Antibiotics for early-onset neonatal infection

NICE CG149; 2012

This guideline covers the diagnosis and management of neonatal infection within 72 hours of birth.

Information and support - see full guideline.

Recognition of early-onset neonatal infection

♦ Identify risk factors for and clinical indicators of early-onset neonatal infection during pregnancy, labour and birth – see full guideline.
♦ Red flag risk factors/clinical indicators should prompt a high level of concern for early-onset neonatal infection.

Table 1. Red flags - see full guideline for complete list of risk factors and clinical indicators.

<table>
<thead>
<tr>
<th>Risk Factor - mother/baby</th>
<th>Clinical indicator - baby</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected/confirmed infection in another baby in the case of a multiple pregnancy</td>
<td>Respiratory distress starting &gt; 4 hours after birth</td>
</tr>
<tr>
<td>Parenteral antibiotics given to the woman for confirmed/suspected invasive bacterial infection at any time during labour, or within 24 hours before or after birth</td>
<td>Seizures</td>
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Before birth

♦ During labour monitor for new risk factors e.g. fever >38°C, chorioamnionitis.

Box 1

Intrapartum antibiotics

♦ Give antibiotic prophylaxis for early-onset neonatal infection to women who have had:
  ➢ a previous baby with an invasive group B streptococcal infection,
  ➢ group B streptococcal colonisation, bacteruria or infection in the current pregnancy.
♦ In preterm labour consider antibiotic prophylaxis if there is:
  ➢ prelabour rupture of membranes of any duration,
  ➢ suspected or confirmed intrapartum rupture of membranes lasting more than 18 hours.

First-line: IV benzylpenicillin. If penicillin allergy then; Second-line: clindamycin*.
*unless sensitivity results or local microbiological surveillance data indicate a different antibiotic.

♦ Give the first dose as soon as possible and continue until birth of the baby.

After the birth

♦ Do NOT routinely give antibiotics to babies without risk factors/clinical indicators of infection or laboratory evidence of possible infection.
♦ Use risk factors/clinical indicators including red flags to direct antibiotic management decisions.
♦ If any risk factors/clinical indicators present then do a careful clinical assessment without delay. Review maternal and neonatal history and carry out a physical examination of the baby including assessment of vital signs.

Treatment and management

♦ In babies with any red flags OR 2 or more ‘non-red flag’ risk factors/clinical indicators:
  ➢ perform investigations and start antibiotics.
  ➢ Do NOT delay starting antibiotics pending test results.
♦ In babies without red flags and only one risk factor/clinical indicator: use clinical judgement. Consider if it is:
  ➢ safe to withhold antibiotics,
  ➢ necessary to monitor baby’s vital signs and clinical condition. If monitoring is required continue for at least 12 hours (at 0,1, 2 hours then 2-hourly).
♦ In babies being monitored for possible infection:
  ➢ if clinical concern increases, perform investigations and start antibiotics.
  ➢ if no further concerns then reassure the family and give advice to parents/carers if baby is discharged.
  ➢ Give antibiotics as soon as possible and always within 1 hour of the decision to treat.
♦ Follow recommendations in the appropriate clinical guideline:
  ➢ NICE CG102; Bacterial meningitis and meningococcal septicaemia
  ➢ NICE CG54; Urinary tract infection in children
♦ In babies without risk factors/clinical indicators:
  ➢ continue routine postnatal care; see NICE CG37; Postnatal care.

Investigations in babies with suspected infection

At the start of antibiotic treatment

♦ Perform a blood culture before giving the first dose.
♦ Measure C-reactive protein concentration at presentation.
♦ Perform a lumbar puncture to obtain a cerebrospinal fluid (CSF) sample before starting antibiotics if it is safe to do so and:
  ➢ there is a strong clinical suspicion of infection, OR
  ➢ there are clinical symptoms or signs suggesting meningitis.
♦ If performing lumbar puncture would delay starting antibiotics, do it as soon as possible after starting antibiotics.
♦ Do NOT routinely perform urine microscopy or culture.
♦ Do NOT perform skin swab microscopy or culture in the absence of clinical signs of a localised infection.

During antibiotic treatment

♦ Measure C-reactive protein concentration 18 to 24 hours after presentation.
♦ Perform a lumbar puncture to obtain CSF if it is safe to do so and the baby;
  ➢ has a C-reactive protein ≥10mg/litre, OR
  ➢ has a positive blood culture, OR
  ➢ does not respond satisfactorily to antibiotics.
If suspected localised eye infection
- Minor conjunctivitis with encrusting of the eyelids is common and often benign, however a purulent discharge may indicate serious infection.
- In babies with a purulent eye discharge take urgent swabs for microbiological investigation, using methods that can detect chlamydia and gonococcus. Start systemic antibiotics for possible gonococcal infection while awaiting swab results.

