NICE National Institute for Health and Care Excellence

Royal College of Obstetricians & Gynaecologists

NICE guideline

Neonatal infection: antibiotics for prevention and treatment

NICE guideline
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www.nice.org.uk/guidance/ng195

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.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

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.

Contents

This guideline partially replaces CG149.

This guideline is the basis of QS75 and QS37.

This guideline should be read in conjunction with NG240.

Overview

This guideline covers preventing bacterial infection in healthy babies of up to and including 28 days corrected gestational age, treating pregnant women whose unborn baby is at risk of infection, and caring for babies of up to and including 28 days corrected gestational age with a suspected or confirmed bacterial infection. It aims to reduce delays in recognising and treating infection and prevent unnecessary use of antibiotics. The guideline does not cover viral infections.

The guideline uses the terms 'woman' or 'mother' throughout. These should be taken to include people who do not identify as women but are pregnant or have given birth. Similarly, where the term 'parents' is used, this should be taken to include anyone who has main responsibility for caring for a baby. We recognise there are many different family arrangements.

Who is it for?

- Healthcare professionals in primary and secondary care
- Commissioners and providers of neonatal and maternity services
- Parents and carers of babies who are at risk of or who have a neonatal infection

Recommendations

Parents and carers have the right to be involved in planning and making decisions about their baby's health and care, and to be given information and support to enable them to do this, as set out in the NHS Constitution and summarised in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Please note that the Royal College of Obstetricians and Gynaecologists has produced guidance on COVID-19 and pregnancy for all midwifery and obstetric services. The Royal College of Paediatrics and Child Health has published guidance on COVID-19 for neonatal services.

Throughout this guideline, unless otherwise specified, the term neonatal infection covers both early-onset and late-onset infections.

1.1 Information and support

1.1.1 For guidance on communication (including different formats and languages), providing information, and shared decision making, see the NICE guidelines on patient experience in adult NHS services, babies, children and young people's experience of healthcare and shared decision making. **[2021]**

Parents and carers of babies at increased risk of neonatal infection

1.1.2 If clinical concerns about possible neonatal infection arise at any point:

- talk to the baby's parents and carers, explaining the reason for concern, and

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explain what neonatal infection is

- discuss the options for management that may be best for their baby (for example, observation, investigations or antibiotic treatment)
- do not delay treatment, but when possible give the baby's parents and carers time to think about the information they have been given and ask any questions they may have before making treatment decisions. **[2021]**

1.1.3 If giving antibiotics because of clinical concerns about possible early- or late-onset neonatal infection, discuss with parents and carers:

- the reason for the treatment
- the risks and benefits in relation to their baby's circumstances
- the observations and investigations that might be needed to guide treatment (for example, to help decide when to stop treatment)
- the preferred antibiotic regimen (including how it will be delivered) and likely duration of treatment
- the impact, if any, on where the woman or her baby will be cared for. **[2021]**

1.1.4 To maintain communication with a woman in labour whose baby is at increased risk of early-onset neonatal infection:

- 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
- include an update in the handover about the presence of any infection.

  For more guidance, see the section on communication in the NICE guideline on intrapartum care. **[2012]**

1.1.5 For babies who are considered to be at increased risk of early-onset infection, inform their parents and GP about this verbally and in writing:

- when the baby is discharged from the hospital or midwifery-led unit **or**

- in the immediate postnatal period, if the baby was born at home. **[2012]**

1.1.6 Reassure parents and carers that babies who have or are at increased risk of neonatal infection can usually continue to breastfeed, and that every effort will be made to help with this. If a baby is temporarily unable to breastfeed, support the mother to express breast milk if she wishes to do so. **[2012]**

1.1.7 When a woman is identified as having group B streptococcal colonisation, bacteriuria or infection during her current pregnancy:

- advise the woman that if she becomes pregnant again:
  - that her new baby will be at increased risk of early-onset group B streptococcal infection
  - she should inform her maternity care team that she has had a positive group B streptococcal infection test in a previous pregnancy
  - her maternity care team will offer her antibiotics in labour
- inform the woman's GP in writing that there is a risk of group B streptococcal infection in babies in future pregnancies. **[2012, amended 2021]**

Parents and carers of babies treated for neonatal infection

1.1.8 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. **[2012]**

1.1.9 Offer parents and carers contact details of organisations that provide parent support, befriending, counselling, information and advocacy. **[2012]**

1.1.10 If a baby has been treated for suspected or confirmed neonatal infection:

- advise 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. **[2021]**

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:
  - that her new baby will be at increased risk of early-onset group B streptococcal infection
  - she should inform her maternity care team that she has had a previous baby with a group B streptococcal infection
  - her maternity care team will offer her antibiotics in labour
- inform the woman's GP in writing that there is a risk of:
  - group B streptococcal infection recurrence in the baby and
  - group B streptococcal infection in babies in future pregnancies. **[2012]**

Parents and carers of babies being treated for bacterial meningitis

1.1.12 Early in the management of confirmed bacterial meningitis, discuss the following with parents and carers:

- what might happen during the course of the disease
- the uncertainty about the initial prognosis, and when they can expect to know more
- the risk of passing on the infection
- whether close contacts need to take any preventative measures (for example, for meningococcal meningitis or Haemophilus influenzae type b). **[2024]**

1.1.13 Repeat information over time and check the parents and carers understand, as they may be distressed and unable to ask questions when their baby is first diagnosed. **[2024]**

1.1.14 Provide emotional and pastoral support for family members and carers during hospitalisation. **[2024]**

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on information and support after diagnosis.

Full details of the evidence and the committee's discussion are in evidence review J: information for confirmed bacterial meningitis and evidence review K: support for confirmed bacterial meningitis.

Parents and carers of all babies

1.1.15 Before any baby is transferred home from the hospital or midwifery-led unit (or in the immediate postnatal period in the case of babies born at home), advise parents and carers to seek urgent medical help (for example, from NHS 111, their GP, or an accident and emergency department) if they are concerned that their baby:

- is showing abnormal behaviour (for example, inconsolable crying or listlessness) **or**
- is unusually floppy **or**
- has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C) **or**
- has abnormal breathing (rapid breathing, difficulty in breathing or grunting) **or**
- has a change in skin colour (for example, where the baby becomes very pale, blue/grey or dark yellow) **or**
- has developed new difficulties with feeding.

Give the advice both in person, and as written information and advice for them to take away. **[2021]**

Post-discharge planning for babies who have not been given antibiotics

1.1.16 When there has been a clinical concern about neonatal infection in a baby, make 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. **[2012]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on information and support.

Full details of the evidence and the committee's discussion are in evidence review A: information and support.

1.2 Preventing early-onset neonatal infection before birth

Intrapartum antibiotics

1.2.1 Offer antibiotics during labour to women who:

- are in pre-term labour **or**
- have group B streptococcal colonisation, bacteriuria or infection during the current pregnancy **or**

- have had group B streptococcal colonisation, bacteriuria or infection in a previous pregnancy, and have not had a negative test for group B streptococcus by enrichment culture or polymerase chain reaction (PCR) on a rectovaginal swab samples collected between 35 and 37 weeks' gestation or 3 to 5 weeks before the anticipated delivery date in the current pregnancy **or**
- have had a previous baby with an invasive group B streptococcal infection **or**
- have a clinical diagnosis of chorioamnionitis. **[2021]**

1.2.2 Use table 1 to decide which antibiotic to use when giving intrapartum antibiotics for neonatal infection.

Table 1 Intrapartum antibiotics

Allergies	Women without chorioamnionitis	Women with chorioamnionitis
No penicillin allergy	Use Benzylpenicillin.	Use Benzylpenicillin plus gentamicin plus metronidazole.
Penicillin allergy that is not severe	Use Cephalosporin with activity against group B streptococcus (for example, cefotaxime). Use with caution. In April 2021 this was an off-label use of cephalosporins. See NICE's information on prescribing medicines.	Use Cephalosporin with activity against group B streptococcus (for example, cefotaxime) plus metronidazole. Use with caution. In April 2021 this was an off-label use of cephalosporins. See NICE's information on prescribing medicines.

Allergies	Women without chorioamnionitis	Women with chorioamnionitis
Severe penicillin allergy	Consider: Vancomycin **or** An alternative antibiotic that would be expected to be active against group B streptococcus based on either sensitivity testing performed on the woman's isolate or on local antibiotic susceptibility surveillance data. In April 2021 this was an off-label use of vancomycin. See NICE's information on prescribing medicines.	Consider: Vancomycin plus gentamicin plus metronidazole **or** An alternative antibiotic to vancomycin that would be expected to be active against group B streptococcus based on either sensitivity testing performed on the woman's isolate or on local antibiotic susceptibility surveillance data plus gentamicin plus metronidazole. In April 2021 this was an off-label use of vancomycin. See NICE's information on prescribing medicines.

1.2.3 If using intravenous gentamicin during labour, use once-daily dosing. **[2021]**

1.2.4 Give the first dose of antibiotics as soon as possible after labour starts (or as soon as infection is suspected, in the case of chorioamnionitis), and continue until the birth of the baby. **[2021]**

1.2.5 Be aware that therapeutic drug monitoring may be needed when using gentamicin or vancomycin during labour. **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on intrapartum antibiotics.

Full details of the evidence and the committee's discussion are in evidence review B: intrapartum antibiotics.

Women with prolonged prelabour rupture of membranes who have group B streptococcal colonisation, bacteriuria or infection

1.2.6 Offer an immediate birth (by induction of labour or caesarean birth) to women who are between 34 and 37 weeks' gestation who:

- have prolonged prelabour rupture of membranes **and**
- have group B streptococcal colonisation, bacteriuria or infection at any time in their current pregnancy. **[2021]**

For a short explanation of why the committee made the 2021 recommendation and how it might affect practice, see the rationale and impact section on women with prolonged prelabour rupture of membranes.

Full details of the evidence and the committee's discussion are in evidence review C: timing of delivery.

