

Neonatal infection (early onset): antibiotics for prevention and treatment

Clinical guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline is the basis of QS75.

Introduction

Early-onset neonatal bacterial infection (infection with onset within 72 hours of birth) is a significant cause of mortality and morbidity in newborn babies. Parent organisations and the scientific literature report that there can be unnecessary delays in recognising and treating sick babies. In addition, concern about the possibility of early-onset neonatal infection is common. This concern is an important influence on the care given to pregnant women and newborn babies. There is wide variation in how the risk of early-onset neonatal infection is managed in healthy babies. The approach taken by the NHS needs to:

- prioritise the treatment of sick babies
- minimise the impact of management pathways on healthy women and babies
- use antibiotics wisely to avoid the development of resistance to antibiotics.

These drivers have not always been addressed consistently in the NHS, and this guideline was commissioned to ensure they would be addressed in future.

Five key principles underpin the recommendations in this guideline.

- Unless it is dangerous, families should be offered choice. The guideline includes recommendations to support families in making choices through provision of information and, where appropriate, reassurance.
- Intrapartum antibiotic prophylaxis should be administered in a timely manner to all eligible women who choose it.
- Babies with suspected early-onset neonatal infection should be treated as quickly as possible.
- Antibiotic exposure should be minimised in babies who do not have an early-onset neonatal infection.
- An integrated system of clinical care is needed to allow full implementation of the guideline recommendations.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual women and babies.

Where dosages recommended in the guideline are based on evidence that is not reflected in the summary of product characteristics, this is indicated in footnotes to the recommendations.

Patient-centred care

This guideline offers best practice advice on the care of babies who are at risk of or who have an early-onset neonatal infection (that is, onset of infection within 72 hours of birth).

Treatment and care should take into account the needs and preferences of parents and carers, as appropriate. Parents and carers whose babies are at risk of or have an early-onset neonatal infection should have the opportunity to make informed decisions about their baby's, and their own, care and treatment, in partnership with their healthcare professionals. If parents and carers do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

If the woman is under 16, healthcare professionals should follow the Department of Health's guidance in [Seeking consent: working with children](#).

Sometimes if a baby appears to have a serious illness that could indicate the need for urgent treatment the medical staff may not have time to fully discuss what is involved in that treatment beforehand. In an emergency, if the person with parental responsibility cannot be contacted, healthcare professionals may give treatment immediately if it is in the baby's best interests.

Good communication between healthcare professionals and the parents or carers is essential. It should be supported by evidence-based written information tailored to their needs. Treatment and care, and the information given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

Terms used in this guideline

Peak gentamicin concentration

The level of gentamicin in the baby's bloodstream shortly after administration. The blood sample is usually taken about 1 hour after giving the drug. High peak concentrations of gentamicin are necessary to kill bacteria.

Therapeutic monitoring

A process of measuring the concentration of a drug in the bloodstream, to avoid excessive levels that might be associated with adverse effects or to ensure adequate levels for therapeutic effect.

Trough gentamicin concentration

The level of gentamicin in the baby's bloodstream shortly before a further dose is given. High trough gentamicin concentrations may be associated with an increased risk of adverse effects.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Information and support

- If there have been any concerns about early-onset neonatal infection before a baby is discharged, advise the parents and carers verbally and in writing that they should seek medical advice (for example, from NHS Direct, their general practice, or an accident and emergency department) if they are concerned that the baby:
 - is showing abnormal behaviour (for example, inconsolable crying or listlessness), or
 - is unusually floppy, or
 - has developed difficulties with feeding or with tolerating feeds, or
 - has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C), or
 - has rapid breathing, or
 - has a change in skin colour.

Risk factors for infection and clinical indicators of possible infection

- Use the following framework based on risk factors and clinical indicators, including red flags (see [tables 1 and 2](#)), to direct antibiotic management decisions:
 - In babies with any red flags, or with two or more 'non-red flag' risk factors or clinical indicators (see [tables 1 and 2](#)), perform investigations (see recommendations 1.5.1.1–1.5.1.3) and start antibiotic treatment. Do not delay starting antibiotics pending the test results (see recommendations 1.6.1.1–1.6.1.3).
 - In babies without red flags and only one risk factor or one clinical indicator, using clinical judgement, consider:
 - ◇ whether it is safe to withhold antibiotics, and
 - ◇ whether it is necessary to monitor the baby's vital signs and clinical condition – if monitoring is required continue it for at least 12 hours (at 0, 1 and 2 hours and then 2-hourly for 10 hours).

