protein (g/l)	Glucose (mmol/l)
Preterm < 28 days	9 (0-30)	1 (0.5-2.5)*	3 (1.5-5.5)
Term < 28 days	6 (0-21)	0.6 (0.3-2.0)*	3 (1.5-5.5)

- Protein values are higher in the first week of life and depend on the red cell count. A white cell count of more than 21/mm3 with a protein value of more than 1 g/l with less than 1000 red cells is suspicious of meningitis.

- Plasma glucose should be taken immediately prior to the LP. CSF glucose is usually 70-80% of plasma glucose (normal). A low CSF glucose can persist for many weeks following IVH. If CSF results are suspicious then always consider a repeat LP in next 12-24 hours (discuss with Consultant).