

Empirical Antibiotic Guideline for Neonates

A clinical guideline recommended for use:

In	JPUH NHS Foundation Trust
By	All medical and non-medical staff involved in the management of infections in neonates
For	Neonates with sepsis
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Key Points

- Babies with any red flag indicators or 2 or more risk factors / clinical indicators should be treated with antibiotics
- Treat within 1 hour of decision to treat
- Blood cultures should be taken prior to commencing antibiotics
- If CRP 10-20 discuss with consultant re: need for lumbar puncture
- Repeat CRP 18- 24 hours after commencing treatment
- Consider lumbar puncture in all late onset infection

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1. Introduction

- 1.1 This guideline sets out the local agreement on antibiotic use for the management of suspected or confirmed sepsis and other neonatal infections
- 1.2 It has been developed in agreement with local microbiologists, infection control, neonatal staff and a pharmacist.
- 1.3 This guideline is designed to be used in conjunction with and not as a replacement for clinical assessment of the baby where decisions are made about the management of suspected and confirmed sepsis.
- 1.4 This guideline should be read in conjunction with the NICE guideline CG149

2. Purpose and scope of the Document

- 2.1 Mortality and morbidity from neonatal sepsis remain significant, with early recognition and treatment likely to improve outcomes. As symptoms and signs of sepsis can be subtle, empirical antibiotic treatment should be started in any neonate who is unwell and in some cases for infants with significant risk factors.
- 2.2 Scope
 - 2.2.1 All newborn infants in the Maternity Unit to include Delivery Suite, Maternity Inpatients, Transitional Care and Neonatal Unit.
 - 2.2.2 All staff managing such infants.

3. Key Principles

- 3.1 Parents should be fully informed of the indications for antibiotics with appropriate provision of information and reassurance.
- 3.2 Babies with suspected neonatal infection should be treated as quickly as possible.
- 3.3 Antibiotic exposure should be minimized in babies who do not have an early-onset neonatal infection to avoid the development of resistance to antibiotics.

4. Audit Standards

- 4.1 100 % of babies should have a blood culture taken before starting antibiotics.
- 4.2 100% of babies should have their C-Reactive Protein (CRP) checked at 18- 24 hours following commencement of antibiotic treatment.
- 4.3 Antibiotics should be given within 1 hour of decision to treat.

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5. Indications for starting antibiotics (see appendix 1 for antibiotic regime)

- RED FLAGS – Investigations and Antibiotics must be started
- 2 or more Risk factors / Clinical indicators – perform investigations and start antibiotics
- No red flags and only 1 risk factor or clinical indicator – use clinical judgement.

5.1 RED FLAGS – Antibiotics must be started

- **Maternal infection.** Parenteral antibiotic treatment of the woman for invasive bacterial infection (such as septicaemia) during labour, or < 24-hour before and after the birth [This does not refer to intrapartum antibiotic prophylaxis]
- **Infection in sibling.** Suspected or confirmed infection in another baby in the case of a multiple pregnancy
- **Respiratory Distress** starting or persisting more than 4 hours after birth
- **Seizures**
- **Ventilation.** Need for mechanical ventilation in a term baby
- **Shock.** Signs of shock

5.2 Risk factors for sepsis:

- Invasive group B Streptococcal infection in a previous baby
- Maternal group B Streptococcal colonisation, bacteriuria or infection in the current pregnancy
- Rupture of membranes > 18 hours
- Preterm birth following spontaneous labour < 37 weeks' gestation
- Intrapartum fever higher than 38 °C
- Chorioamnionitis

5.3 Clinical indicators of sepsis:

- Altered behaviour, responsiveness
- Altered muscle tone (for example, floppiness)
- Feeding difficulties (for example feed refusal)
- Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension
- Signs of respiratory distress
- Hypoxia
- Jaundice within 24 hours of birth
- Apnoea
- Signs of neonatal encephalopathy
- Need for cardio–pulmonary resuscitation
- Need for mechanical ventilation in a preterm baby
- Persistent fetal circulation (persistent pulmonary hypertension)
- Temperature instability (< 36 °C or > 38 °C) unexplained by environmental factors
- Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation (International Normalised Ratio greater than 2.0)
- Oliguria persisting beyond 24 hours after birth

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- Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)
- Metabolic acidosis (base deficit of 10mmol/l or greater)
- Local signs of infection (for example, affecting the skin or eye)

5.4 Remember

- 5.4.1 The clinical opinion of an experienced neonatal nurse/midwife should be taken very seriously as should parental concerns about their own infant's condition.
- 5.4.2 A baby with respiratory symptoms persisting 4 hours after birth should be treated with antibiotics even if felt likely to be due to surfactant deficiency or retained lung fluid. Sepsis may be contributing or may be the primary cause, even if there are no known risk factors.
- 5.4.3 Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs.
- 5.4.4 Do not delay starting antibiotics; these should be administered within an hour of the decision to treat.
- 5.4.5 When using clinical judgment, consider whether it is safe to withhold antibiotics, and whether it is necessary to monitor the baby's vital signs and clinical condition – if monitoring is required continue it for at least 12 hours (at 0, 1 and 2 hours and then 2-hourly for 10 hours).
- 5.4.6 Regularly reassess the clinical condition and results of investigations in babies receiving antibiotics. Consider whether to change the antibiotic regimen taking account of:
- the baby's clinical condition (for example, if there is no improvement)
 - the results of microbiological investigations
 - expert microbiological advice, taking account of local surveillance data