1.3 Risk factors for and clinical indicators of possible early-onset neonatal infection

Before birth

1.3.1 For women in labour, identify and assess any risk factors for early-onset neonatal infection (see box 1). Throughout labour, monitor for any new risk factors. **[2021]**

1.3.2 For guidance on managing prelabour rupture of membranes at term, see the NICE guideline on intrapartum care. **[2021]**

Assessing and managing the risk of early-onset neonatal infection after birth

1.3.3 If there are any risk factors for early-onset neonatal infection (see box 1), or if there are clinical indicators of possible early-onset neonatal infection (see box 2):

- perform an immediate clinical assessment
- review the maternal and neonatal history
- carry out a physical examination of the baby, including an assessment of vital signs. **[2021]**

1.3.4 If group B streptococcus is first identified in the mother within 72 hours after the baby's birth:

- ask those directly involved in the baby's care (for example, a parent, carer, or healthcare professional) whether they have any concerns in relation to the clinical indicators listed in box 2 **and**
- identify any other risk factors present **and**
- look for clinical indicators of infection.

  Use this assessment to decide on clinical management (see recommendation 1.3.5). **[2021]**

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

Red flag risk factor:

- Suspected or confirmed infection in another baby in the case of a multiple pregnancy.

Other risk factors:

- Invasive group B streptococcal infection in a previous baby or maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy.
- Pre-term birth following spontaneous labour before 37 weeks' gestation.
- Confirmed rupture of membranes for more than 18 hours before a pre-term birth.
- Confirmed prelabour rupture of membranes at term for more than 24 hours before the onset of labour.
- Intrapartum fever higher than 38°C if there is suspected or confirmed bacterial infection.
- Clinical diagnosis of chorioamnionitis.

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

Red flag clinical indicators:

- Apnoea (temporary stopping of breathing)
- Seizures
- Need for cardiopulmonary resuscitation
- Need for mechanical ventilation
- Signs of shock

Other clinical indicators:

- 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 (including grunting, recession, tachypnoea)
- Hypoxia (for example, central cyanosis or reduced oxygen saturation level)
- Persistent pulmonary hypertension of newborns
- Jaundice within 24 hours of birth
- Signs of neonatal encephalopathy
- Temperature abnormality (lower than 36°C or higher than 38°C) unexplained by environmental factors
- Unexplained excessive bleeding, thrombocytopenia, or abnormal coagulation

- Altered glucose homeostasis (hypoglycaemia or hyperglycaemia)
- Metabolic acidosis (base deficit of 10 mmol/litre or greater)

1.3.5 Use the following framework, based on the risk factors in box 1 and the clinical indicators in box 2, to make antibiotic management decisions as directed:

- In babies with any red flag, or with 2 or more 'non-red-flag' risk factors or clinical indicators:
  - follow recommendations 1.4.1 to 1.4.18 on investigations before starting antibiotics **and**
  - start antibiotic treatment according to recommendations 1.5.1 to 1.6.6 **and**
  - do not wait for the test results before starting antibiotics
- in babies without red flags and only 1 risk factor or 1 clinical indicator, use clinical judgement to decide:
  - whether it is safe to withhold antibiotics **and**
  - whether the baby's vital signs and clinical condition need to be monitored. If monitoring is needed, continue for at least 12 hours using a newborn early warning system
- for babies without risk factors or clinical indicators of possible infection, continue routine postnatal care as covered in the NICE guideline on postnatal care. **[2021]**

Kaiser Permanente neonatal sepsis calculator

1.3.6 The Kaiser Permanente neonatal sepsis calculator can be used as an alternative to the framework outlined in recommendation 1.3.5 for babies born after 34+0 weeks of pregnancy who are being cared for in a neonatal unit, transitional care or postnatal ward. It should only be used if it is part of a prospective audit,

which should record:

- total number of babies assessed using the calculator
- number of babies correctly identified by the calculator who develop a culture-confirmed neonatal infection
- number of babies incorrectly identified by the calculator who do not develop a culture-confirmed neonatal infection
- number of babies missed by the calculator who develop a culture-confirmed neonatal infection. **[2021]**

1.3.7 If using the Kaiser Permanente neonatal sepsis calculator (see recommendation 1.3.6) to assess the risk of early-onset neonatal infection, use the classification given by the calculator to direct management decisions. **[2021]**

Management for babies at increased risk of infection

1.3.8 In babies being monitored for possible early-onset neonatal infection:

- Consider starting antibiotic treatment (see recommendations 1.4.1 to 1.4.18 on investigations before starting antibiotics, and recommendations 1.5.1 to 1.5.9 on which antibiotics to use).
- If no further concerns arise during observation reassure the family and, if the baby is to be discharged, give information and advice to the parents and carers (see recommendations 1.1.15 and 1.1.16). **[2021]**

1.3.9 If a baby needs antibiotic treatment, give this as soon as possible and always within 1 hour of the decision to treat. **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on risk factors for and clinical indicators of possible early-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review D: maternal and neonatal risk factors.

1.4 Investigations before starting antibiotics in babies who may have early-onset infection

1.4.1 When starting antibiotic treatment in babies who may have early-onset neonatal infection (see recommendations on recognising risk factors and clinical indicators), perform a blood culture before giving the first dose. **[2012]**

1.4.2 Measure baseline C-reactive protein concentration when starting antibiotic treatment in babies who may have early-onset neonatal infection. **[2012]**

1.4.3 Do not routinely perform urine microscopy or culture as part of the investigations for early-onset neonatal infection. **[2012]**

1.4.4 Do not perform skin swab microscopy or culture as part of the investigations for early-onset neonatal infection if there are no clinical signs of a localised infection. **[2012]**

Lumbar puncture

1.4.5 If it is safe to do so, perform a lumbar puncture to obtain a cerebrospinal fluid sample when:

- there is a strong clinical suspicion of early-onset neonatal infection **or**
- there are clinical symptoms or signs suggesting meningitis. **[2012]**

1.4.6 Treat and stabilise any of the following before performing a lumbar puncture:

- unprotected airway
- respiratory compromise
- shock
- uncontrolled seizures
- bleeding risk. **[2024]**

1.4.7 Do not perform lumbar puncture if there is:

- extensive or rapidly spreading purpura
- infection at the lumbar puncture site
- risk factors for an evolving space-occupying lesion
- any of these symptoms or signs, which might indicate raised intracranial pressure:
  - new focal neurological features (including seizures or posturing)
  - abnormal pupillary reactions
  - a progressive and sustained or rapid fall in level of consciousness. **[2024]**

1.4.8 Measure blood glucose in babies immediately before lumbar puncture, so that the cerebrospinal fluid to blood glucose ratio can be calculated. **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on lumbar puncture.

Full details of the evidence and the committee's discussion are in evidence review L: investigating and diagnosing suspected bacterial meningitis with cerebrospinal fluid parameters.

Cerebrospinal fluid investigations in babies with suspected bacterial

meningitis

1.4.9 Perform the following cerebrospinal fluid investigations in babies with suspected bacterial meningitis:

- red and white cell count and cell type (including differential white cell count)
- total protein
- glucose concentration (to calculate cerebrospinal fluid to blood glucose ratio)
- microscopy for bacteria (using gram stain)
- microbiological culture and sensitivities
- PCR for relevant pathogens. **[2024]**

1.4.10 Store the remaining cerebrospinal fluid in case more tests are needed. **[2024]**

1.4.11 Ensure that cerebrospinal fluid, cell counts, total protein and glucose concentrations are available within 4 hours of lumbar puncture. **[2024]**

1.4.12 When interpreting the results of cerebrospinal fluid investigations, take into account:

- red cells in the sample, which may suggest blood contamination or a different diagnosis
- whether earlier antibiotics may have reduced the diagnostic reliability of these investigations. **[2024]**

1.4.13 Interpret cerebrospinal fluid results using standard age-appropriate threshold values (taking into account factors such as gestational age, chronological age, birth weight, and earlier antibiotic use or suspected immunodeficiency). **[2024]**

1.4.14 Interpret cerebrospinal fluid results in babies alongside the clinical presentation and maternal history. **[2024]**

1.4.15 If cerebrospinal fluid results are abnormal, consider alternative viral, mycobacterial, fungal or non-infectious causes as well as bacterial meningitis.

[2024]

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on cerebrospinal fluid investigations in babies with suspected bacterial meningitis.

Full details of the evidence and the committee's discussion are in evidence review L: investigating and diagnosing suspected bacterial meningitis with cerebrospinal fluid parameters.

Advice for site-specific infections

1.4.16 Be aware that, although minor conjunctivitis with encrusted eyelids is common and often benign, a purulent discharge may indicate a serious infection (for example, with chlamydia or gonococcus). **[2012]**

1.4.17 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 waiting for the swab microbiology results. **[2012]**

1.4.18 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 **and**
- take a swab sample for microscopy and culture **and**
- start antibiotic treatment with intravenous flucloxacillin and gentamicin (see recommendations 1.5.3 and 1.5.4).

  If the microbiology results show that the infection is not caused by a Gram-negative bacterium, stop the gentamicin. **[2012]**

1.5 Antibiotics for suspected early-onset infection

1.5.1 Use intravenous benzylpenicillin with gentamicin as the first-choice antibiotic regimen for empirical treatment of suspected early-onset infection, unless microbiological surveillance data show local bacterial resistance patterns that indicate the need for a different antibiotic. **[2012]**

1.5.2 Give benzylpenicillin in a dosage of 25 mg/kg every 12 hours. Consider shortening the dose interval to every 8 hours, based on clinical judgement (for example, if the baby appears very ill). **[2012]**

1.5.3 Give gentamicin in a starting dose of 5 mg/kg (see recommendation 1.5.4). **[2012]**

1.5.4 When prescribing gentamicin, be aware that:

- the summary of product characteristics recommends a dosage of 4 to 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.