- If a baby needs antibiotic treatment it should be given as soon as possible and always within 1 hour of the decision to treat.

Intrapartum antibiotics

- Offer intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women who have had:
 - a previous baby with an invasive group B streptococcal infection
 - group B streptococcal colonisation, bacteriuria or infection in the current pregnancy.

Investigations before starting antibiotics in the baby

- Measure the C-reactive protein concentration at presentation when starting antibiotic treatment in babies with risk factors for infection or clinical indicators of possible infection.

Antibiotics for suspected infection

- Use intravenous benzylpenicillin with gentamicin as the first-choice antibiotic regimen for empirical treatment of suspected infection unless microbiological surveillance data reveal local bacterial resistance patterns indicating a different antibiotic.

Investigations during antibiotic treatment

- In babies given antibiotics because of risk factors for infection or clinical indicators of possible infection, measure the C-reactive protein concentration 18–24 hours after presentation.

Decisions 36 hours after starting antibiotic treatment

- In babies given antibiotics because of risk factors for infection or clinical indicators of possible infection consider stopping the antibiotics at 36 hours if:
 - the blood culture is negative, and
 - the initial clinical suspicion of infection was not strong, and
 - the baby's clinical condition is reassuring with no clinical indicators of possible infection, and
 - the levels and trends of C-reactive protein concentration are reassuring.

- Consider establishing hospital systems to provide blood culture results 36 hours after starting antibiotics to facilitate timely discontinuation of treatment and discharge from hospital.

Care setting

- When deciding on the appropriate care setting for a baby, take into account the baby's clinical needs and the competencies necessary to ensure safe and effective care (for example, the insertion and care of intravenous cannulas).

1 Guidance

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

This guideline should be read in conjunction with:

- [Caesarean section](#) (NICE clinical guideline 132).
- [Bacterial meningitis and meningococcal septicaemia](#) (NICE clinical guideline 102).
- [Induction of labour](#) (NICE clinical guideline 70).
- [Antenatal care](#) (NICE clinical guideline 62).
- [Intrapartum care](#) (NICE clinical guideline 55).
- [Urinary tract infection in children](#) (NICE clinical guideline 54).
- [Feverish illness in children](#) (NICE clinical guideline 47).
- [Postnatal care](#) (NICE clinical guideline 37).

Unless otherwise indicated, all references to infection in the guideline recommendations refer to early-onset neonatal infection (that is, onset of infection within 72 hours of birth).

1.1 Information and support

1.1.1.1 If clinical concerns about possible early-onset neonatal infection arise during pregnancy or in the first 72 hours after birth (for example, in relation to risk factors [see [table 1](#)] or clinical indicators [see [table 2](#)]):

- tell the baby's parents and carers
- explain the reason for concern (including the nature of early-onset neonatal infection)
- discuss the preferred options for management (for example, observation, investigations or antibiotic treatment)
- give the baby's parents and carers time to consider the information provided, and offer further opportunities for discussion if necessary.

- 1.1.1.2 If considering antibiotic treatment because of clinical concerns about possible early-onset neonatal infection, discuss:
- the rationale for the treatment
 - the risks and benefits in the individual circumstances
 - the observations and investigations that may be needed to guide clinical management (for example, when to stop treatment)
 - the preferred antibiotic regimen and likely duration of treatment
 - the impact, if any, on where the woman or her baby will be cared for.
- 1.1.1.3 To maintain communication with a woman in labour whose baby is at increased risk of infection, healthcare professionals should involve the woman in any handover of care, either when additional expertise is brought in because of the risk of infection or during planned changes in staff. The handover should include an update about the presence of any infection. [This recommendation is adapted from recommendation 1.3.2 in [Intrapartum care](#) (NICE clinical guideline 55).]
- 1.1.1.4 Reassure parents and carers that they will be able to continue caring for, and holding, their baby according to their wishes unless the baby is too ill to allow this. If the severity of the baby's illness means they need to change the way they care for the baby, discuss this with them.
- 1.1.1.5 Reassure parents and carers that babies at increased risk of, or with, early-onset neonatal infection can usually continue to breastfeed, and that every effort will be made to facilitate this. If a baby is temporarily unable to breastfeed, support the mother to express breast milk if she wishes to do so.
- 1.1.1.6 If the woman had group B streptococcal colonisation in a previous pregnancy but without infection in the baby, reassure her that this will not affect the management of the birth in the current pregnancy.
- 1.1.1.7 Offer parents and carers contact details of organisations that provide parent support, befriending, counselling, information and advocacy. They may signpost families to other sources of help. [This recommendation is adapted from recommendation 1.5.2 in [Bacterial meningitis and meningococcal septicaemia](#) (NICE clinical guideline 102).]

