Early onset sepsis in Neonates

This guideline aims to identify well babies who are at risk of sepsis and unwell babies with sepsis. It is important to differentiate between these two groups and remember that most neonates will fall into the former group. If sepsis is subsequently ruled out, the well babies can ideally avoid unnecessary antibiotic courses and be discharged safely.

“RED FLAG” RISK FACTORS for Early Onset Sepsis (NICE guidance)

- Maternal infection 24hrs around labour
- Infection in other baby if multiple pregnancy
- Documented chorioamnionitis
- Maternal GBS colonisation/UTI/infection in current pregnancy with inadequate maternal intrapartum antibiotic prophylaxis (IAP) (<2hrs before delivery)

Neonates who definitely need TESTS and ANTIBIOTICS and OBSERVATIONS

- Any RED FLAG risk factors (see box, above)
- Signs of shock
- Seizures

Neonates who definitely need OBSERVATIONS but not (necessarily) tests or treatment

- All babies started on antibiotics
- Invasive GBS infection in previous baby + adequate IAP (≥2h before birth)
- Maternal GBS colonisation/UTI/infection in current pregnancy + adequate IAP (≥2h before birth)
- PROM >24hrs
- Prematurity (<37 weeks) (not including induced or non-labour / elective C/S)
- Maternal intrapartum fever >38°C (or fever >37.5°C on two consecutive occasions 1 hour apart)
- Required cardiac massage at birth
- Meconium stained liquor
- Jaundice <24hrs (not explained by Rh/ABO incompatibility) (See Jaundice guideline)

Maternal antibiotic treatment (e.g. for pyrexia 37.5°C on two consecutive occasions) does NOT mean the baby automatically needs bloods and antibiotics. A review of the risk factors and clinical examination of the baby is needed.
At least 12 hrs of observations; 0hrs, 1hr, 2hrs and 2hrly for 12 hrs (on neonatal observation chart – including temperature, colour, capillary refill time, HR, RR)

If there is maternal GBS then observations to continue until 24h of age (4hrly from 12-24 hrs)

Abnormal observations → review by doctor within 1 hour

1. **Start antibiotic treatment if:**
   
a) **Risk factor + clinical concern**
   
   2. **Persistent abnormal clinical indicators (2 consecutive readings)**
      
      • signs of respiratory distress >4hours of age
      • hypoxia
      • apnoea
      • tachy/bradycardia
      • temperature instability
      • altered tone/behaviour/responsiveness

2. **Grey areas – discuss with senior colleague**
   
   • ≥ 2 risk factors
   • persistent feed difficulty/intolerance (vomiting, distension, large aspirates)
   • Anuria >24hrs of age
   • persistent hypo/hyper-glycaemia
   • metabolic acidosis (BE > -10) or lactate >2

3. **Maternal GBS colonisation first identified after birth but within 72hrs of life:**
   
   • Check if other risk factors
   • Assess baby – by hospital doctor if inpatient/midwife or GP if community
   • If positive maternal colonisation identified after discharge but within 24h of birth → readmit, assess and consider treatment. (For these cases please discuss with consultant)
   • If abnormal observations/unwell baby → readmit and treat
   • If normal observations/well baby + identified GBS >24h after birth → routine postnatal care and advice for parents

Note that GBS colonisation only in a previous pregnancy is not deemed to be a significant risk factor, provided no other risk factors are present.