  In 2021, a dosage of 5 mg/kg every 36 hours is an off-label use of gentamicin. See NICE's information on prescribing medicines. **[2012]**

1.5.5 If a second dose of gentamicin is given (see recommendation 1.6.3) this should usually be 36 hours after the first dose. Use a shorter interval if clinical judgement suggests this is needed, for example, if:

- the baby appears very ill
- the blood culture shows a Gram-negative infection. **[2012]**

1.5.6 Take account of blood gentamicin concentrations when deciding on subsequent gentamicin dosing regimen (see recommendations 1.15.1 to 1.15.8). **[2012]**

1.5.7 Record the times of:

- gentamicin administration

- sampling for therapeutic monitoring. **[2012]**

1.5.8 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, including local surveillance data. **[2012]**

1.5.9 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. **[2012]**

1.6 Duration of antibiotic treatment for early-onset neonatal infection

Investigations during antibiotic treatment for early-onset neonatal infection

1.6.1 In babies given antibiotics because of risk factors for infection or clinical indicators of possible early-onset infection, measure the C-reactive protein concentration 18 to 24 hours after presentation. **[2012]**

1.6.2 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 positive blood culture (other than coagulase negative staphylococcus) **or**
- the baby does not respond satisfactorily to antibiotic treatment, **or**

- there is a strong clinical suspicion of infection **or**
- there are clinical symptoms or signs suggesting meningitis. **[2012, amended 2021]**

Decisions 36 hours after starting antibiotic treatment

1.6.3 In babies given antibiotics because of risk factors for early-onset 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. **[2012]**

1.6.4 Consider establishing hospital systems to provide blood culture results 36 hours after starting antibiotics, to allow timely stopping of treatment and discharge from hospital. **[2012]**

1.6.5 Healthcare professionals with specific experience in neonatal infection should be available every day to give clinical microbiology or paediatric infectious disease advice. **[2012]**

Treatment duration for early-onset neonatal infection without meningitis

1.6.6 Give antibiotic treatment for 7 days for babies with a positive blood culture, and for babies with a negative blood culture if sepsis has been strongly suspected. Consider continuing antibiotic treatment for more than 7 days if:

- the baby has not yet fully recovered **or**
- this is advisable because of the pathogen identified on blood culture (seek expert microbiological advice if necessary). **[2012]**

1.6.7 If continuing antibiotics for longer than 36 hours despite negative blood cultures, review the baby at least once every 24 hours. Consider at each review whether it is appropriate to stop antibiotic treatment, taking account of:

- the level of initial clinical suspicion of infection **and**
- the baby's clinical progress and current condition **and**
- the levels and trends of C-reactive protein concentration. **[2012]**

1.7 Antibiotic-impregnated intravascular catheters for reducing the risk of late-onset neonatal infection

1.7.1 Do not use rifampicin-miconazole-impregnated catheters for newborn babies. **[2021]**

For a short explanation of why the committee made the 2021 recommendation and how it might affect practice, see the rationale and impact section on antibiotic-impregnated intravascular catheters for reducing the risk of late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review F: intravascular catheters.

1.8 Risk factors for and clinical indicators of possible late-onset neonatal infection

1.8.1 When assessing or reviewing a baby:

- Check for, the possible clinical indicators of late-onset neonatal infection shown in table 2.
- take into account that prematurity, mechanical ventilation, history of surgery and presence of a central catheter are associated with greater risk of late-onset neonatal infection.
- Think about infection in the other babies when one baby from a multiple birth has infection. **[2021]**

1.8.2 Seek early advice from a paediatrician when late-onset infection is suspected in non-inpatient settings. **[2021]**

1.8.3 Refer to the NICE guidelines on fever in under 5s and suspected sepsis when assessing babies for late-onset neonatal infection who have been admitted to the hospital from home. **[2021]**

Be aware that some pulse oximeters can underestimate or overestimate oxygen saturation levels, especially if the saturation level is borderline. Overestimation has been reported in people with dark skin. See also the NHS England Patient Safety Alert on the risk of harm from inappropriate placement of pulse oximeter probes.

Table 2 Clinical indicators of possible late-onset neonatal infection (observations and events in the baby)

Category	Indicators
Behaviour	Parent or care-giver concern for change in behaviour Appears ill to a healthcare professional Does not wake, or if roused does not stay awake Weak high-pitched or continuous cry

Category	Indicators
Respiratory	Raised respiratory rate: 60 breaths per minute or more Grunting Apnoea Oxygen saturation of less than 90% in air or increased oxygen requirement over baseline
Circulation and hydration	Persistent tachycardia: heart rate 160 beats per minute or more Persistent bradycardia: heart rate less than 100 beats per minute
Skin	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin
Other	Temperature 38°C or more unexplained by environmental factors Temperature less than 36°C unexplained by environmental factors Alterations in feeding pattern Abdominal distension Seizures Bulging fontanelle

This table has been adapted from the high-risk criteria in table 1 of the NICE guideline on suspected sepsis.

Timing of antibiotics for late-onset neonatal infection

1.8.4 If a baby needs antibiotic treatment, give this as soon as possible and always within 1 hour of the decision to treat. **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on risk factors for and clinical indicators of possible late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review E: risk factors for late-onset neonatal infection.

1.9 Investigations before starting antibiotics in babies who may have late-onset infection

1.9.1 When starting antibiotic treatment in babies who may have late-onset neonatal infection (see recognising risk factors and clinical indicators), perform a blood culture before giving the first dose. **[2021]**

1.9.2 Measure baseline C-reactive protein concentration when starting antibiotic treatment in babies who may have late-onset neonatal infection. Use this together with later readings to assess the likelihood of infection and response to treatment. **[2021]**

1.9.3 Do not routinely perform urine microscopy or culture as part of the investigations for late-onset neonatal infection for babies in neonatal units. **[2021]**

1.9.4 Perform urine microscopy and culture for babies outside of neonatal units in line with the NICE guideline on urinary tract infection in under 16s.

1.9.5 Do not perform skin swab microscopy or culture as part of the investigations for late-onset neonatal infection if there are no clinical signs of a localised infection. **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on investigations for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review G: investigations before starting treatment.

Lumbar puncture

1.9.6 If it is safe to do so, perform a lumbar puncture to obtain a cerebrospinal fluid sample when:

- there is a strong clinical suspicion of neonatal infection **or**

- there are clinical symptoms or signs suggesting meningitis. **[2021]**

For a short explanation of why the committee made the 2021 recommendation and how it might affect practice, see the rationale and impact section on investigations for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review G: investigations before starting treatment.

1.9.7 Treat and stabilise any of the following before performing a lumbar puncture:

- unprotected airway
- respiratory compromise
- shock
- uncontrolled seizures
- bleeding risk. **[2024]**

1.9.8 Do not perform lumbar puncture if there is:

- extensive or rapidly spreading purpura
- infection at the lumbar puncture site
- risk factors for an evolving space-occupying lesion
- any of these symptoms or signs, which might indicate raised intracranial pressure:
  - new focal neurological features (including seizures or posturing)
  - abnormal pupillary reactions
  - a progressive and sustained or rapid fall in level of consciousness. **[2024]**

1.9.9 Measure blood glucose in babies immediately before lumbar puncture, so that the

cerebrospinal fluid to blood glucose ratio can be calculated. **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on lumbar puncture.

Full details of the evidence and the committee's discussion are in evidence review L: investigating and diagnosing suspected bacterial meningitis with cerebrospinal fluid parameters.

Cerebrospinal fluid investigations in babies with suspected bacterial meningitis

1.9.10 Perform the following cerebrospinal fluid investigations in babies with suspected bacterial meningitis:

- red and white cell count and cell type (including differential white cell count)
- total protein
- glucose concentration (to calculate cerebrospinal fluid to blood glucose ratio)
- microscopy for bacteria (using gram stain)
- microbiological culture and sensitivities
- PCR for relevant pathogens. **[2024]**

1.9.11 Store the remaining cerebrospinal fluid in case more tests are needed. **[2024]**

1.9.12 Ensure that cerebrospinal fluid, cell counts, total protein and glucose concentrations are available within 4 hours of lumbar puncture. **[2024]**

1.9.13 When interpreting the results of cerebrospinal fluid investigations, take into account:

- red cells in the sample, which may suggest blood contamination or a different diagnosis

- whether earlier antibiotics may have reduced the diagnostic reliability of these investigations. **[2024]**

1.9.14 Interpret cerebrospinal fluid results using standard age-appropriate threshold values (taking into account factors such as gestational age, chronologic age, birth weight, and earlier antibiotic use or suspected immunodeficiency). **[2024]**

1.9.15 Interpret cerebrospinal fluid results in babies alongside the clinical presentation and maternal history. **[2024]**

1.9.16 If cerebrospinal fluid results are abnormal, consider alternative viral, mycobacterial, fungal or non-infectious causes as well as bacterial meningitis. **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on cerebrospinal fluid investigations in babies with suspected bacterial meningitis.

Full details of the evidence and the committee's discussion are in evidence review L: investigating and diagnosing suspected bacterial meningitis with cerebrospinal fluid parameters.