1.1.1.8 If there have been any concerns about early-onset neonatal infection before a baby is discharged, advise the parents and carers verbally and in writing that they should seek medical advice (for example, from NHS Direct, their general practice, or an accident and emergency department) if they are concerned that the baby:

- is showing abnormal behaviour (for example, inconsolable crying or listlessness), or
- is unusually floppy, or
- has developed difficulties with feeding or with tolerating feeds, or
- has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C), or
- has rapid breathing, or
- has a change in skin colour.

1.1.1.9 When the baby is discharged from the hospital or midwifery-led unit (or in the immediate postnatal period in the case of babies born at home), inform the parents and carers and the baby's GP, verbally and in writing, if the baby is considered to be at increased risk of infection.

1.1.1.10 If a baby has been treated for suspected or confirmed early-onset neonatal infection:

- inform the parents and carers about potential long-term effects of the baby's illness and likely patterns of recovery, and reassure them if no problems are anticipated
- take account of parents' and carers' concerns when providing information and planning follow-up.

1.1.1.11 When a baby who has had a group B streptococcal infection is discharged from hospital:

- advise the woman that if she becomes pregnant again:
 - there will be an increased risk of early-onset neonatal infection
 - she should inform her maternity care team that a previous baby has had a group B streptococcal infection

- antibiotics in labour will be recommended

- inform the woman's GP in writing that there is a risk of:

- recurrence of group B streptococcal infection in the baby, and

- group B streptococcal infection in babies in future pregnancies.

1.1.1.12 If the woman has had group B streptococcal colonisation in the pregnancy but without infection in the baby, inform her that if she becomes pregnant again, this will not affect the management of the birth in the next pregnancy.

1.1.1.13 For every baby about whom there has been a clinical concern regarding early-onset neonatal infection, formulate a post-discharge management plan, taking into account factors such as:

- the level of the initial clinical concern

- the presence of risk factors

- parents' and carers' concerns.

1.2 *Risk factors for infection and clinical indicators of possible infection*

1.2.1 Recognising risk factors and clinical indicators

1.2.1.1 Use table 1 to identify risk factors for early-onset neonatal infection and table 2 to identify clinical indicators of early-onset neonatal infection.

1.2.1.2 Use tables 1 and 2 to identify red flags (risk factors and clinical indicators that should prompt a high level of concern regarding early-onset neonatal infection).

Table 1 Risk factors for early-onset neonatal infection, including 'red flags'

Risk factor	Red flag
Invasive group B streptococcal infection in a previous baby	
Maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy	

Prelabour rupture of membranes	
Preterm birth following spontaneous labour (before 37 weeks' gestation)	
Suspected or confirmed rupture of membranes for more than 18 hours in a preterm birth	
Intrapartum fever higher than 38°C, or confirmed or suspected chorioamnionitis	
Parenteral antibiotic treatment given to the woman for confirmed or suspected invasive bacterial infection (such as septicaemia) at any time during labour, or in the 24-hour periods before and after the birth [This does not refer to intrapartum antibiotic prophylaxis]	Yes
Suspected or confirmed infection in another baby in the case of a multiple pregnancy	Yes

Table 2 Clinical indicators of possible early-onset neonatal infection (observations and events in the baby), including 'red flags'

Clinical indicator	Red flag
Altered behaviour or responsiveness	
Altered muscle tone (for example, floppiness)	
Feeding difficulties (for example, feed refusal)	
Feed intolerance, including vomiting, excessive gastric aspirates and abdominal distension	
Abnormal heart rate (bradycardia or tachycardia)	
Signs of respiratory distress	
Respiratory distress starting more than 4 hours after birth	Yes
Hypoxia (for example, central cyanosis or reduced oxygen saturation level)	
Jaundice within 24 hours of birth	
Apnoea	
Signs of neonatal encephalopathy	
Seizures	Yes
Need for cardio-pulmonary resuscitation	