<table>
<thead>
<tr>
<th>Antibiotic Choices</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cefotaxime</strong> for post natal ward / SCU babies</td>
</tr>
<tr>
<td><strong>Pen + Gent</strong> for babies admitted Neonatal Unit</td>
</tr>
</tbody>
</table>

If in doubt, discuss with neonatal registrar / consultant
STAGES OF MANAGEMENT OF BABY AT RISK OF EARLY ONSET SEPSIS: TIMELINE

BABY RED FLAG RISK OF SEPSIS or CLINICALLY SEPTIC

0hr

Antibiotics should have been given

1hr

Treatment (Choose and start within ONE hour)

Baby is well
Cefotaxime² twice daily for babies who are remaining on SCU or on the Postnatal Wards

Babies who are unwell should be admitted to the Neonatal Unit and commenced on IV Benzylpenicillin (3) and Gentamicin (4)

Investigation¹
Blood cultures / CRP. (FBC, Clotting +/- LFT if unwell)

18hrs

Baby well no significant clinical concerns

Repeat CRP after 18 hrs

Second CRP ≤10mg/L

Baby well continue Cefotaxime

Second CRP >10mg/L

Clinical review

Repeat CRP after 18 hrs

36hr

DECISION – Can antibiotics be ceased? Clinical Review

At 36 hours
If baby well and observations normal
If both CRPs ≤10 mg/L
If blood cultures negative after 24h incubation =>Stop cefotaxime

Baby unwell or rapid rise in CRP
Admit to Neonatal Unit, change to Pen + Gent

Decide if:
  o Gentamicin to be given 24 hourly or 36 hourly?
  o Dose of Benzylpenicillin sufficient?
  o Further tests (LP, SPA, CXR, bloods needed)?

The key question is: - is this baby at risk of sepsis but not septic, or is the baby septic, regardless of risk?
Notes

(1) **Investigations:** Lumbar Puncture

Perform LP as part of initial investigation if:
- Strong clinical suspicion of septicaemia or severe generalised infection
- Clinical symptoms/signs of meningitis

Consider LP on babies who are on antibiotics and did not have LP as part of initial investigation if:
- CRP >20mg/L or rising quickly
- Positive blood culture
- Unsatisfactory response to antibiotic treatment including - persistent/re-emergent fever, deterioration in clinical condition, persistently abnormal inflammatory markers
- New clinical findings (especially neurological findings)
- Consider a repeat LP if baby is not making a good clinical recovery

Do not perform LP if:
- No clinical concerns i.e. don’t just treat a CRP
- Contraindicated: local infection over proposed LP site; unstable patient e.g. respiratory insufficiency; shock; on-going convulsions; coagulation abnormalities or thrombocytopenia

(2) **IV Cefotaxime 50mg/kg bd** – this is the first line treatment for babies with suspected EOS who are generally well on SCU/PNW. This does not cover Listeria so discuss with Consultant if Listeria sepsis suspected. Cefotaxime can be given IM if venous access if not available.

(3) **IV Benzylpenicillin**

NICE CG149 suggests 25mg/kg BD. (However, clinical judgement may suggest an 8hrly regime or increased dosage). Pen + Gent is the regime if babies are unwell or admitted to NICU

(4) **Gentamicin**

- See flow chart below to guide decision making on dose and interval
- MUST be prescribed correctly on Gentamicin chart only
- Some babies at risk of delayed clearance – babies <32 weeks gestation, <1000g birth weight and for babies undergoing therapeutic hypothermia (cooling) and/or if there is suspicion/evidence of renal dysfunction should have lower dose (4mg/kg) less frequently (36 hourly) with pre-second dose levels checked.
- Rarely - consider measuring peak blood gentamicin concentrations in selected babies such as in those with:
  - oedema
  - macrosomia (birthweight more than 4.5 kg)
  - an unsatisfactory response to treatment
  - proven Gram-negative infection.

  Measuring peak concentrations 1 hour after starting the gentamicin infusion (D/W Consultant first)

- If a baby has a Gram-negative or staphylococcal infection, consider increasing the dose of gentamicin if the peak concentration is less than 8 mg/litre
Discuss with parents at all stages and ensure parental understanding and provide WRITTEN information (parent information leaflet)
Ensure the baby is managed in an appropriate care setting

Once antibiotics stopped/at discharge:
- Give parents/carers advice re: when to seek medical attention – VERBALLY and in WRITING (patient information leaflet)
- Give parents/carers a point of contact for advice
- Give parents/carers and GP a copy of the discharge summary

**Gentamicin Prescribing Guidance**

This is based on NICE and NPSA guidance, as well as local audit findings and published data.