1.10 Antibiotics for late-onset neonatal infection

Choice of antibiotics

1.10.1 For babies with suspected late-onset neonatal infection who are already in a neonatal unit:

- give a combination of narrow-spectrum antibiotics (such as intravenous flucloxacillin plus gentamicin) as first-line treatment
- use local antibiotic susceptibility and resistance data (or national data if local data are inadequate) when deciding which antibiotics to use

- give antibiotics that are effective against both Gram-negative and Gram-positive bacteria
- if necrotising enterocolitis is suspected, also include an antibiotic that is active against anaerobic bacteria (such as metronidazole). **[2021]**

1.10.2 For babies with suspected late-onset neonatal infection or meningitis who have been admitted from home, treat according to recommendation 1.14.6 in the NICE guideline on suspected sepsis. **[2021]**

1.10.3 When using gentamicin, see recommendations 1.15.1 to 1.15.8 on therapeutic drug monitoring for gentamicin. **[2021]**

1.11 Duration of antibiotic treatment for late-onset neonatal infection

Investigations during antibiotic treatment for late-onset neonatal infection

1.11.1 In babies given antibiotics because of risk factors for infection or clinical indicators of possible late-onset neonatal infection, measure the C-reactive protein concentration 18 to 24 hours after starting antibiotics. **[2021]**

1.11.2 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 positive blood culture (other than coagulase negative staphylococcus) **or**
- the baby does not respond satisfactorily to antibiotic treatment, **or**
- there is a strong clinical suspicion of infection **or**
- there are clinical symptoms or signs suggesting meningitis. **[2021]**

Decisions 48 hours after starting antibiotic treatment

1.11.3 For babies given antibiotics because of suspected late-onset infection, consider stopping the antibiotics at 48 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. **[2021]**

1.11.4 Healthcare professionals with specific experience in neonatal infection should be available every day to give clinical microbiology or paediatric infectious disease advice. **[2021]**

Treatment duration for late-onset neonatal infection without meningitis

1.11.5 Give antibiotic treatment for 7 days for babies with a positive blood culture. Consider continuing antibiotic treatment for more than 7 days if:

- the baby has not yet fully recovered **or**
- longer treatment is needed because of the pathogen identified on blood culture (for example, Gram-negative bacteria or *Staphylococcus aureus*; seek expert microbiological advice if necessary) **or**
- longer treatment is needed because of the site of the infection (such as intra-abdominal co-pathology, necrotising enterocolitis, osteomyelitis or infection of a central venous catheter). **[2021]**

1.11.6 Use a shorter treatment duration than 7 days when the baby makes a prompt recovery, and either no pathogen is identified or the pathogen identified is a common commensal (for example, coagulase negative staphylococcus). **[2021]**

1.11.7 If continuing antibiotics for longer than 48 hours for suspected late-onset neonatal infection despite negative blood culture, review the baby at least once every 24 hours. At each review, decide whether to stop antibiotics, taking account of:

- the level of initial clinical suspicion of infection **and**
- the baby's clinical progress and current condition **and**
- the levels and trends of C-reactive protein. **[2021]**

1.11.8 For guidance on treatment duration for suspected or confirmed meningitis, refer to the section on meningitis (babies in neonatal units). **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on antibiotics for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review H: antibiotics.

1.12 Antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection

1.12.1 Give prophylactic oral nystatin to babies treated with antibiotics for suspected late-onset neonatal bacterial infection if they:

- have a birthweight of up to 1,500 g **or**
- were born at less than 30 weeks' gestation. **[2021]**

  If oral administration of nystatin is not possible, give intravenous fluconazole. In April 2021, this was an off-label use of fluconazole. See NICE's information on prescribing medicines and use clinical judgement to determine the dosage. **[2021]**

For a short explanation of why the committee made the 2021 recommendations and how they might affect practice, see the rationale and impact section on antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review I: antifungals.

1.13 Avoiding routine use of antibiotics in babies

1.13.1 Do not routinely give antibiotic treatment to babies without risk factors for infection or clinical indicators or laboratory evidence of possible infection. **[2012]**

1.14 Early- and late-onset meningitis (babies in neonatal units)

1.14.1 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. **[2012, amended 2021]**

1.14.2 If a baby is in a neonatal unit and meningitis is shown (by either cerebrospinal fluid Gram stain or culture) to be caused by Gram-negative infection, stop amoxicillin and treat with cefotaxime alone. **[2012, amended 2021]**

1.14.3 If a baby is in a neonatal unit and meningitis is shown (by cerebrospinal fluid Gram stain) to be caused by a Gram-positive bacterium:

- continue treatment with intravenous amoxicillin and cefotaxime while waiting for the cerebrospinal fluid culture result **and**
- seek expert microbiological advice. **[2012, amended 2021]**

1.14.4 If the cerebrospinal fluid culture is positive for group B streptococcus, consider changing the antibiotic treatment to:

- benzylpenicillin 50 mg/kg every 12 hours, normally for at least 14 days **and**
- gentamicin, with:
  - a starting dosage of 5 mg/kg every 36 hours (see recommendation 1.5.3)
  - subsequent doses and intervals adjusted if necessary based on clinical judgement (see recommendation 1.5.5) and blood gentamicin concentrations (see recommendations 1.15.1 to 1.15.3)
  - treatment lasting for 5 days. **[2012, amended 2021]**

1.14.5 If the blood culture or cerebrospinal fluid culture is positive for listeria, consider stopping cefotaxime and treating with amoxicillin and gentamicin. **[2012, amended 2021]**

1.14.6 If the cerebrospinal fluid culture identifies a Gram-positive bacterium other than group B streptococcus or listeria, seek expert microbiological advice on management. **[2012, amended 2021]**

For a short explanation of why the committee amended the 2012 recommendations and how they might affect practice, see the rationale and impact section on early- and late-onset meningitis.

Fluid restriction

1.14.7 Do not routinely restrict fluid intake to below routine maintenance needs in babies with bacterial meningitis. **[2024]**

1.14.8 Give maintenance fluids orally or by enteral tube, if tolerated. **[2024]**

For more guidance on fluid therapy, see the NICE guideline on intravenous fluid therapy in children and young people.

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on fluid restriction for confirmed bacterial meningitis.

Full details of the evidence and the committee's discussion are in evidence review M: fluid restriction in bacterial meningitis.

Assessing for immunodeficiency and recurrence risk in babies with bacterial meningitis

1.14.9 Refer babies with pneumococcal meningitis to a paediatric immunology and infectious disease specialist to assess for primary immunodeficiency. **[2024]**

1.14.10 For babies with bacterial meningitis, examine their back and scalp for signs of a sinus tract. **[2024]**

1.14.11 For babies with bacterial meningitis, take a history of:

- head trauma, surgery or cerebrospinal fluid leak
- immunisations
- medicines, including drugs that suppress the immune system (such as complement inhibitors). **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on assessing for immunodeficiency and recurrence risk in babies with bacterial meningitis.

Full details of the evidence and the committee's discussion are in evidence review N: factors associated with recurrent bacterial meningitis.

Discharge after antibiotic treatment

1.14.12 After antibiotic treatment, consider prompt discharge of the baby from hospital,

with support for the parents and carers and a point of contact for advice. **[2012]**

Preparing for hospital discharge

See also the recommendations on planning for care after discharge for all babies who have had an infection.

Identifying and managing complications

1.14.13 Identify follow-up needs for babies who have had bacterial meningitis, taking into account potential cognitive, neurological, developmental, hearing, psychosocial, education, and renal complications. **[2024]**

Cognitive, neurological and developmental complications

1.14.14 Refer babies for community neurodevelopmental follow-up. **[2024]**

1.14.15 For babies who are taking anti-epileptic drugs, refer for a medicines review 3 months after hospital discharge, with a clinician with an interest in epilepsy, an epilepsy specialist nurse, or a neurologist. **[2024]**

Audiological assessment

1.14.16 Offer an audiological assessment within 4 weeks of the baby being well enough for testing (and preferably before discharge). **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on identifying and managing complications.

Full details of the evidence and the committee's discussion are in evidence review O: long-term complications and follow-up for bacterial meningitis.

Psychosocial support

1.14.17 Consider referral to psychosocial support for family members and carers of babies who have had bacterial meningitis. **[2024]**

For a short explanation of why the committee made the 2024 recommendation and how it might affect practice, see the rationale and impact section on planning for care after hospital discharge.

Full details of the evidence and the committee's discussion are in evidence review Q: support for confirmed bacterial meningitis.

Care after hospital discharge

First review

1.14.18 For babies who have had bacterial meningitis, arrange for a review with a neonatologist or paediatrician at 4 to 6 weeks after discharge from hospital. As part of this review, cover:

- the results of their audiological assessment, and whether cochlear implants are needed
- damage to bones and joints
- skin complications (including scarring from necrosis)
- psychosocial problems (if relevant, see the NICE guideline on post-traumatic stress disorder)
- neurological and developmental problems, in liaison with community child development services. **[2024]**

1.14.19 Arrange a review with a neonatologist or paediatrician for 1 year after discharge. At this review, assess for possible late-onset neurodevelopmental, sensory and psychosocial complications. **[2024]**

1.14.20 Healthcare professionals (such as school nurses, health visitors and GPs) with responsibility for monitoring the health and wellbeing of babies should be alert for late-onset complications of bacterial meningitis. **[2024]**

1.14.21 Be aware that late-onset complications may not be apparent until transition points (such as starting nursery or school). **[2024]**

1.14.22 Community child development services should follow up and assess the risk of long-term neurodevelopmental complications for at least 2 years after discharge. **[2024]**

1.14.23 If a neurodevelopmental deficit is identified, refer to the appropriate services (for example, neurodisability services) and agree with them who will be responsible for follow-up, to ensure that nobody misses out on care. **[2024]**

1.14.24 Advise parents and carers to get advice from their GP if their child develops possible neurodevelopmental complications more than 2 years after discharge. **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on care after hospital discharge.

Full details of the evidence and the committee's discussion are in evidence review O: long-term complications and follow-up for bacterial meningitis and evidence review Q: support for confirmed bacterial meningitis.

Recurrent bacterial meningitis

Risk factors

1.14.25 Risk factors for recurrent bacterial meningitis are:

- primary or secondary immunodeficiency, including:
  - HIV

  - congenital complement deficiency or acquired inhibition
  - reduced or absent spleen function
  - hypogammaglobulinaemia
- communication between the cerebrospinal fluid and external surface, for example, caused by:
  - prior trauma or surgery
  - a congenital anomaly. **[2024]**

Management

1.14.26 For babies who have had a recurrent episode of bacterial meningitis:

- review with a paediatric immunology and infectious disease specialist **and**
- agree which tests, investigations, vaccines and other interventions are needed to prevent re-occurrence. **[2024]**

1.14.27 Examine the baby's back and scalp for signs of a sinus tract. **[2024]**

1.14.28 Get specialist radiological advice on investigations for a cerebrospinal fluid leak. **[2024]**

1.14.29 Take an immunisation and medicine history, including for drugs that suppress the immune system (such as complement inhibitors). **[2024]**

1.14.30 In babies with recurrent meningitis with unconfirmed bacterial cause, consider other causes and get advice from an infection specialist. **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on recurrent bacterial meningitis.