6. Investigations

- 6.1 Initial investigations:
- Blood Culture
 - CRP, Full Blood Count (FBC)
 - Repeat CRP 18-24 hours after presentation
- 6.2 Lumbar puncture
- 6.2.1 Lumbar puncture (LP) if:
- Strong clinical suspicion of infection
 - Clinical symptoms or signs of meningitis.
 - C-reactive protein >20 mg/litre
 - Positive blood culture
 - Poor response to antibiotic treatment
 - Consider in all suspected late onset sepsis

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- 6.2.2 Babies with an initial or repeat CRP between 10 -20 mg/litre should be discussed with a Consultant Paediatrician and the need to perform an LP considered taking into account the overall clinical picture. Decisions should be clearly documented in the baby's notes.
(Consultant discussion and lumbar punctures need not be done overnight and may be within normal day shift if the baby is asymptomatic of meningitis)
- 6.2.3 If performing the lumbar puncture would unduly delay starting antibiotics, perform it as soon as possible after starting antibiotics.
- 6.2.4 Inability to obtain CSF sample should not delay treatment. CSF for PCR diagnostics may be an option.
- 6.2.5 Do not perform lumbar puncture if platelets $< 50 \times 10^9/l$. Consider correction prior to procedure being undertaken.
- 6.3 Decision for treatment and management should not be based on CRP levels alone. Consider white cell count (high and low significant) and broader clinical picture.
- 6.4 If Gentamicin used, assess renal function and levels as per EOE guideline
- 6.5 If chorioamnionitis suspected, placenta should be sent for histological examination and culture

7. Other Investigations

- Urine microscopy and culture – may be useful in late onset sepsis.
- Eye Swab - swab discharge for culture. Consider Chlamydia and Gonococcus. Start systemic antibiotic treatment for possible Gonococcal infection.
- Chest X-ray if respiratory symptoms.
- Surface swabs if appropriate.
- If Herpes Simplex Suspected. EDTA blood, LP, Surface skin swabs, HSV PCR

8. Information and support

- 8.1 Inform parents of concerns.
- 8.2 Explain rationale for treatment and nature of neonatal infection.
- 8.3 Discuss management options including risks and benefits.
- 8.4 Discuss observations and investigations to include where the baby will be cared for.
- 8.5 Inform parents on discharge, if any further concerns who to contact.
- 8.6 Reassure re long term effects and answer questions honestly.
- 8.7 Inform GP / Health visitor on discharge.

9. Stopping Antibiotics

- 9.1 Consider stopping antibiotics at 48 hours if:
- Blood culture negative AND
 - No strong clinical indication for infection
 - Clinical condition of baby is good
 - CRP levels / trend reducing

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9.2 Continue antibiotics if:

- Positive culture, discuss length of treatment with microbiologist
- Significant rise in CRP
- Strong suspicion of sepsis with negative culture – minimum 5 days antibiotics
- Meningitis –14 to 21 days. Always discuss with microbiologist. Check viral PCR on CSF if no bacterial growth. Lumbar puncture may be repeated prior to stopping antibiotics

10. Central lines

Consider:

- 10.1 Removal in suspected central line infection and send tip for culture.
- 10.2 Exceptional circumstances (difficult access) consider leaving the line in situ and treating with vancomycin administered via the long line if left in-situ.
- 10.3 Removal in any septic infant who fails to improve.
- 10.4 Removal in presence of culture positive sepsis.
- 10.5 Repeated bacteraemia related to line sepsis.
- 10.6 Administer vancomycin for suspected or proven Coagulase negative Staphylococcus in the presence of a long line (via the long line).
- 10.7 Fungal sepsis with long line in situ. Remove long line and treat for 2 weeks with anti-fungal agents .Always discuss with microbiologist

11. Parent Information

- 11.1 If considering antibiotic treatment because of clinical concerns about possible early-onset neonatal infection, discussions with parents should include:
 - the rationale for the treatment
 - the risks and benefits in the individual circumstances
 - the observations and investigations that may be needed to guide clinical management (for example, when to stop treatment)
 - the preferred antibiotic regimen and likely duration of treatment
 - the impact, if any, on where the woman or her baby will be cared for
 - potential long-term effects of the baby's illness and likely patterns of recovery
 - Provide reassurance if no problems are anticipated

12. Endorsement

- 12.1 This guideline will be approved by the Paediatricians and Antimicrobial Management Group

13. Distribution

- 13.1 Available on the Trust intranet site

14. References

- 14.1 National Institute for Health and Clinical Excellence, (NICE), (2012), Clinical Guideline 149, Antibiotics for Early Onset Infection, Available from:

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<http://www.nice.org.uk/nicemedia/live/13867/60633/60633.pdf> [Accessed 4th March 2014]

14.2 East of England Perinatal Networks, 2013, Neonatal Antibiotic Guideline

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Appendix 1

ANTIBIOTIC REGIME

ANTIBIOTICS SHOULD BE GIVEN WITHIN AN HOUR OF DECISION TO TREAT

Indication	Drug Dose and Route	Route	Dose Interval	Notes
		Age		
<p>SEPSIS First Line MRSA Negative</p>	<p>AMOXICILLIN 50 mg / kg / dose</p> <p>+</p> <p>CEFOTAXIME 50 mg / kg / dose</p>	<p>Intravenous</p> <p>< 7 days 12 hourly</p> <p>7-28 days 8 hourly</p> <p>> 1 month 6 hourly</p>	<p>< 7 days 12 hourly</p> <p>7-21 days 8 hourly</p> <p>21-28 days 6 hourly</p> <p>> 28 days 8-12 hourly (6 hourly in severe infection)</p>	<ul style="list-style-type: none"> • Use Amoxicillin and Cefotaxime as first line antibiotics for suspected infection • Course length dependant on CRP, Culture and suspected site of infection • Well baby and CRP <10 x 2, stop if Negative cultures • If MRSA Positive / Suspected add vancomycin – see SEPSIS 2nd line
<p>NEC For suspected NEC when on 1st or 2nd line antibiotics Add</p> <p>If not already on antibiotics start on Cefotaxime and Metronidazole</p>	<p>METRONIDAZOLE 15mg / kg stat dose IV Followed by 7.5mg / kg</p>	<p><26 weeks <u>corrected</u> gestational age 24 hourly</p> <p>26-34+6 weeks <u>corrected</u> gestational age 12 hourly</p> <p>≥35 weeks <u>corrected</u> gestational age 8 hourly</p>	<p>Increase the dosing interval of Metronidazole in hepatic but not renal failure</p>	

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Indication	Drug Dose and Route	Route	Dose Interval	Notes
		Age		
SEPSIS 2nd Line – Or MRSA positive Or Suspected line sepsis	CEFOTAXIME 50 mg / kg AND VANCOMYCIN 15mg/Kg	Intravenous < 7 days 12 hourly 7-21 days 8 hourly 21-28 days 6 hourly	24 hourly 12 hourly 8 hourly	Course dependant on Consultant and Microbiologist If baby is to remain on vancomycin for more than 7 days. Discuss with microbiologist Adjust dose according to plasma levels
		Intravenous <29 weeks corrected age 29-35 weeks corrected age >35 weeks corrected age		8 hourly

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<p>SEPSIS 3rd line or Suspected Pseudomonas</p>	<p>CEFTAZIDIME 50 mg / kg dose</p> <p>AND</p> <p>VANCOMYCIN15mg/kg</p>	<p>Intravenous < 7 days 24 hourly 7-21 days 12 hourly 21-28 days 8 hourly > 28 days 8 hourly</p> <p>Intravenous <29 weeks corrected age 24 hourly</p> <p>29-35 weeks corrected age 12 hourly</p> <p>>35 weeks corrected age 8 hourly</p>	<p>If Pseudomonas confirmed – Discuss with Paediatric Consultant and Microbiologist</p> <p>If GI involvement add Metronidazole – See NEC</p>
<p>Skin Infection or Umbilical Flare</p>	<p>FLUCLOXACILLIN 50mg / kg dose</p>	<p>Intravenous < 7 days 12 hourly 7-21 days 8 hourly 21-28 days 6 hourly</p>	<p>Consider MRSA status of mother</p>
<p>Confirmed / Suspected Invasive Candidias</p>	<p>FLUCONAZOLE Treatment 12 mg / kg</p>	<p>Intravenous < 2 weeks every 72 hours 2- 4 weeks every 48 hours 1 month - daily</p>	<ul style="list-style-type: none"> • Suspected - Review at day 5 • Confirmed - Treat for 2 weeks • Discuss with Paediatric Consultant and Microbiologist prior to stopping treatment • LP, ECHO and Ophthalmology examination required in cases of confirmed invasive candidiasis

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Prophylactic antifungal	FLUCONAZOLE Prophylactic 3mg / kg	Intravenous < 2 weeks every 72 hours 2- 4 weeks every 48 hours 1 month - daily	Please refer to Joint Trust Guideline for the Use of Antifungal Prophylaxis on the Neonatal Intensive Care Unit
Topical antifungal	MICONAZOLE CREAM	Topically	Apply twice daily for 5 days and review
Oral antifungal	MICONAZOLE ORAL GEL	1ml 2-4 times daily	Smear around mouth after feeds Review day 5
Eye infection	Chloramphenicol Eye Ointment	3-4 times daily	Swab and tailor to susceptibility Treat for 5 days and review

Gentamicin – see EOE Guideline – May be used on the advice of Microbiologist for organism sensitive bacteria or baby transferred to unit on gentamicin

Other antibiotics may be used according to bacteria, microbiology or consultant request