If suspected localised umbilical infection
- In babies with clinical signs of umbilical infection, such as a purulent discharge or signs of periumbilical cellulitis (e.g. redness, increased skin warmth or swelling), perform a blood culture, take a swab for microscopy and culture, and start antibiotic treatment with IV fluclaxacillin and gentamicin.
- If microbiology results indicate that the infection is not due to a gram-negative infection, stop gentamicin.

Antibiotics for suspected neonatal infection without meningitis
For empirical treatment of suspected infection, unless local bacterial resistance patterns indicate a different antibiotic:

**First-line:** IV benzylpenicillin 25mg/kg every 12 hours + gentamicin starting dose 5mg/kg

**Benzylenpicillin**
- Consider a shorter 8-hourly dosage interval based on clinical judgement e.g. if the baby appears very ill.

**Gentamicin**
- If a second dose is needed give 36 hours after first dose. Interval may be shortened if:
  - the baby appears very ill,
  - blood cultures show a gram-negative infection.
- Decide on subsequent dose and dosage interval taking account of blood gentamicin concentrations – see Box 2.
- Record times of gentamicin administration and blood sampling for therapeutic monitoring.

Duration of antibiotic treatment
- Regularly reassess clinical condition and results of investigations in babies receiving antibiotics.
- Consider if a change of antibiotic is needed taking into account:
  - the clinical condition of the baby,
  - results of microbiological investigations,
  - expert microbiological advice and local surveillance data.
- If there is microbiological evidence of gram-negative bacterial sepsis ADD another antibiotic active against gram-negative bacteria e.g. cefotaxime. If gram-negative infection is confirmed stop benzylpenicillin.
- Consider stopping antibiotics at 36 hours if:
  - blood culture is negative, **AND**
  - initial clinical suspicion of infection was not strong, **AND**
  - baby’s clinical condition is reassuring with no clinical indicators of possible infection, **AND**
  - levels and trends of C-reactive protein are reassuring.
- Establish hospital systems which provide blood culture results 36 hours after starting antibiotics to facilitate timely discharge.
- If continuing antibiotics for >36 hours despite negative blood cultures review the baby at least once every 24 hours. At every review consider if it is appropriate to stop antibiotics.

Visit the NICE pathway: Antibiotics for early-onset neonatal infection

**Usual duration of antibiotic treatment is 7 days in babies with a positive blood culture or negative blood culture with strong suspicion of sepsis. Consider continuing treatment if the baby has not fully recovered or it is advisable based on the pathogen identified on blood culture.**

**Box 2**

**Gentamicin: Therapeutic Drug Monitoring**

**Trough concentrations**
- If a second dose is to be given measure the trough blood gentamicin concentration immediately before giving the second dose and consider the results before giving a third dose.
- Hospital services should make blood gentamicin concentrations available in time to inform the next dosage decision (e.g. within 30 hours of sampling).
- Repeat the trough measurement immediately before every third dose of gentamicin, or more frequently if necessary (e.g. if there has been concern about previous trough concentrations or renal function).
- Adjust the gentamicin dose interval, aiming to achieve trough concentrations of <2 mg/litre.
- If giving >3 doses of gentamicin a trough concentration of <1 mg/litre is advised.
- If a trough concentration is not available, do not withhold the next dose of gentamicin unless there is evidence of renal dysfunction (e.g. an elevated serum urea or creatinine concentration, or anuria).

**Peak concentrations**
- Consider measuring the peak blood gentamicin concentration in selected babies such as those with:
  - oedema,
  - macrosonia (birthweight>4.5 kg),
  - an unsatisfactory response to treatment,
  - proven gram-negative infection.
- Measure peak concentrations 1 hour after starting gentamicin.
- If a baby has a gram-negative or staphylococcal infection, consider increasing the gentamicin dose if the peak concentration is <8 mg/litre.

**Meningitis**
- For babies in neonatal units and in whom meningitis is:
  - suspected but causative pathogen is unknown - give IV amoxicillin and cefotaxime,
  - due to gram-negative infection as shown by CSF fluid gram stain or culture - stop amoxicillin and give IV cefotaxime alone,
  - due to gram-positive infection as shown by CSF gram stain - continue with IV amoxicillin and cefotaxime while waiting for CSF culture result and seek expert microbiological advice.
- If CSF culture is positive for group B streptococcus consider changing antibiotics to:
  - benzylpenicillin 50mg/kg every 12 hours** for at least 14 days + gentamicin (starting dose 5mg/kg) every 36 hours for 5 days.**
- If blood culture or CSF culture is positive for listeria consider stopping cefotaxime and give IV amoxicillin and gentamicin.
- If CSF culture identifies a gram-positive bacterium other than group B streptococcus or listeria seek expert microbiological advice.

**See Summary of Prescribing Characteristics for full prescribing information.**