Full details of the evidence and the committee's discussion are in evidence review N: factors associated with recurrent bacterial meningitis.

1.15 Therapeutic drug monitoring for babies receiving gentamicin

Trough concentrations

1.15.1 If giving a second dose of gentamicin, measure the trough blood gentamicin concentration immediately before giving the second dose. Take the trough concentrations into account before giving the third dose of gentamicin. **[2012]**

1.15.2 Repeat the measurement of trough concentrations immediately before every subsequent third dose of gentamicin, or more frequently if necessary (for example, if there has been concern about previous trough concentrations or renal function). **[2012]**

1.15.3 Hospital services should make blood gentamicin concentrations available to healthcare professionals in time to inform the next dosage decision. **[2012]**

1.15.4 Adjust the gentamicin dose interval, aiming to achieve trough concentrations of less than 2 mg/litre. If the course of gentamicin lasts for more than 3 doses, aim for a trough concentration of less than 1 mg/litre. **[2012]**

1.15.5 Do not withhold a dose of gentamicin because of delays in getting a trough concentration measurement, unless there is evidence of impaired renal function (for example, an elevated serum urea or creatinine concentration, or anuria). **[2012]**

Peak concentrations

1.15.6 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. **[2012]**

1.15.7 When measuring peak blood gentamicin concentrations, take the measurement 1 hour after starting gentamicin. **[2012]**

1.15.8 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. **[2012]**

1.16 Care setting

1.16.1 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 and for whom there are no ongoing concerns if there is adequate local support. **[2012]**

1.16.2 When deciding on the appropriate care setting for a baby, take into account the baby's clinical needs and the competencies needed to ensure safe and effective care (for example, the insertion and care of intravenous cannulas). **[2012]**

1.17 Planning for care after discharge

1.17.1 For babies who have had an infection, tell their GP (and health visitor if relevant), and explain any follow-up plans. **[2024]**

1.17.2 Tell the parents and carers who their main point of contact will be after discharge.

[2024]

1.17.3 Document the follow-up plan for managing complications in the discharge summary. **[2024]**

1.17.4 The hospital team should coordinate with the following professionals for care after discharge:

- tertiary and primary care and other specialists
- allied professionals and community teams that will be involved in follow-up (for example, audiology and speech and language therapy departments). **[2024]**

For a short explanation of why the committee made the 2024 recommendations and how they might affect practice, see the rationale and impact section on planning for care after hospital discharge.

Full details of the evidence and the committee's discussion are in evidence review O: long-term complications and follow-up for bacterial meningitis, evidence review P: information for confirmed bacterial meningitis and evidence review Q: support for confirmed bacterial meningitis.

Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline. For other definitions see the NICE glossary and the Think Local, Act Personal Care and Support Jargon Buster.

Early-onset neonatal infection

Neonatal infection less than 72 hours after birth.

Late-onset neonatal infection

Neonatal infection 72 hours or more after birth.

Peak blood 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.

Severe penicillin allergy

A history of allergy to penicillin with effects that are clearly likely to be allergic in nature such as anaphylaxis, respiratory distress, angioedema or urticaria.

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 blood 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.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

Risk factors for and clinical indicators of early-onset infection

What is the accuracy of clinical prediction models for early-onset neonatal infection in the UK and what is their effectiveness in guiding management in the baby? **[2021]**

What is the risk of early-onset neonatal infection with maternal obesity and how does this change with increasing body mass index? **[2021]**

For a short explanation of why the committee made these recommendations for research, see the rationale on risk factors for and clinical indicators of possible early-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review D: maternal and neonatal risk factors.

Investigations for babies who may have early-onset infection

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? **[2012]**

Antibiotics for suspected early-onset neonatal infection

What is the optimal duration of treatment (course length) in babies who receive antibiotics for confirmed early-onset neonatal infection? **[2012]**

Risk factors for and clinical indicators of late-onset infection

What is the accuracy of new or existing clinical prediction models for late-onset neonatal infection in the UK and what is their effectiveness in guiding management:

- for babies already on a neonatal unit?
- for babies admitted from home? **[2021]**

For a short explanation of why the committee made the recommendation for research, see the rationale on risk factors for and clinical indicators of possible late-onset infection.

Full details of the evidence and the committee's discussion are in evidence review E: risk factors for late onset neonatal infection.

Antibiotics for suspected late-onset neonatal infection

What is the optimal antibiotic treatment regimen for suspected late-onset neonatal infection? **[2021]**

For a short explanation of why the committee made the recommendation for research, see the rationale on antibiotics for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review H: antibiotics.

Impact of neonatal infection on the baby's family

What is the impact of neonatal infection on the health-related quality of life of the baby's family? **[2021]**

For a short explanation of why the committee made the recommendation for research, see the rationale on women with prolonged prelabour rupture of membranes.

Full details of the evidence and the committee's discussion are in evidence review C: timing of delivery.

Other recommendations for research

Information and support

How does each step in the care pathway for prevention and treatment of early-onset neonatal infection impact on babies and their families? **[2012]**

What is the clinical and cost effectiveness of information and support offered to parents and carers of babies who have received antibiotics for suspected or proven early-onset neonatal infection? **[2012]**

Intrapartum antibiotics

What is the clinical and cost effectiveness of intrapartum antibiotics for women with meconium-stained amniotic fluid? **[2021]**

For a short explanation of why the committee made the recommendation for research, see the rationale on intrapartum antibiotics.

Full details of the evidence and the committee's discussion are in evidence review B: intrapartum antibiotics.

Antibiotics for suspected early-onset infection

What is the incidence in England and Wales of resistance to commonly used antibiotics among bacteria that cause early-onset neonatal infection? **[2012]**

What is the optimal antibiotic dosage regimen for the treatment of early-onset neonatal

infection? **[2012]**

What is the incidence and severity of adverse effects with antibiotics used to prevent or treat early-onset neonatal infection? **[2012]**

What are the core exposures and outcomes that should be used to evaluate clinical effectiveness of antibiotics to prevent or treat early- onset neonatal infection? **[2012]**

Intravascular catheters for reducing the risk of late-onset neonatal infection

What is the effectiveness of antimicrobial-impregnated catheters other than those impregnated with rifampicin and miconazole for preventing late-onset catheter-related bloodstream infections in newborn babies? **[2021]**

What is the effectiveness of catheters impregnated with silver zeolite for preventing late-onset catheter-related bloodstream infections in newborn babies? **[2021]**

For a short explanation of why the committee made these recommendations for research, see the rationale on antibiotic-impregnated intravascular catheters for reducing the risk of late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review F: intravascular catheters.

Antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection

What is the optimum regimen (including treatment duration and dose) for using antifungals to prevent secondary fungal infection associated with antibiotic treatment for late-onset neonatal infection? **[2021]**

For a short explanation of why the committee made this recommendation for research, see the rationale on antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection.

Full details of the evidence and the committee's discussion are in evidence review I: antifungals.

Early and late-onset meningitis

What is the optimal antibiotic treatment regimen for early-onset neonatal meningitis? **[2012]**

Care setting

What is the clinical and cost effectiveness of different models of care for the prevention and treatment of early-onset neonatal infection? **[2012]**

Long-term outcomes of bacterial meningitis

What are the long-term outcomes after bacterial meningitis in infancy? **[2024]**

For a short explanation of why the committee made this recommendation for research and how it might affect practice, see the rationale section on identifying and managing complications.

Full details of the evidence and the committee's discussion are in evidence review O: long-term complications and follow-up for bacterial meningitis.

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

Information and support

Recommendations 1.1.1 to 1.1.11, and 1.1.15 to 1.1.16

Why the committee made the recommendations

The committee decided that some of the information and support recommendations in the 2012 version of the NICE guideline on neonatal infection for the families of babies with early-onset infection were also applicable to the families of babies who may develop late-onset infection.

The 2012 version of the guideline on early-onset infection recommended that parents and carers of babies with risk factors for early-onset infection should be given verbal and written information on the signs and symptoms of infection. This is particularly important when the baby already has risk factors that indicate they may develop infection. However, the committee noted that any baby can develop an infection, even if they are not identified as high risk at the time of discharge. The committee therefore thought it was important that all parents and carers should be given information about the signs and symptoms of neonatal infection before their baby is discharged from hospital.

The committee also wanted to ensure that the signs of infection listed in the recommendations were written in simple language that families could understand, rather than using clinical terminology. Therefore, examples of the most common breathing problems experienced by babies with neonatal infection were added to the recommendation on signs and symptoms.

The committee thought it was important that information was given in accessible formats, including different languages where appropriate to ensure that information was equally accessible to all. They noted these principles are outlined in the NICE guideline on patient experience in adult NHS services and so cross-referred to this guideline.

How the recommendations might affect practice

These recommendations have been adapted from the existing guidelines for early-onset neonatal infection, reflecting standard practice. As such, they are not expected to have a substantial impact on practice. Expanding the recommendation on signs and symptoms so that advice is given to all parents and carers will mean that more families will be aware of the signs of infection and will know to seek medical help if their baby develops any of them.

Return to recommendations

Information and support after diagnosis

Recommendations 1.1.12 to 1.1.14

Why the committee made the recommendations

The committee made recommendations based on evidence on the views of parents and carers, and based on their knowledge and experience.

The committee emphasised the need to discuss the issues covered in the recommendations with parents and carers of babies with bacterial meningitis, to give them the chance to ask questions, and to repeat information over time. This is because people may be distressed and unable to ask questions or understand information when their baby is first admitted to hospital.

Emotional and pastoral support is recommended for parents and carers because of the severe impact meningitis can have on a baby.

How the recommendations might affect practice

The recommendations largely reflect current practice and they should not have a significant resource impact.

