Infants of any gestational age are at high risk for acute bacterial infections for several reasons, both innate and extrinsic. Preterm infants acquire infection more readily than term infants; and with increasing survival of premature infants, infection has become an important cause of mortality and morbidity. Although successful management requires prompt recognition and early initiation of treatment, it is important to remember that preventing infection is a priority for all neonatal unit staff. The most important intervention for preventing infection is careful and frequent hand washing.

**Early-onset sepsis (EOS): < 72 hours**
Acquired in the intra-partum period and usually presents in the first 24-72 hours after birth. The incidence of EOS is 0.98 cases per 1000 live births, and is higher in preterms.¹
The principal organisms responsible are group B streptococci (GBS) and Escherichia coli.¹ Listeria monocytogenes is a rare but important cause of neonatal sepsis.²

**Late-onset sepsis: ≥ 72 hours**
Both group B streptococci and listeria can cause late-onset infection. Late onset infection is predominantly hospital acquired.
A recent review has shown 36% of preterms ≤28 weeks infants developed LOS.³ 70% of late onset infection is caused by gram-positive organisms, with coagulase-negative staphylococci (CoNS) responsible for 48%.⁴ Gram-negative organisms cause some specific infections, such as urinary tract infections.
Fungal infections (Candida albicans) occur frequently in small preterm infants.⁴

**Criteria for starting antibiotics:**
Postnatal management for EOS depends on both maternal and neonatal risk factors and clinical indicators or signs of infection.
Look at the maternal notes, talk with the midwife looking after Mum, take a history from the parents and examine the baby carefully to assess for clinical indicators of infection. Explain to the parents your findings and explain why their baby may or may not need observations and antibiotics.
Be aware some risk factors carry more weight than others; these are considered as red flags.

**Start IV antibiotics for all babies who have:**
- Clinical concerns of sepsis or if considered systemically unwell
- one red flag risk factor or clinical sign
- two or more other risk factors or clinical signs.
Perform neonatal observations 4 hourly for duration of antibiotic therapy.

Babies with only one “other risk factor”:
- consider if safe to withhold antibiotics
- and observe for a minimum of 24 hours. Perform observations at 0, 2, 4, 8, 12, 16, 20 and 24 hours. Observations at 0 hr taken and recorded by the staff present at birth.

**Red flag risk factors for infection⁵:**
- Mother on the “sepsis pathway” ie IV antibiotics given to the mother for confirmed or suspected invasive bacterial infection during labour, or in the 24-hour periods before and after birth (not intrapartum antibiotic prophylaxis).
- Encephalopathy requiring total body cooling.
- Suspected or confirmed infection in another baby in the case of a multiple pregnancy.
- Invasive GBS infection in a previous baby.

**Other risk factors⁵:**
- Maternal GBS colonisation and intrapartum antibiotics either declined or given to mother less than 2 hours pre delivery. GBS bacteriuria or infection in the current pregnancy. Please see the GBS colonisation guideline.
- Prelabour/Prolonged rupture of membranes (>18 hours).
- Prematurity (<37 weeks).

D Gallacher, S Barr, R Howe – August 2014. To be reviewed August 2017
Red Flag Clinical Signs:
- Respiratory distress starting more than 4 hours after birth.
- Need for mechanical ventilation in a term baby.
- Signs of shock.
- Seizures, unless clear underlying cause.

Other Clinical Signs that may represent infection:
- Resp: Hypoxia, Apnoea, Resp distress.
- CVS: PPHN, Tachycardia, Bradycardia.
- Neuro: ↓tone, ↓Responsiveness, encephalopathy.
- GI: Feeding difficulties, abdo distention, vomiting (including bilious).
- Other: Jaundice <24hrs, ↓or↑Temp, Hypo or hyper glycaemia.

Remember neonatal sepsis may present in many different ways, often non-specific in nature. Always be vigilant.

