1. Guideline title

Antibiotics for early-onset neonatal infection: antibiotics for the prevention and treatment of early-onset neonatal infection

1.1 Short title

Antibiotics for early-onset neonatal infection

2. The remit

The Department of Health has asked NICE: ‘To produce a clinical guideline on the use of antibiotics for the prevention and treatment of early onset neonatal infection.’

3. Clinical need for the guideline

3.1 Epidemiology

a) Bacterial infection is a major cause of morbidity and mortality in newborn babies, especially those born prematurely. Babies with birth weights below 1500 g have the highest risk of infection. In these babies infection is associated with adverse outcomes, including a prolonged hospital stay. In both preterm and term babies, perinatal infection is an important factor in the pathogenesis of cerebral cortical lesions and subsequent neurodevelopmental delay.

b) Early-onset neonatal infection (within 72 hours of birth) is less common than late-onset neonatal infection. Early-onset infection is usually caused by organisms from the mother's genital tract and occurs in 1.9% of babies with very low birth weight. Early-onset
infection is often more severe than late-onset infection. It may develop suddenly and rapidly, and mortality is high, particularly in premature babies and those with low birth weight. Even with antibiotic treatment, the mortality rate for low birth weight babies with early-onset infection is 26%. Babies that survive early-onset infection have prolonged hospital stays.

c) Although group B Streptococcus (GBS) is common in newborn babies and may not result in infection, it can cause serious infection that frequently presents in the first 72 hours of life. Overall mortality is reported to be about 10%, but is even higher in premature babies. Up to 7% of babies who survive GBS infection have a consequent disability.

d) Although systemic candidiasis is a rare cause of early neonatal infection, it is associated with a very high mortality rate.

e) Early-onset neonatal infection with methicillin-resistant Staphylococcus aureus (MRSA) is uncommon. However, the choice of antibiotics in the neonatal period is important because limiting the use of broad-spectrum antibiotics, such as cephalosporins, may reduce the emergence of resistant bacteria.

f) Administration of antibiotics to pregnant women may have significant consequences for the newborn baby. Co-amoxiclav administration has been associated with an increased risk of necrotising enterocolitis in the baby. Antenatal or intrapartum administration of antibiotics may be an important consideration in the prevention and treatment of early-onset neonatal infection.

g) Most newborn babies who are given antibiotics do not have an infection. Stopping unnecessary antibiotics as soon as possible will help reduce the emergence of resistant bacterial strains. and help to ‘normalise’ neonatal care.
3.2 **Current practice**

a) Antibiotics are increasingly prescribed for maternal or fetal indications, and in the neonatal period. Their effective use reduces the incidence of invasive neonatal infections such as GBS septicaemia. The potential clinical benefits must be balanced against possible harms.

b) About 10% of all newborn babies (whatever their gestational age) are screened for early-onset infection and then treated with antibiotics. Suspected or confirmed infections are, however, identified in fewer than 5% of these babies. Babies who need respiratory support receive antibiotics because it is difficult to distinguish respiratory distress syndrome from pneumonia.

c) Some healthcare professionals use narrow-spectrum antibiotics, such as benzylpenicillin and gentamicin, which are specific for GBS and *Escherichia coli* (the most frequently identified organisms). Others use broad-spectrum antibiotics, such as cephalosporins, amoxicillin and co-amoxiclav, which are active against a wide range of organisms but may increase the risk of antibiotic resistance and may be expensive.

d) Ampicillin and cephalosporins are used as antibacterial prophylaxis in women undergoing caesarean section to reduce the risk of maternal infection. This can change the endocervical flora, leading to overgrowth of potential pathogens. Widespread use of broad-spectrum antibiotics in maternity units also encourages the persistence of antibiotic-resistant organisms within the units and the risk of hospital-acquired colonisation or infection.

e) The care of babies at risk of early-onset infection is variable, with many receiving antibiotics, perhaps unnecessarily. Some neonatologists treat bacterial colonisation more readily than others.
f) In ‘Antenatal care’ (NICE clinical guideline 62, 2008) NICE recommends that women should be screened in the antenatal period for various infections, including syphilis and asymptomatic bacteriuria. Screening for GBS, asymptomatic bacterial vaginosis and chlamydia is not recommended as part of routine antenatal care. ‘Intrapartum care’ (NICE clinical guideline 55, 2007) recommends that if there are no signs of infection in the mother, antibiotics should not be given to a term baby immediately after birth, even when the membranes have been ruptured for more than 24 hours. Close observation of the asymptomatic baby is recommended with immediate referral for investigation and possible treatment if sepsis is suspected.

g) Prompt antibiotic treatment for neonatal infection can save lives. However, there is concern that the range of effective antibiotics is being reduced by the development of bacterial resistance. There is therefore a need for guidance for all healthcare professionals who care for newborn babies about when antibiotics should and should not be used, the selection of appropriate antibiotics and optimal antibiotic regimens (in terms of dosage and duration) for the prevention and treatment of infection.