Need for mechanical ventilation in a preterm baby	
Need for mechanical ventilation in a term baby	Yes
Persistent fetal circulation (persistent pulmonary hypertension)	
Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors	
Signs of shock	Yes
Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation (International Normalised Ratio greater than 2.0)	
Oliguria persisting beyond 24 hours after birth	
Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)	
Metabolic acidosis (base deficit of 10 mmol/litre or greater)	
Local signs of infection (for example, affecting the skin or eye)	

1.2.2 Before the birth

- 1.2.2.1 For women in labour identify and assess any risk factors for early-onset neonatal infection (see [table 1](#)). Throughout labour monitor for the emergence of new risk factors, such as intrapartum fever higher than 38°C, or the development of chorioamnionitis.
- 1.2.2.2 Manage prelabour rupture of membranes at term according to the recommendations in [Intrapartum care](#) (NICE clinical guideline 55).

1.2.3 After the birth

- 1.2.3.1 If there are any risk factors for early-onset neonatal infection (see [table 1](#)) or if there are clinical indicators of possible early-onset neonatal infection (see [table 2](#)) perform a careful clinical assessment without delay. Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs.
- 1.2.3.2 Use the following framework based on risk factors and clinical indicators, including red flags (see [tables 1 and 2](#)), to direct antibiotic management decisions:

- In babies with any red flags, or with two or more 'non-red flag' risk factors or clinical indicators (see [tables 1 and 2](#)), perform investigations (see recommendations 1.5.1.1–1.5.1.3) and start antibiotic treatment. Do not delay starting antibiotics pending the test results (see recommendations 1.6.1.1–1.6.1.3).
- In babies without red flags and only one risk factor or one clinical indicator, using clinical judgement, consider:
 - whether it is safe to withhold antibiotics, and
 - whether it is necessary to monitor the baby's vital signs and clinical condition – if monitoring is required continue it for at least 12 hours (at 0, 1 and 2 hours and then 2-hourly for 10 hours).

1.2.3.3 In babies being monitored for possible infection:

- if clinical concern increases, consider performing necessary investigations (see recommendations 1.5.1.1–1.5.1.3) and starting antibiotic treatment (see recommendations 1.6.1.1–1.6.1.3)
- if no further concerns arise during the period of observation reassure the family and, if the baby is to be discharged, give advice to the parents and carers (see recommendation 1.1.1.8).

1.2.3.4 If a baby needs antibiotic treatment it should be given as soon as possible and always within 1 hour of the decision to treat.

1.2.3.5 Manage suspected bacterial meningitis according to the recommendations in [Bacterial meningitis and meningococcal septicaemia](#) (NICE clinical guideline 102) unless the baby is already receiving care in a neonatal unit.

1.2.3.6 Manage suspected urinary tract infection according to the recommendations in [Urinary tract infection in children](#) (NICE clinical guideline 54).

1.2.3.7 Continue routine postnatal care (see [Postnatal care](#), NICE clinical guideline 37) for babies without risk factors (see [table 1](#)) or clinical indicators of possible infection (see [table 2](#)).

1.2.3.8 If maternal colonisation with group B streptococcus is first identified after the birth but within the first 72 hours of life, ask the person directly involved in the

baby's care (for example, a parent, carer or healthcare professional) whether they have any concerns, identify any other risk factors present and look for clinical indicators of infection. Use this assessment to decide on clinical management (see recommendation 1.2.3.2).

1.3 *Intrapartum antibiotics*

1.3.1.1 Offer intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women who have had:

- a previous baby with an invasive group B streptococcal infection
- group B streptococcal colonisation, bacteriuria or infection in the current pregnancy.

1.3.1.2 If the woman decides to take intrapartum antibiotic prophylaxis, give the first dose as soon as possible and continue prophylaxis until the birth of the baby.

1.3.1.3 Consider intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women in preterm labour if there is prelabour rupture of membranes of any duration.

1.3.1.4 Consider intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women in preterm labour if there is suspected or confirmed intrapartum rupture of membranes lasting more than 18 hours.

1.3.1.5 Offer benzylpenicillin as the first choice for intrapartum antibiotic prophylaxis. If the woman is allergic to penicillin, offer clindamycin unless individual group B streptococcus sensitivity results or local microbiological surveillance data indicate a different antibiotic.

1.4 *Avoiding routine use of antibiotics in the baby*

1.4.1.1 Do not routinely give antibiotic treatment to babies without risk factors for infection or clinical indicators or laboratory evidence of possible infection.