Return to recommendations

Intrapartum antibiotics

Recommendations 1.2.1 to 1.2.5

Why the committee made the recommendations

No new evidence was identified since 2012, when the previous version of the guideline was published. The committee extended the 2012 recommendation on antibiotics for group B streptococcus to cover women who had colonisation in a previous pregnancy. This was because group B streptococcus colonisation in a previous pregnancy greatly increases the chance of being colonised in future pregnancies. The committee were concerned about a woman not receiving treatment because of a false negative test result, and so they decided to specify that a negative test should be from enrichment culture or polymerase chain reaction (PCR) on rectovaginal swab samples. Although some tests may have higher false positive rates, all women with positive tests should be treated as if they have GBS so that no babies who are at higher risk of infection are missed.

For women in pre-term labour and women with a clinical diagnosis of chorioamnionitis, there was no evidence identified on the effects on intrapartum antibiotics on the number of neonatal infections. However, antibiotics did reduce the number of maternal infections in women in pre-term labour. The committee also agreed that pre-term labour and chorioamnionitis are important risk factors for neonatal infection, so intrapartum antibiotics are very likely to reduce the risk to the baby. Chorioamnionitis is a serious infection that needs to be treated with antibiotics to prevent harm to the mother. The committee thought that it was important to make recommendations for antibiotic treatment that would simultaneously treat infection in the mother and prevent early-onset group B streptococcal infection in the baby to make the best use of antibiotics.

The committee retained the recommendations on using benzylpenicillin as first-choice antibiotic from the 2012 guideline. Based on their knowledge and experience, gentamicin and metronidazole are also now recommended for women with chorioamnionitis, because chorioamnionitis can be caused by Gram positive or negative aerobic and anaerobic bacteria, so clinicians need to use broad-spectrum antibiotics that are effective against both. Once-daily dosing for gentamicin was recommended based on the knowledge and experience of the committee because 8 hourly dosing has additional monitoring requirements and would need additional nursing time for administration.

The committee also provided guidance on alternatives for women with a penicillin allergy,

based on their knowledge and experience. The committee amended the 2012 recommendation on antibiotic alternatives for women who are allergic to penicillin. They changed the recommended antibiotic from clindamycin because there is evidence of resistance to group B streptococcus emerging with clindamycin, meaning that this antibiotic should no longer be used routinely. Based on their knowledge and experience, the committee recommended a cephalosporin with activity against group B streptococcus as an alternative for women with a penicillin allergy that was not severe, and vancomycin or an alternative antibiotic with activity against group B streptococcus in the case of severe penicillin allergy. The committee were aware of the possibility of allergic reaction to cephalosporins in women with a history of penicillin allergy. For women with a history of penicillin allergy that was not severe they thought that this risk was small and was outweighed by the benefits of using cephalosporins to treat chorioamnionitis and prevent neonatal infection. They noted that cephalosporins should be used with caution in these women. Cephalosporins were not recommended in the case of severe penicillin allergy because of an increased chance of a severe allergic reaction to cephalosporins. Severe penicillin allergy refers to a history of allergy to penicillin with effects that are clearly likely to be allergic in nature such as anaphylaxis, respiratory distress, angioedema or urticaria.

How the recommendations might affect practice

Many of the recommendations remain the same as in the 2012 guideline. The recommendations on intrapartum antibiotics have been extended to cover women in pre-term labour without prelabour rupture of membranes, women with chorioamnionitis and women with group B streptococcus colonisation in a previous pregnancy. However, these changes reflect current practice, as many of these women already receive intrapartum antibiotics.

The committee expected that the recommendation on intrapartum antibiotics for chorioamnionitis would have the greatest impact on clinical practice. There is currently variation in which antibiotics are given to women with chorioamnionitis, with some units prescribing broad-spectrum antibiotics to treat infection in the mother and benzylpenicillin to prevent infection in the baby. Recommending a combination of narrow-spectrum antibiotics for women without an allergy to penicillin is likely to reduce the use of broad-spectrum antibiotics, which will improve antibiotic stewardship.

Return to recommendations

Women with prolonged prelabour rupture of membranes who have group B streptococcal colonisation, bacteriuria or infection

Recommendation 1.2.6

Why the committee made the recommendation

The evidence suggested that immediate delivery can result in a reduced risk of a baby developing neonatal infection when a mother is between 34 and 37 weeks' gestation and has prolonged prelabour rupture of membranes and a positive test result for group B streptococcus. The evidence did not indicate any significant harms to the baby from choosing immediate delivery over expectant management. Therefore, the committee decided that, given the potential serious consequences of a baby developing neonatal infection, a recommendation in favour of immediate delivery was important. This was further supported by the economic evidence, which showed not only a clinical benefit to immediate delivery but also lower associated costs in comparison to expectant management, which has increased antenatal costs and higher rates of infections.

The committee made a recommendation for research on examining the health-related quality of life impact on parents or carers when a baby has neonatal infection. This information was not available and would have improved how well the economic model truly reflected the costs and health consequences of neonatal infection.

How the recommendation might affect practice

This recommendation could increase the number of women who are offered immediate delivery when they have both prolonged prelabour rupture of membranes and a positive test for group B streptococcus. This in turn could reduce the number of babies who need to be treated for neonatal infection and also reduce the number of mothers who need to be monitored throughout the expectant management period. The exact impact of these recommendations will vary between those hospitals where group B streptococcus screening and testing is more routinely performed and those where it is not. Recommendations on group B streptococcus screening were outside of the scope of this guideline. An economic model suggested that increasing the number of women offered immediate delivery would reduce costs overall.

Return to recommendation

Risk factors for and clinical indicators of possible early-onset neonatal infection

Recommendations 1.3.1 to 1.3.9

Why the committee made the recommendations

Before birth

No evidence was found that related specifically to this topic, and the committee agreed that the recommendations from the previous version of this guideline still reflected current best practice so did not need to be changed. These recommendations apply to all women with risk factors, including those who decline antibiotics, or those who either do not receive antibiotics or receive their first dose of antibiotics shortly before birth because of precipitate birth. As such, any women with risk factors should be monitored throughout labour, and these factors should be taken into account when assessing the risk of infection in the baby.

Assessing and managing the risk of early-onset neonatal infection after birth

The committee based their recommendations on evidence on the accuracy of clinical decision models for early-onset neonatal infection, as well as evidence on individual neonatal and maternal risk factors.

There was uncertainty about how well the Kaiser Permanente neonatal sepsis calculator identified true cases of early-onset infection, because the studies included very few cases of infection that were confirmed by blood culture. This was a problem for the framework outlined in the 2012 version of the guideline as well, but the committee believed that the framework is more conservative and would lead to more antibiotics being prescribed than the Kaiser Permanente calculator (both appropriately and inappropriately). Evidence on the Kaiser Permanente neonatal sepsis calculator suggests that it is good at correctly identifying babies without neonatal infection, so reducing the amount of antibiotics that are prescribed unnecessarily. However, given the very serious consequences of missing an infection, the committee preferred the conservative approach from the framework in the 2012 guideline, with some amendments as outlined. However, as the evidence does not

clearly show one option to be better and some UK centres currently use the Kaiser Permanente calculator, they also recommended this as an alternative, but only in the context of a research or audit project. By using the Kaiser Permanente calculator as part of an audit, centres will be able to collect detailed data on the use of the tool within NHS practice, including the number of babies who correctly received treatment, those who received antibiotics unnecessarily, and any who were not recommended antibiotics but did have infection. This information will provide a more detailed understanding of the effectiveness and safety of the Kaiser Permanente calculator which can be used to inform decisions on its use in future updates of this guideline.

The committee decided to specify that the Kaiser Permanente calculator should only be used for babies who are being cared for in a neonatal unit (neonatal intensive care units, local neonatal units and special care units), transitional care or a postnatal ward. The committee highlighted how it would be more difficult to collect the information needed for the audit in other settings. They did not think the calculator should be recommended for use in the emergency department, as babies who are brought in from home are likely to already be showing signs of being unwell and therefore need more immediate treatment than babies who are being assessed for risk of infection in a neonatal unit. In these cases, waiting to consult the calculator could instead delay treatment. The committee also thought that the calculator was not appropriate for use in a midwife-led unit or freestanding midwifery unit as there is currently no evidence that has used the calculator in these settings.

As there was only limited new evidence, the framework for assessing and managing risk, involving red flag indicators and other indicators of infection, has been retained from the 2012 guideline. The committee selected the red flag indicators as those that, based on their clinical experience, are the most high-risk factors that need immediate treatment. Non-red flag indicators are those that can have causes other than neonatal infection and therefore do not always signal the need for immediate treatment. Many of the clinical indicators matched those in the 2012 guideline, with the following changes.

Parenteral antibiotics are no longer a risk factor. Since the 2012 guideline, awareness of the risks of maternal sepsis has increased and there has been a focus on early treatment with antibiotics. This has led to more babies being prescribed antibiotics even when a maternal infection is not strongly suspected. This rise in antibiotic use can result in babies being unnecessarily exposed to the side effects associated with antibiotics, such as nephrotoxicity, as well as increasing a baby's length of stay in hospital. Increased antibiotic use is also associated with an increase in the development of antibiotic resistance.

Chorioamnionitis and intrapartum fever are now separate risk factors because intrapartum fever has other potential causes. This change means that women with chorioamnionitis and intrapartum fever will have 2 risk factors, so their babies will receive antibiotics.

Invasive group B streptococcal infection in a previous baby and maternal group B streptococcal colonisation, bacteriuria or infection in the current pregnancy have been combined into a single risk factor, because having a previous baby with invasive group B streptococcal infection increases the risk of future colonisation and infection, but does not confer additional risk if infection, bacteriuria or infection in the current pregnancy is already known about.

Mechanical ventilation, which was previously a red flag risk factor pre-term babies, and a non-red flag risk factor for term babies has been merged into one recommendation. The committee agreed that mechanical ventilation is a risk factor for infection regardless of prematurity, and so they decided to merge these into one red flag risk factor which did not refer to whether a baby was born pre-term or at term.

