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 / TREATMENT for sepsis AND observations**

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

**Neonates who definitely need OBSERVATIONS but not (necessarily) tests/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
- Required cardiac massage at birth
- Meconium stained liquor
- Jaundice <24hrs (not explained by Rh/ABO incompatibility) (See Jaundice guideline)

Maternal antibiotic treatment does NOT mandate neonatal antibiotic treatment, a close review of the risk factors and neonatal clinical examination 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
   b) 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.

Antibiotic Choices
Tazocin for post natal ward / SCU babies
Pen + Gent for babies admitted Neonatal Unit

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**

- **Investigation (1)**
  - Blood cultures / CRP. (FBC, Clotting +/- LFT if unwell)

- **Treatment (Choose and start within ONE hour)**
  - IV Tazocin (2) 8hrly for babies who are remaining on SCU or on the Postnatal Wards and are well
  - If baby is unwell, admit to Neonatal Unit and commence IV Benzylpenicillin (3) and Gentamicin (4)

**0hr**

- Baby well and initial CRP≤10mg/L
  - Repeat CRP after 18 hrs
  - Second CRP ≤10mg/L
    - Baby well – admit to SCU if not already, continue Tazocin
  - Second CRP >10mg/L
    - Clinical review
    - Second CRP >10mg/L and baby unwell
      - Admit to Neonatal Unit, change to Pen + Gent

**1hr**

- Second CRP >10 mg/L
  - Baby well – admit to SCU if not already, continue Tazocin

**18hrs**

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

**36hr**

- 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:
- Contraindicated: local infection over proposed LP site; unstable patient e.g. respiratory insufficiency; shock; on-going convulsions; coagulation abnormalities or thrombocytopenia

(2) **IV Tazocin** – is used as a single agent in this context. It is preferred to a cephalosporin due to the emergence of ESBL-producing gram negative organisms.

(3) **IV Benzylpenicillin**
NICE CG149 suggests 25mg/kg BD. (However, clinical judgement may suggest an 8hrly regime or increased dosage)

(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

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**Yes**

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

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**No**

**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

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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.

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**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**

**Intravenous GENTAMICIN PRESCRIPTION CHART FOR USE IN NEONATES**

*Reference on main drug chart "as per chart"*

<table>
<thead>
<tr>
<th>Write in CAPITAL LETTERS or use addressograph</th>
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</thead>
<tbody>
<tr>
<td>Surname: ..................................</td>
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<tr>
<td>First Names: ................................</td>
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<tr>
<td>Hospital number: ................................</td>
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<tr>
<td>Date of Birth: ................................</td>
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</tbody>
</table>

| Consultant: .................................. |
| Gestation: .................. Weight: .................K |

**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.

<table>
<thead>
<tr>
<th>PRESCRIPTION</th>
<th>ADMINISTRATION</th>
<th>MONITORING</th>
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</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>Date to be</td>
<td>Time to be</td>
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<td>given</td>
<td>given (24hr</td>
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<td>(24hr clock)</td>
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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>
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1. Check the date and time of the next blood level required. Are any blood levels required prior to, or post administration?  
   - 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

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

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

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

### Prescription chart details:

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</table>

**Signature checker A**

**Signature checker B**
Neonatal gentamicin care bundle compliance chart

Patient ID: ________________________________________________________________

<table>
<thead>
<tr>
<th>Complete for each dose of gentamicin administered</th>
<th>Dose 1</th>
<th>Dose 2</th>
<th>Dose 3</th>
<th>Dose 4</th>
<th>Dose 5</th>
</tr>
</thead>
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<tr>
<td>Date:</td>
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<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</td>
<td>Y/N</td>
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<td>Y/N</td>
<td>Y/N</td>
<td>Y/N</td>
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<tr>
<td>administration of Gentamicin must be avoided</td>
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<td>by the wearing of a disposable red apron by staff</td>
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<td>to indicate that they must not be disturbed.</td>
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<td>3. A double-checking prompt must be used during</td>
<td>Y/N</td>
<td>Y/N</td>
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<td>the preparation and administration of Gentamicin</td>
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<td>4. The prescribed dose of Gentamicin must be</td>
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<td>given within one hour of the prescribed time</td>
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<td>Compliant with all FOUR elements of the care</td>
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If gentamicin was not administered within one hour of the prescribed time then please indicate any relevant reasons:

<table>
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<th>Reason</th>
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<td>Prescription not signed</td>
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<td>Incorrect drug</td>
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<td>Incorrect date</td>
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</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
   http://trustnet/docsdata/paed/Audit%20Competition/Neonatal%20Sepsis.ppt
6. CDC. Prevention of Perinatal Group B Streptococcal Disease Revised Guideline. 2010

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With advice from ASPH Drugs and Therapeutics Committee

Approved for use October 2013
Updated March 2015 Dr Reynolds (discussed with Microbiologists)

Next review March 2020