1.5 *Investigations before starting antibiotics in the baby*

- 1.5.1.1 When starting antibiotic treatment in babies with risk factors for infection or clinical indicators of possible infection, perform a blood culture before administering the first dose.
- 1.5.1.2 Measure the C-reactive protein concentration at presentation when starting antibiotic treatment in babies with risk factors for infection or clinical indicators of possible infection.
- 1.5.1.3 Perform a lumbar puncture to obtain a cerebrospinal fluid sample before starting antibiotics if it is thought safe to do so and:
- there is a strong clinical suspicion of infection, or
 - there are clinical symptoms or signs suggesting meningitis.
- If performing the lumbar puncture would unduly delay starting antibiotics, perform it as soon as possible after starting antibiotics.
- 1.5.1.4 Do not routinely perform urine microscopy or culture as part of the investigation for early-onset neonatal infection.
- 1.5.1.5 Do not perform skin swab microscopy or culture as part of the investigation for early-onset neonatal infection in the absence of clinical signs of a localised infection.
- 1.5.1.6 Be aware that, although minor conjunctivitis with encrusting of the eyelids is common and often benign, a purulent discharge may indicate the presence of a serious infection (for example, with chlamydia or gonococcus).
- 1.5.1.7 In babies with a purulent eye discharge take swab samples urgently for microbiological investigation, using methods that can detect chlamydia and gonococcus. Start systemic antibiotic treatment for possible gonococcal infection while awaiting the swab microbiology results.
- 1.5.1.8 In babies with clinical signs of umbilical infection, such as a purulent discharge or signs of periumbilical cellulitis (for example, redness, increased skin warmth or swelling), perform a blood culture, take a swab sample for microscopy and

culture, and start antibiotic treatment with intravenous flucloxacillin and gentamicin (see recommendation 1.6.1.3)^[1]. If the microbiology results indicate that the infection is not due to a Gram-negative infection, stop the gentamicin.

1.6 Antibiotics for suspected infection

1.6.1.1 Use intravenous benzylpenicillin with gentamicin as the first-choice antibiotic regimen for empirical treatment of suspected infection unless microbiological surveillance data reveal local bacterial resistance patterns indicating a different antibiotic.

1.6.1.2 Give benzylpenicillin in a dosage of 25 mg/kg every 12 hours^[2]. Consider shortening the dose interval to 8-hourly based on clinical judgement (for example, if the baby appears very ill).

1.6.1.3 Give gentamicin in a starting dosage of 5 mg/kg^[1].

1.6.1.4 If a second dose of gentamicin is to be given (see recommendation 1.7.2.1) it should usually be given 36 hours after the first dose. The interval may be shortened, based on clinical judgement, for example if:

- the baby appears very ill
- the blood culture shows a Gram-negative infection.

1.6.1.5 Decide on subsequent gentamicin doses and intervals taking account of blood gentamicin concentrations (see recommendations [1.8.1.1–1.8.2.3](#)).

1.6.1.6 Record the times of:

- gentamicin administration
- sampling for therapeutic monitoring.

1.6.1.7 Regularly reassess the clinical condition and results of investigations in babies receiving antibiotics. Consider whether to change the antibiotic regimen taking account of:

- the baby's clinical condition (for example, if there is no improvement)

- the results of microbiological investigations
- expert microbiological advice, taking account of local surveillance data.

1.6.1.8 If there is microbiological evidence of Gram-negative bacterial sepsis, add another antibiotic to the benzylpenicillin and gentamicin regimen that is active against Gram-negative bacteria (for example, cefotaxime). If Gram-negative infection is confirmed stop benzylpenicillin.

1.7 *Duration of antibiotic treatment*

1.7.1 Investigations during antibiotic treatment

1.7.1.1 In babies given antibiotics because of risk factors for infection or clinical indicators of possible infection, measure the C-reactive protein concentration 18–24 hours after presentation.

1.7.1.2 Consider performing a lumbar puncture to obtain a cerebrospinal fluid sample in a baby who did not have a lumbar puncture at presentation who is receiving antibiotics, if it is thought safe to do so and if the baby:

- has a C-reactive protein concentration of 10 mg/litre or greater, or
- has a positive blood culture, or
- does not respond satisfactorily to antibiotic treatment.

1.7.2 Decisions 36 hours after starting antibiotic treatment

1.7.2.1 In babies given antibiotics because of risk factors for infection or clinical indicators of possible infection, consider stopping the antibiotics at 36 hours if:

- the blood culture is negative, and
- the initial clinical suspicion of infection was not strong, and
- the baby's clinical condition is reassuring with no clinical indicators of possible infection, and
- the levels and trends of C-reactive protein concentration are reassuring.