Confirmed prelabour rupture of membranes was removed from the table because the committee decided that it is now covered by other risk factors in the table (pre-term birth and confirmed rupture of membranes in a pre-term or term birth). Babies born to mothers with prelabour rupture of membranes will therefore still receive treatment when using the updated version of the framework.

To address the limited evidence, the committee recommended further research on the accuracy of the Kaiser Permanente neonatal sepsis calculator and other clinical prediction models.

Management of babies at increased risk of infection

No evidence was found that related specifically to this topic, and the committee agreed that the recommendations from the previous version of this guideline still reflected current best practice so did not need to be changed.

How the recommendations might affect practice

Many neonatal units use the framework from the 2012 version of the NICE guideline. Removal of parenteral antibiotics as a risk factor is expected to reduce the number of babies given antibiotics unnecessarily.

Some centres use the Kaiser Permanente neonatal sepsis calculator as an alternative, and the recommendations may increase the number of centres who use this calculator in the context of a research or audit project. Current evidence suggests that this may reduce the number of babies who are unnecessarily given antibiotics, but there was substantial uncertainty about how well the calculator identified true cases of infection. If an increase in use of the Kaiser calculator resulted in more cases of infection being missed, this could increase costs associated with treating neonatal infections, as well as the very serious impact on the baby and their families.

Reducing the number of babies being given antibiotics may reduce costs for the NHS, both by reducing prescriptions and by reducing the amount of time babies and their mothers spend in hospital.

Return to recommendations

Lumbar puncture

Recommendations 1.4.6 to 1.4.8 and recommendations 1.9.6 to 1.9.9

Why the committee made the recommendations

Lumbar puncture is the only test that can directly confirm a diagnosis of bacterial meningitis.

Antibiotics can affect the results of cerebrospinal fluid tests, so lumbar puncture needs to be performed before antibiotics when possible. The committee did not recommend a specific timeframe for performing lumbar puncture because they were concerned that it would be interpreted as a hard cutoff. The key timeframe is the 1-hour timeframe for giving antibiotics, but clinical judgement is needed for decisions on how to fit lumbar puncture around this. For example, for some people it may be safe to delay the antibiotics by slightly longer than 1 hour, if this would allow a lumbar puncture to be performed first.

The committee used their experience to highlight situations that need treating or stabilising before a lumbar puncture, because these are potentially life-threatening and present a greater risk than delayed meningitis investigations.

How the recommendations might affect practice

Lumbar punctures can often be performed more quickly on acute medical wards than in emergency departments. Because of this, hospitals may need to be able to urgently transfer people with suspected bacterial meningitis out of emergency departments (following stabilisation). Hospitals may also need to streamline their processes so that acute medical wards can perform lumbar punctures within the 1-hour timeframe for giving antibiotics.

Return to recommendations 1.4.6 to 1.4.8

Return to recommendations 1.9.6 to 1.9.9

Cerebrospinal fluid investigations in babies with suspected bacterial meningitis

Recommendations 1.4.9 to 1.4.15 and recommendations 1.9.10 to 1.9.16

Why the committee made the recommendations

There was evidence on various cerebrospinal fluid investigations for diagnosing bacterial meningitis:

- studies looked at multiple thresholds for white cell count, finding that it was at least moderately sensitive and specific at most thresholds, and very specific and sensitive at some thresholds
- overall, the evidence showed that protein concentration was at least moderately sensitive and specific
- gram staining and culture was very specific for identifying all causes of bacterial meningitis
- there was a large, consistent body of evidence showing that PCR was at least moderately sensitive and very specific for identifying particular causes of bacterial meningitis.

The committee highlighted that cerebrospinal fluid cell counts, total protein and glucose concentrations are important for clinical decision making and to guide antibiotic treatment,

and agreed that these results should be available within 4 hours.

It is important to look at the whole clinical picture and take a full clinical history, including maternal history for babies aged 28 days or under. This is because there are factors that may reduce the reliability of cerebrospinal fluid investigations. Based on their knowledge and experience the committee highlighted the most important of these factors.

Age-appropriate threshold values for cerebrospinal fluid should be used. Values for some parameters (such as protein and cell counts) are higher in newborn babies than in older babies and children.

The committee highlighted the need to consider alternative diagnoses because there could be serious consequences if a potentially treatable alternative cause is missed.

How the recommendations might affect practice

The recommendations largely support current practice, and they should not have a significant resource impact.

PCR was not included as part of cerebrospinal fluid investigations in the 2010 meningitis guideline, but it has since become standard practice in most hospitals.

Return to recommendations 1.4.9 to 1.4.15

Return to recommendations 1.9.10 to 1.9.16

Antibiotic-impregnated intravascular catheters for reducing the risk of late-onset neonatal infection

Recommendation 1.7.1

Why the committee made the recommendation

There were only 2 studies looking at antimicrobial-impregnated catheters in newborn babies:

- One study looked at rifampicin-miconazole-impregnated catheters. These provided no

benefit over standard catheters. In addition, they are more expensive than standard catheters.

- The other study looked at silver-zeolite-impregnated catheters. They showed some benefit compared with standard catheters, but the study was small and the committee had concerns about its quality. It was also conducted in Italy, and there are differences in clinical practice and infection rates between Italy and the UK.

The committee agreed they could not recommend antimicrobial-impregnated catheters based on the available evidence. The recommendation against the use of rifampicin-miconazole-impregnated catheters was made on the basis of the evidence that they provide no additional benefit over a standard catheter, and not because of any safety concerns over their use. There is a wider range of antimicrobials that can be used to impregnate catheters than have currently been investigated in newborn babies and uncertainty over which type of impregnated catheter is the most effective and whether monotherapy or the use of more than one antimicrobial would provide the most benefits. To address the shortage of evidence they made recommendations for further research.

How the recommendation might affect practice

The recommendation will reduce the use of rifampicin-miconazole-impregnated catheters. However, antimicrobial-impregnated catheters are not commonly used for newborn babies, so this should have a limited impact.

Return to recommendation

Risk factors for and clinical indicators of possible late-onset neonatal infection

Recommendations 1.8.1 and 1.8.4

Why the committee made the recommendations

The committee did not feel that there was sufficient, high-quality evidence for any individual model to make a recommendation on clinical prediction models for late-onset neonatal infection. Instead, they recommended a review of the individual risk factors that may predict a baby's risk of having or developing late-onset neonatal infection.

Although there was evidence on a number of tools aimed at predicting late-onset neonatal infection, the committee did not think that there was sufficient, high quality, evidence including external validation to recommend any of them for use in practice. Most of the evidence was not from recent studies, the models were not readily available as web-based tools or in other formats that could be easily used by clinicians and it was thought that implementing them would have needed considerable changes in clinical practice.

Given the limited evidence currently available for prognostic models for late-onset infection, the committee decided that they should make a recommendation for research. The recommendation is designed to encourage the development of new models to identify babies at risk of late-onset neonatal infection as well as promoting the validation of these models and evaluation of their effects on practice. This should help to improve the understanding of the factors associated with late-onset neonatal infection so that committees can make recommendations on this area in future guideline updates.

With limited evidence on prognostic models, the committee agreed that it was instead important for clinicians to be aware of the clinical indicators and risk factors for late-onset neonatal infection. There was very limited evidence on maternal risk factors for late-onset infection and so the recommendations were based on the risk factors and signs and symptoms in the baby. The committee decided that the list of high-risk criteria from the risk stratification tool in the NICE guideline on suspected sepsis (table 1) covered the most important indicators that clinicians in both community and specialist settings should be aware of. They included the recommendation to seek early advice from a paediatrician to highlight the importance of early treatment if any of the main clinical indicators are present. Early specialist advice was thought to be particularly important when caring for babies in the community as they need to be taken to hospital and admitted before treatment can begin, while babies who are on a neonatal unit can be monitored and treated more quickly. It was agreed that in addition to clinical indicators, it was also important to highlight potential risk factors for infection. This will help to ensure that babies who are at greater risk for infection are closely monitored for the presence of any of the clinical indicators. The committee also recommended that clinicians should think about infection in the other babies when one baby from a multiple birth has infection. Evidence was not found on this, but the committee thought that it was in line with current best practice because of the risk that all the babies from the pregnancy will have the same risk of infection.

There was very limited evidence on the signs and symptoms of infection. The committee was aware of existing recommendations on clinical indicators of infection in the NICE

guideline on suspected sepsis and so it considered this information when deciding on recommendations. It was agreed that the high-risk indicators listed in the sepsis guideline were an accurate reflection of the committee's experience with babies who develop late-onset infection. Parental or carer concern over changes in behaviour was added to the list of high-risk criteria as this was highlighted as an important indicator of potential infection for babies in the community. Other potential clinical indicators were discussed, but the committee were concerned about the risk of over-treatment if too many clinical indicators were listed in the recommendation, especially if some of those indicators could have causes other than neonatal infection. The committee decided that the signs included in the recommendation were those that were most likely to indicate infection and therefore the most important to consider when assessing whether a baby may need treatment.

How the recommendations might affect practice

The recommendations are consistent with current practice and therefore a large resource impact is not anticipated. The table of clinical indicators may increase awareness of when a baby is at greater risk of late-onset neonatal infection. This may increase the number of babies who receive early treatment in hospital and reduce the negative effects and costs associated with infection.

Clinicians working on a neonatal or paediatric ward are already likely to be aware of the risk factors that were identified in the evidence review. As such, the recommendations are helpful to reinforce the knowledge of these clinicians about the risk factors but may not have a substantial effect on current practice in a hospital setting.