**Risk factor for delayed clearance of gentamicin?**
- Preterm ≤ 32 weeks
- HIE with cooling
- Renal impairment
- IUGR <1kg
- Concurrent NSAID therapy

**Is baby clinically stable and well?**
- Yes
- No

**Gentamicin 4 mg/kg 36 hourly**
- Check level 4 hours pre-second dose (36 hourly regimen)
- Level <2mg/L – continue on 36 hourly regimen

**Gentamicin 5 mg/kg 36 hourly**
- Level <2mg/L – continue
- Level >2mg/L – omit and repeat level after 12 hours (or 24 hours if very high). Level must be <1 mg/L before re-dosing and interval must be extended accordingly

**Gentamicin 5mg/kg 24 hourly**
- Take level 4 hours pre-second dose
- Level <2mg/L – continue
- Level >2mg/L – omit and repeat level after 12 hours (or 24 hours if very high). Level must be <1 mg/L before re-dosing and interval must be extended accordingly

All second doses onwards should be prescribed on the Gentamicin prescribing Chart (Appendix 1). The times need to be according to the 24 hour clock.

Clinical judgement is used to determine the safest prescription which should be double checked with the nursing staff.

**Nursing Staff**

Arrangements to be in place such as use of the red plastic apron to indicate that staff are preparing gentamicin and should not be disturbed. Double signature checks are required for gentamicin checking and administration. The care bundle compliance chart must be completed (see Appendix 2)
## Appendix 1
### Intravenous Gentamicin Prescribing Chart for Neonates

**Write in CAPITAL LETTERS or use addressograph**

<table>
<thead>
<tr>
<th>Surname:</th>
<th>First Names:</th>
<th>Hospital number:</th>
<th>Date of Birth:</th>
</tr>
</thead>
</table>

**Consultant:** __________________

**Gestation:** .............  **Weight:** ............. Kg

**Administration**

As slow intravenous injection over 3-5 minutes Gentamicin may be injected neat or diluted with sodium chloride 0.9% or glucose 5%. Flush with sodium chloride 0.9% A red disposable apron should be worn during preparation and administration. The double checking prompt and care bundle compliance chart should be used. The prescribed dose of gentamicin should be given within one hour of the prescribed time. If not, subsequent dose times must take this into account.

**Monitoring**

Take trough levels 4 hours before the 2nd dose. Interpretation of results for doses: Trough level <2mg/L: Continue with current dosing. If level >2mg/L omit dose and repeat level after 12 hours (or 24 hours if more than 3). Level must be <1mg/l before re-dosing and interval adjusted accordingly.

### Prescription

<table>
<thead>
<tr>
<th>Dose</th>
<th>Date to be given</th>
<th>Time to be given (24hr clock)</th>
<th>Dose (mg/kg)</th>
<th>Gentamicin Dose (mg)</th>
<th>Dr's Signature</th>
<th>Time dose given (24hr clock)</th>
<th>Given by Signature</th>
<th>Check by signature</th>
<th>Level needed yes/no</th>
<th>Time level needed</th>
<th>Time of sample</th>
<th>Result of sample</th>
<th>Action and signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>Y/N</td>
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</tbody>
</table>

Note: Infants on 35 hour dosing should not require more than 3 doses for a standard 5-day course of treatment. Infant on 24 hour dosing should not require more than 5 doses for a standard course of treatment. If longer is required state reason below and continue below. A supplementary double prompt and compliance care bundle will be required.

**Reason for continuing after 5 days..............................**
Double-checking prompt for the preparation and administration of intravenous gentamicin to neonates

- Both members of staff (Checker A and B) are to use the prompt every time a dose of gentamicin is prepared and administered. Circle Yes, No or N/A (Not applicable) for first 5 questions, thereafter tick for yes.
- Ultimate responsibility for the process lies with checker A one whose additional responsibilities are highlighted in blue/bold.