1.7.2.2 Consider establishing hospital systems to provide blood culture results 36 hours after starting antibiotics to facilitate timely discontinuation of treatment and discharge from hospital.

1.7.2.3 Clinical microbiology or paediatric infectious disease advice should be available every day from healthcare professionals with specific experience in neonatal infection.

1.7.3 Early-onset neonatal infection without meningitis

1.7.3.1 The usual duration of antibiotic treatment for babies with a positive blood culture, and for those with a negative blood culture but in whom there has been strong suspicion of sepsis, should be 7 days. Consider continuing antibiotic treatment for more than 7 days if:

- the baby has not yet fully recovered, or
- this is advisable, based on the pathogen identified on blood culture (seek expert microbiological advice if necessary).

1.7.3.2 If continuing antibiotics for longer than 36 hours despite negative blood cultures, review the baby at least once every 24 hours. On each occasion, using clinical judgement, consider whether it is appropriate to stop antibiotic treatment, taking account of:

- the level of initial clinical suspicion of infection
- the baby's clinical progress and current condition, and
- the levels and trends of C-reactive protein concentration.

1.7.4 Meningitis (babies in neonatal units)

1.7.4.1 If a baby is in a neonatal unit and meningitis is suspected but the causative pathogen is unknown (for example, because the cerebrospinal fluid Gram stain is uninformative), treat with intravenous amoxicillin and cefotaxime.

1.7.4.2 If a baby is in a neonatal unit and meningitis is shown to be due to Gram-negative infection either by cerebrospinal fluid Gram stain or culture, stop amoxicillin and treat with cefotaxime alone.

- 1.7.4.3 If a baby is in a neonatal unit and meningitis is shown by cerebrospinal fluid Gram stain to be due to a Gram-positive infection, continue treatment with intravenous amoxicillin and cefotaxime while awaiting the cerebrospinal fluid culture result and seek expert microbiological advice.
- 1.7.4.4 If the cerebrospinal fluid culture is positive for group B streptococcus consider changing the antibiotic treatment to:
- benzylpenicillin 50 mg/kg every 12 hours^[2], normally for at least 14 days, and
 - gentamicin in a starting dosage of 5 mg/kg every 36 hours^[1], with subsequent doses and intervals adjusted if necessary based on clinical judgement (see recommendation 1.6.1.4) and blood gentamicin concentrations (see recommendations 1.8.1.1–1.8.2.3); gentamicin treatment should continue for 5 days.
- 1.7.4.5 If the blood culture or cerebrospinal fluid culture is positive for listeria consider stopping cefotaxime and treating with amoxicillin and gentamicin.
- 1.7.4.6 If the cerebrospinal fluid culture identifies a Gram-positive bacterium other than group B streptococcus or listeria seek expert microbiological advice on management.

1.7.5 Discharge after antibiotic treatment

- 1.7.5.1 On completing antibiotic treatment, consider prompt discharge of the baby from hospital, with support for the parents and carers and a point of contact for advice.

1.8 Therapeutic drug monitoring for gentamicin

1.8.1 Trough concentrations

- 1.8.1.1 If a second dose of gentamicin is to be given (see recommendation 1.6.1.4) measure the trough blood gentamicin concentration immediately before giving the second dose. Consider the trough concentration before giving a third dose of gentamicin.

- 1.8.1.2 Hospital services should make blood gentamicin concentrations available to healthcare professionals in time to inform the next dosage decision (for example, within 30 hours of sampling).
- 1.8.1.3 Consider repeating the measurement of trough concentrations immediately before every third dose of gentamicin, or more frequently if necessary (for example, if there has been concern about previous trough concentrations or renal function).
- 1.8.1.4 Adjust the gentamicin dose interval, aiming to achieve trough concentrations of less than 2 mg/litre. If the course of gentamicin lasts more than three doses a trough concentration of less than 1 mg/litre is advised.
- 1.8.1.5 If an intended trough concentration measurement is not available, do not withhold the next dose of gentamicin unless there is evidence of renal dysfunction (for example, an elevated serum urea or creatinine concentration, or anuria).

1.8.2 Peak concentrations

- 1.8.2.1 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.
- 1.8.2.2 Measure peak concentrations 1 hour after starting the gentamicin infusion.
- 1.8.2.3 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.