4. **The guideline**

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.
4.1 Population

4.1.1 Groups that will be covered

a) Unborn babies who may be at risk of early-onset neonatal bacterial infection (onset of infection before 72 hours of age).

b) Newborn babies (term and preterm) with an increased risk of infection because of transmission of bacteria from the mother.

c) Newborn babies (term and preterm) with suspected or confirmed early-onset neonatal bacterial infection.

d) Preterm babies will receive special consideration because they have an increased risk of infection, and because they may need different strategies for the prevention, diagnosis and treatment of infection.

4.1.2 Groups that will not be covered

a) Babies with suspected or confirmed late-onset neonatal bacterial infection (onset of infection after 72 hours of age).

b) Babies with suspected or confirmed non-bacterial infections.

c) Babies with suspected or confirmed bacterial infection resulting from therapeutic interventions such as surgery.

d) Babies with suspected or confirmed syphilis.

4.2 Healthcare setting

a) All settings in which care for the newborn baby is delivered by the NHS (including community care).

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) Risk factors for early-onset neonatal bacterial infection (including antenatal, intrapartum and postnatal risk factors).
b) Which risk factors, individually or in combination, indicate the need for prophylactic antibiotic treatment (that is, intrapartum antibiotic prophylaxis) to prevent early-onset neonatal infection.

c) Which risk factors, individually or in combination, indicate the need for observation or treatment strategies for asymptomatic babies.

d) Signs and symptoms of early-onset neonatal infection in term and preterm babies.

e) Clinical and cost effectiveness of diagnostic tests (including lumbar puncture for cerebrospinal fluid examination) for the identification and exclusion of early-onset neonatal infection.

f) Clinical and cost effectiveness of antibiotics for the prevention and treatment of early-onset neonatal infection, including:

- duration of treatment
- dosage and frequency
- choice of antibiotic, for example penicillins (benzylpenicillin, ampicillin), cephalosporins (cefotaxime), carbapenems (meropenem), glycopeptides (vancomycin) and aminoglycosides (gentamicin)
- therapeutic drug monitoring.

g) Clinical and cost effectiveness of antibiotic treatment as:

- intrapartum antibiotic prophylaxis
- prophylactic treatment of the asymptomatic newborn baby
- empirical treatment of the newborn baby with suspected early onset neonatal infection
- treatment of the newborn baby with confirmed early onset neonatal infection

h) Information and support for parents and carers.
4.3.2 Clinical issues that will not be covered

a) Non-antibiotic management of suspected or confirmed early-onset neonatal infection.

b) Matters specific to the diagnosis and management of necrotising enterocolitis.

c) Recognition and treatment of bacterial meningitis and meningococcal septicaemia in neonates who are not receiving care in neonatal units. This is covered in ‘Bacterial meningitis and meningococcal septicaemia in children’ (NICE clinical guideline 102, publication expected June 2010).

d) Antenatal screening and antibiotic prophylaxis for bacterial infections. This is covered in ‘Antenatal care’ (NICE clinical guideline 62, 2008).

e) Antibiotic prophylaxis and management in term pregnancies with prelabour rupture of membranes. This is covered in ‘Intrapartum care’ (NICE clinical guideline 55, 2007).

4.4 Main outcomes

a) Neonatal mortality.

b) Neonatal morbidity (including respiratory distress syndrome, intraventricular haemorrhage and necrotising enterocolitis).

c) Health-related quality of life of the baby and the impact on the baby’s family.

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually
be only from an NHS and personal social services (PSS) perspective. Further
detail on the methods can be found in 'The guidelines manual' (see 'Further
information').

4.6 Status

4.6.1 Scope
This is the consultation draft of the scope. The consultation dates are 15 June
to 13 July 2010.

4.6.2 Timing
The development of the guideline recommendations will begin in
September 2010.

5. Related NICE guidance

5.1 Published guidance
- Induction of labour. NICE clinical guideline 70 (2008). Available from
  www.nice.org.uk/guidance/CG70
  www.nice.org.uk/guidance/CG62
  www.nice.org.uk/guidance/CG55
  from www.nice.org.uk/guidance/CG47
  www.nice.org.uk/guidance/CG37
- Caesarean section. NICE clinical guideline 13 (2004). Available from
  www.nice.org.uk/guidance/CG13

5.2 Guidance under development
NICE is currently developing the following related guidance (details available
from the NICE website):
• Bacterial meningitis and meningococcal septicaemia in children. NICE clinical guideline. Publication expected June 2010.

6. Further information

Information on the guideline development process is provided in:

• ‘How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS’
• ‘The guidelines manual’.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).