<table>
<thead>
<tr>
<th>Date:</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
<th>Dose 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood level monitoring: Any actions required in the section below should be prioritised to ensure doses are not delayed:</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
</tbody>
</table>

1. Check the date and time of the next blood level required. Are any blood levels required prior to, or post administration? | YES | NO | YES | NO | YES | NO |

2. Do any blood level results need action prior to administration of this dose? I.e. results chasing or results interpreted? | YES/NO | N/A | YES/NO | N/A | YES/NO | N/A |

3. If yes to question two, has the person responsible for the interpretation of result been informed? | YES/NO | N/A | YES/NO | N/A | YES/NO | N/A |

4. Has the blood level result been interpreted correctly? If not escalate as per policy. | YES/NO | N/A | YES/NO | N/A | YES/NO | N/A |

5. Does the dose or dosing interval need changing as a result of the blood level result? If yes ensure this is actioned as per policy. | YES/NO | N/A | YES/NO | N/A | YES/NO | N/A |

**Prescription chart details:**

6. Check the time recorded when dose last given and the frequency prescribed. Is a dose due now? | A | B | A | B |

7. Is the patient’s current weight recorded on the prescription chart correct? (Caution: Ensure the weight is recent and realistic). | A | B | A | B |

8. Has the correct dose been prescribed based on the weight? Each checker to calculate the dose separately. | A | B | A | B |

9. Is the dosing regimen and frequency correct for gestational age? Check against neonatal gentamicin policy. | A | B | A | B |

10. Has the prescription been signed by the prescriber? | A | B | A | B |

**Vial or CIVAS details:**

11. Is this the correct medication? | A | B | A | B |

12. Is this the correct strength of gentamicin, i.e. 20mgs/2mls? | A | B | A | B |

13. Has the correct volume been drawn up? (Each checker to calculate dose separately) | A | B | A | B |

**Administration:**


15. Has the prescription chart been signed by the administrator with details of the time of administration? | A | B | A | B |

Signature checker A

Signature checker B
Neonatal gentamicin care bundle compliance chart

Patient ID: ____________________________________________________________

Complete for each dose of gentamicin administered

<table>
<thead>
<tr>
<th></th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
<th>Dose 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date:</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1. Use of 24 hour clock format</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
<tr>
<td>2. Interruptions during the preparation and administration of Gentamicin must be avoided by the wearing of a disposable red apron by staff to indicate that they must not be disturbed.</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
<tr>
<td>3. A double-checking prompt must be used during the preparation and administration of Gentamicin</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
<tr>
<td>4. The prescribed dose of Gentamicin must be given within one hour of the prescribed time</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
<tr>
<td>Compliant with all FOUR elements of the care bundle</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
</tr>
</tbody>
</table>

If gentamicin was not administered within one hour of the prescribed time then please indicate any relevant reasons:

<table>
<thead>
<tr>
<th></th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
<th>Dose 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>No addressograph</td>
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<tr>
<td>Not prescribed but due</td>
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<tr>
<td>Prescription not signed</td>
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<td>Incorrect drug</td>
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<td>Level result not available</td>
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<tr>
<td>Abnormal level results</td>
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<td>No weight</td>
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</tr>
</tbody>
</table>
Sources of Information

1. NICE Guidance CG 149 Antibiotics for early onset neonatal infection August 2012
2. ASPH Maternity GBS guidelines (updated 2013)
3. ASPH Drugs and Therapeutics Committee and Microbiologist opinion
4. ASPH Audit on Gentamicin Use in Neonates
   [link](http://trustnet/docsdata/paed/Audit%20Competition/Neonatal%20Sepsis.ppt)
6. CDC. Prevention of Perinatal Group B Streptococcal Disease Revised Guideline. 2010
   Obstetrics and Gynecology Vol 117, No 4 ; April 2011

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