1.9 Care setting

- 1.9.1.1 Using clinical judgement, consider completing a course of intravenous antibiotics outside of hospital (for example, at home or through visits to a

midwifery-led unit) in babies who are well without ongoing concerns if there is adequate local support.

- 1.9.1.2 When deciding on the appropriate care setting for a baby, take into account the baby's clinical needs and the competencies necessary to ensure safe and effective care (for example, the insertion and care of intravenous cannulas).

^[1] Gentamicin is licensed for use in newborn babies. The summary of product characteristics recommends a dosage of 4–7 mg/kg/day administered in a single dose. The evidence reviewed for the guideline supports a starting dosage of 5 mg/kg every 36 hours administered in a single dose.

^[2] Benzylpenicillin is licensed for use in newborn babies. The summary of product characteristics recommends a dosage of 50 mg/kg/day in two divided doses in babies under 1 week of age. In babies aged 1–4 weeks the dosage should be increased to 75 mg/kg/day in three divided doses, as recommended in the summary of product characteristics.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Women's and Children's Health to develop this guideline. The Centre established a Guideline Development Group (see [appendix A](#)), which reviewed the evidence and developed the recommendations.

There is more information about [how NICE clinical guidelines are developed](#) on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is also [available](#).

3 Implementation

NICE has developed tools to help organisations implement this guidance.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the [full guideline](#) (see section 5).

4.1 *Screening and intrapartum antibiotic prophylaxis for group B streptococcal colonisation*

What is the clinical and cost effectiveness of intrapartum antibiotic prophylaxis targeting group B streptococcus and guided by routine antenatal screening?

Why this is important

[Antenatal care](#) (NICE clinical guideline 62) considers the clinical and cost effectiveness of routine antenatal screening for group B streptococcus separately from the clinical and cost effectiveness of intrapartum antibiotic prophylaxis once group B streptococcus has been identified. This guideline considers the clinical and cost effectiveness of intrapartum antibiotic prophylaxis separately from the clinical and cost effectiveness of routine antenatal screening to identify women colonised with group B streptococcus.

Further research is needed to evaluate the clinical and cost effectiveness of routine antenatal screening for group B streptococcus combined with intrapartum antibiotic prophylaxis in women identified as carriers. The research could take the form of health economic modelling based on published studies or new studies (for example, randomised controlled trials or observational studies) comparing outcomes from different screening and treatment strategies. The research should also consider the gestational age at which screening should occur.

4.2 *Risk factors for early-onset neonatal infection and symptoms and signs*

Which risk factors for early-onset neonatal infection, clinical symptoms and signs of infection, and laboratory investigations should be used to identify babies who should receive antibiotics?

Why this is important

The evidence reviewed for the guideline included several risk scoring models designed to identify babies at risk of developing an early-onset neonatal infection and in whom antibiotic treatment

should be started. The models – which incorporated maternal and fetal risk factors for infection, clinical symptoms and signs of infection, and the results of laboratory investigations (such as C-reactive protein concentrations) – were intended for use before or after birth of the baby. However, the models were suboptimal because they were not specific to early-onset neonatal infection, or they were based on data collected using a case-control design (which tends to overestimate predictive accuracy because it includes extremes of the risk spectrum but not the harder to classify patients who are not obviously free from infection or confirmed as having an infection), or they did not examine predictive accuracy in independent training and validation sets.

Further research is needed, particularly to examine risk scoring models that incorporate measurements from novel laboratory investigations, such as molecular diagnostics (polymerase chain reaction and 16S approaches). The ideal study design would be a randomised controlled trial that compares clinical outcomes associated with particular investigation and treatment initiation strategies. The next best design would be a prospective cohort study to determine the predictive accuracy of an investigation strategy or a risk scoring model evaluated in a clinically relevant group of babies that is independent of the study population used to derive the risk scoring model.

4.3 *Intrapartum antibiotic prophylaxis in preterm labour*

What is the clinical and cost effectiveness of intrapartum antibiotic prophylaxis using benzylpenicillin in women with preterm labour?

Why this is important

In the absence of unequivocal evidence of clinical and cost effectiveness of intrapartum antibiotic prophylaxis to prevent early-onset neonatal infection in the babies of all women with preterm labour, the recommendation to consider intrapartum antibiotic prophylaxis for women with preterm labour and either prelabour rupture of membranes or confirmed or suspected rupture of membranes of 18 hours' duration or longer was based on the Guideline Development Group's consensus view and knowledge of current practice.