Immediate Management:
1) History – identify presence of any maternal risk factors.
2) Examination – thorough clinical examination.
3) Investigation - Blood Culture, FBC, CRP – in all cases, prior to starting antibiotics,
   - take a venous sample for blood cultures after skin disinfection with chloraprep (2% chlorhexidine /70% Isopropyl alcohol).
   - minimum 1ml should be sent for blood culture.
4) Low threshold for CXR, Urine MC+S, Blood Gas
   - Urine samples should be obtained either by suprapubic aspiration, an “in out” aseptic catherisation of bladder or a clean catch. Send urine for urgent microscopy.
   - Do not delay antibiotics administration in order to obtain CSF/CXR/Urine.
5) Consider CSF – if neurological concerns
   - acceptable to wait for blood results before lumbar puncture.
6) Antibiotics - IV antibiotics given (prescribed and administered) within 1 hour of decision to start antibiotics.

Further Management:
- Serial CRP measurements can aid monitoring the response to treatment and guide duration of antibiotic therapy.
  Two reassuring CRP measurements 24hrs apart have a negative predictive value of 99.7% for culture-confirmed neonatal sepsis.
- Repeat CRP 24-48 hrs after starting antibiotics, usually done with the Gentamicin level.
- Consider Lumbar Puncture if CRP elevated, discuss with seniors.
- Antibiotics can be discontinued at 48 hrs if:
  - No ongoing signs of sepsis
  - Cultures confirmed as negative
  - Bloods reassuring
- Rationalise antibiotics if blood cultures positive when appropriate sensitivities are available (liaise with microbiology).
- In the presence of positive blood cultures or a specific underlying diagnosis, the duration of antimicrobial treatment should be a neonatal consultant decision; usually in consultation with a microbiologist.
- Please remember: Sepsis is not the only reason for a raised CRP.
**First line Antibiotics:**

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Choice of antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early onset Sepsis (&lt;72 hours)</td>
<td>Benzyl Penicillin plus Gentamicin</td>
</tr>
<tr>
<td>Late onset sepsis (&gt;72 hours)</td>
<td>Flucloxacillin plus Gentamicin</td>
</tr>
<tr>
<td>In suspected meningitis</td>
<td>Benzyl Penicillin, Gentamicin plus Cefotaxime</td>
</tr>
<tr>
<td>In suspected Necrotising Enterocolitis</td>
<td>Flucloxacillin, Gentamicin plus Metronidazole</td>
</tr>
<tr>
<td>In suspected long-line infections</td>
<td>Vancomycin plus Gentamicin</td>
</tr>
</tbody>
</table>

**Dose and Frequency of Antibiotics:** Please refer to individual drug monographs for further details

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dose (mg/kg/dose)</th>
<th>Frequency</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzy Penicillin</td>
<td>50</td>
<td>BD (&lt; 7days) TDS (7-27 days) QDS (≥ 28 days)</td>
<td>Loading dose 15mg/kg/dose &lt; 28 days</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>7.5</td>
<td>BD (&lt;28 days) TDS (≥ 28 days)</td>
<td>▲ dose interval in renal failure</td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td>25</td>
<td>BD (&lt; 7days) TDS (7-21 days) QDS (&gt; 21 days)</td>
<td>Loading dose 15mg/kg/dose &lt; 28 days</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>50</td>
<td>BD (&lt; 7days) TDS (≥7days)</td>
<td>Dose reduction in renal failure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dose (mg/kg/dose)</th>
<th>Frequency</th>
<th>Monitoring*</th>
</tr>
</thead>
</table>
| Gentamicin        | 4                 | 36hrly <32wks 24hrly ≥32wks | Trough prior to 3<sup>rd</sup> dose  
Oliguric/ high creatinine prior to 2<sup>nd</sup> dose  
Accept trough <2mg/L  |
| Vancomycin        | 15                | OD <29wks BD 29-34wks TDS ≥35wks | Trough prior to 4<sup>th</sup> dose  
Accept levels between 10-15mg/L  |

*Note: If routine drug level is required out of hours, take blood, give dose and await result in working hours. However if there are clinical concerns such as oliguria/renal impairment etc, discuss with Consultant microbiologist regarding urgent out of hours requests.

References:

6) Benitz WE, Han MY, Madan A, Ramachandra P. Serial serum C-reactive protein levels in the diagnosis of neonatal infection. Pediatrics 1998; 102: E41