Further research is needed to evaluate the clinical and cost effectiveness of intrapartum antibiotic prophylaxis using benzylpenicillin compared with placebo in women with preterm labour (including women with intact membranes and those with ruptured membranes). The research should be conducted through multicentre randomised controlled trials, including some UK centres to allow subgroup analysis of UK data. The primary outcome for evaluating the clinical effectiveness of benzylpenicillin should be the incidence of early-onset neonatal group B streptococcal infection (infection within 72 hours of birth). Secondary outcomes should include long-term outcomes in the

baby. The research should include subgroup analyses for women in spontaneous preterm labour with intact membranes and those with membranes that rupture before or during labour.

4.4 *Investigations during antibiotic treatment*

What is the clinical and cost effectiveness of laboratory investigations used individually or in combination to exclude early-onset neonatal infection in babies receiving antibiotics for suspected infection?

Why this is important

The systematic reviews conducted for the guideline identified limited evidence relating to investigations used to guide the decision to stop antibiotic treatment in babies receiving antibiotics for suspected early-onset neonatal infection. One study evaluated procalcitonin-guided decision making for identifying babies in whom antibiotic treatment could safely be stopped, but the approach used was at an early stage of development and had not been evaluated fully.

The guideline recommendations reflected uncertainty about the diagnostic test accuracy of laboratory investigations used individually or in combination, and further research involving sufficiently powered studies is needed to evaluate this. The ideal study design would be a randomised controlled trial that compares clinical outcomes associated with particular investigation and treatment termination strategies. The next best design would be a prospective cohort study to determine the diagnostic test accuracy of an investigation strategy evaluated in a clinically relevant group of babies. The research should examine clinical effectiveness or diagnostic test accuracy in preterm and term babies separately.

4.5 *Duration of antibiotic treatment*

What is the optimal duration of treatment (course length) in babies who receive antibiotics for confirmed early-onset neonatal infection?

Why this is important

The Guideline Development Group identified no evidence to inform the choice of duration of antibiotic treatment (course length) for confirmed early-onset neonatal infection. In the absence of evidence, the Guideline Development Group based its recommendations on its knowledge of current clinical practice. Further research is needed to evaluate different course lengths in the following clinical circumstances:

- babies with group B streptococcal bacterial meningitis
- babies with group B streptococcal septicaemia
- babies with Gram-negative bacterial meningitis (such as *Escherichia coli* meningitis)
- babies with Gram-negative septicaemia.

The research should ideally take the form of multinational randomised controlled trials. The primary outcome should be relapse within 10 days of stopping treatment. Secondary outcomes should include long-term neurodevelopment.

5 Other versions of this guideline

5.1 *Full guideline*

The full guideline, [Antibiotics for early-onset neonatal infection: antibiotics for the prevention and treatment of early-onset neonatal infection](#) contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Women's and Children's Health.

5.2 *NICE pathway*

The recommendations from this guideline have been incorporated into a [NICE pathway](#).

5.3 *Information for the public*

NICE has produced [information for the public](#) explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this information in their own materials about antibiotics for early-onset neonatal infection.

6 Related NICE guidance

Published

- [Caesarean section](#). NICE clinical guideline 132 (2011).
- [Bacterial meningitis and meningococcal septicaemia](#). NICE clinical guideline 102 (2010).
- [Induction of labour](#). NICE clinical guideline 70 (2008).
- [Antenatal care](#). NICE clinical guideline 62 (2008).
- [Intrapartum care](#). NICE clinical guideline 55 (2007). Update in progress. Publication date to be confirmed.
- [Urinary tract infection in children](#). NICE clinical guideline 54 (2007).
- [Feverish illness in children](#). NICE clinical guideline 47 (2007). Update in progress. Publication expected May 2013.
- [Postnatal care](#). NICE clinical guideline 37 (2006).

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations. Please see our website for information about updating the guideline.

Appendix A: The Guideline Development Group, National Collaborating Centre and NICE project team

Guideline Development Group

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About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

The guideline was developed by the National Collaborating Centre for Women's and Children's Health, which is based at the Royal College of Obstetricians and Gynaecologists. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

The recommendations from this guideline have been incorporated into a [NICE pathway](#). We have produced [information for the public](#) explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also [available](#).

Changes after publication

October 2012: Minor maintenance

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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