Return to recommendations

Investigations for late-onset neonatal infection

Recommendations 1.9.1 to 1.9.6

Why the committee made the recommendations

Blood culture is the current 'gold standard' for identifying neonatal infection. However, babies with late-onset infection can still sometimes have a negative blood culture. It can also take hours or days to get the results of blood cultures. These inaccuracies and delays mean that many babies receive treatment before blood culture results are returned,

because delaying treatment could lead to complications or death. Having another diagnostic test as an alternative or an addition to blood culture results could therefore reduce unnecessary antibiotic treatment. The committee reviewed the evidence for late-onset infection. Of the other diagnostic tests, only C-reactive protein has enough evidence to recommend it. It is not accurate enough to be used as an alternative to blood culture, but when used in combination it can improve the accuracy of the diagnosis. The committee discussed how a single C-reactive protein measurement is not sufficient to diagnose infection, as this can vary between babies. They therefore decided to recommend that a C-reactive protein sample is taken when starting antibiotics. This will provide clinicians with a baseline against which to compare future C-reactive protein results, to indicate whether a baby is likely to have infection, whether they are responding to treatment and when to consider stopping antibiotics. Blood culture is still considered the gold standard test for diagnosing neonatal infection but using it in combination with C-reactive protein measurements will allow babies who do not need antibiotics to stop taking them sooner.

As the evidence for late-onset infection lined up with the evidence from the 2012 guideline for early-onset infection, the committee amended the 2012 recommendations to cover all neonatal infection.

There was limited evidence on lumbar puncture specifically for late-onset infection. However, lumbar puncture is the 'gold standard' test for identifying meningitis, and it was recommended in the 2012 guideline for babies with early-onset infection. The committee extended this recommendation to cover both early- and late-onset neonatal infection, as they felt that the benefits of identifying meningitis outweighed the risks of the procedure.

No evidence was identified that supported using urine culture or skin swabs in the neonatal unit. These tests were also not recommended in the 2012 guideline for babies with early-onset infection and so the committee decided to recommend against their use for babies in neonatal units. However, they also discussed how urine culture can be an important test for babies in a paediatric ward if a urinary tract infection is suspected, so included a recommendation which supported its use in babies who are being cared for outside of neonatal units. This is consistent with the recommendations from the NICE guideline on urinary tract infection in under 16s.

How the recommendations might affect practice

The recommendations are not expected to have a major impact on practice as they reflect

the procedures currently followed in most hospitals.

Return to recommendations

Antibiotics for late-onset neonatal infection

Recommendations 1.10.1 to 1.11.7

Why the committee made the recommendations

There is variation across the country in antibiotic resistance patterns and in which organisms are most likely to cause late-onset neonatal infection. Because of this, local data needs to be used when choosing antibiotics.

Babies in a neonatal unit are likely to have been exposed to different bacteria than babies at home, so the committee made separate recommendations for the 2 groups.

For babies in a neonatal unit, the committee did not believe there was enough evidence to recommend specific antibiotics, and so made a recommendation for research into the best antibiotic regimen to treat late-onset infection. However, the evidence available did show that combinations of narrower-spectrum antibiotics are as effective as broader-spectrum antibiotics. The committee were aware that using broad-spectrum antibiotics in babies is associated with altered gut flora, increased risk of invasive fungal infection and the development of antibiotic resistance, and so a combination of narrow spectrum antibiotics was recommended as first-line treatment.

For babies who have been admitted from home, there was also limited evidence on which antibiotics to use. The NICE guideline on suspected sepsis recommends treating community-acquired sepsis with ceftriaxone or cefotaxime depending on gestational age. The committee agreed that these antibiotics would be appropriate for late-onset neonatal infection in babies who have been admitted from home, and none of the evidence for this group contradicted it.

There was no evidence on duration of antibiotic treatment for late-onset infection. However, the 2012 guideline made recommendations on this for early-onset infection, and the committee adapted these so that they were applicable to late-onset infection. The duration of initial treatment is recommended to be 48 hours rather than 36 hours as recommended for early-onset infection. This is thought to reflect the different bacteria

that cause late-onset infection, which grow more slowly and have a lower load in the bloodstream. This means that it can take longer for a blood culture to become positive for late-onset than early-onset infection and so treatment needs to continue for longer until a negative blood culture result can be confirmed. To help with treatment decisions, the 2012 version of the guideline recommended that healthcare professionals with experience in neonatal infection should be available to provide microbiological or paediatric infection disease advice. The committee decided that this recommendation is also important when making decisions about antibiotic treatment for late-onset infection.

No evidence on treatment duration was identified, and so the committee made recommendations based on their knowledge and experience. The committee recommended a treatment of 7 days for babies with a positive blood culture, consistent with the recommendation on early-onset neonatal infection from the 2012 version of the guideline. The committee recommended that a shorter treatment duration should be used when no pathogen is identified (the blood culture is negative) or the pathogen is a common commensal. In these situations, the committee noted that infection was likely to be less severe and could be safely treated with a shorter treatment duration, which would have the advantage of reducing exposure to antibiotics, which is consistent with the principles of good antibiotic stewardship. The committee also specified situations when a longer treatment duration should be used, such as when there is intra-abdominal co-pathology, necrotising enterocolitis, osteomyelitis or infection of a central venous catheter. There was no evidence for the specific situations where longer treatment would be required, but the committee based their decisions on their knowledge and experience.

How the recommendations might affect practice

These recommendations will help to reduce the use of broad-spectrum antibiotics as first-line treatment for babies in neonatal units, which may help reduce antibiotic resistance. However, use of narrow-spectrum antibiotics is already standard practice in many units, and the costs of antibiotics are low, so there is expected to be very little impact on resource use, especially as most of the affected babies are already receiving intensive care and monitoring.

The recommendation for babies admitted from home may not have a substantial impact on practice, as it refers to an existing recommendation in the NICE guideline on suspected sepsis.

The recommendations on duration of treatment are consistent with current practice.

Return to recommendations

Antifungals to prevent fungal infection during antibiotic treatment for late-onset neonatal infection

Recommendation 1.12.1

Why the committee made the recommendations

Evidence from randomised controlled trials showed that both nystatin and fluconazole can reduce the risk of a baby developing an invasive fungal infection in comparison to placebo or no treatment. Evidence marginally favoured the use of nystatin over fluconazole for reducing the risk of fungal infection and based on the knowledge and experience of the committee, nystatin is better tolerated and there is a lower risk of fungi developing resistance to this antifungal than fluconazole. Economic evidence showed that nystatin was also likely to be the most cost-effective option, and so the committee recommended oral nystatin for antifungal prophylaxis when a baby is being given antibiotics for late-onset neonatal infection. The recommendation for antifungal prophylaxis was limited to babies below 1,500 g or 30 weeks' gestational age because the evidence was from babies in these population groups.

Although oral nystatin was the committee's first choice for antifungal prophylaxis, oral administration of antifungals may not be possible for all babies, particularly those who are very premature. The committee therefore specified that the use of intravenous fluconazole is appropriate when oral administration is not possible.

The committee made a recommendation for research for studies investigating the optimum regimen for giving antifungal prophylaxis when treating a baby with antibiotics for late-onset infection, because evidence was not available to support specific recommendations on the duration and dose of antifungal treatment that should be used.

How the recommendations might affect practice

This recommendation may increase the number of babies who are given nystatin as antifungal prophylaxis when they are prescribed antibiotics for late-onset infection. This should decrease the number of babies who need to be treated for fungal infection which,

although rare, can have serious consequences. Economic modelling showed that giving antifungal prophylaxis is likely to be cost saving because of a reduction in costs associated with treating invasive fungal infections and their consequences.

Return to recommendation

Early- and late-onset meningitis (babies in neonatal units)

Recommendations 1.14.1 to 1.14.6

Why the committee amended the recommendations

These recommendations were carried forward from the 2012 version of NICE's guideline on early-onset neonatal infection, but were expanded to cover both early- and late-onset neonatal meningitis for babies in neonatal units based on the knowledge and experience of the committee. Evidence relating to these recommendations was not reviewed for late-onset meningitis, but the committee agreed that the recommendations that were made in 2012 for early-onset infection would also apply to late-onset meningitis for babies treated in neonatal units.

Return to recommendations

Fluid restriction for confirmed bacterial meningitis

Recommendations 1.14.7 and 1.14.8

Why the committee made the recommendations

Fluid restriction for bacterial meningitis

For babies over 28 days, children and young people, there was a small amount of evidence comparing fluid restriction with routine maintenance fluids. This evidence showed that fluid restriction reduces pulmonary and facial oedema. However, it also increases rates of neurological impairment and epilepsy. There was no evidence in newborn babies aged 28 days or under, or in adults. However, the committee extended the recommendations to

cover these groups because they agreed the risks were likely to be the same, based on their knowledge and experience.

The committee were particularly concerned about the increased rate of neurological impairment, as this could be the most important clinical outcome. Based on the evidence and their knowledge and experience, the committee agreed not to recommend routine fluid restriction for bacterial meningitis. They specified 'routine' because they did not want to stop healthcare professionals from restricting fluids in babies with fluid overload.

There are potential complications to providing fluids intravenously, and in the committee's experience babies with bacterial meningitis can often tolerate oral or enteral fluids. Because of this the committee recommended providing fluids orally or by enteral tube when possible.

How the recommendations might affect practice

Fluid restriction is not part of routine practice, although it may be used for people with fluid overload.

Return to recommendations

Assessing for immunodeficiency and recurrence risk in babies with bacterial meningitis

Recommendations 1.14.9 to 1.14.11

Why the committee made the recommendations

The committee had concerns about the reliability of the evidence, because the sample sizes were not large enough to detect rare events and because people with known immunodeficiency will often receive interventions to prevent recurrent infections. Because of this, the committee used their knowledge and expertise to make recommendations.

The committee agreed that primary immunodeficiency is present in 8 to 26% of children with invasive pneumococcal disease.

The committee agreed that referral to specialists was needed for babies with

pneumococcal meningitis, because this disease may indicate a lack of immune response to pneumococcal vaccination and may be associated with primary immune deficiencies.

Some anatomical factors increase the risk of bacterial meningitis. The committee agreed that babies should be checked for these factors (including signs of a sinus tract), to assess whether they may need intervention to prevent future episodes.

How the recommendations might affect practice

The recommendations are in line with current practice.

Return to recommendations

Identifying and managing complications

Recommendations 1.14.13 to 1.14.16

Why the committee made the recommendations

Evidence showed that meningitis can result in a range of long-term complications, such as:

- learning disability, which can lead to speech and language problems in babies, as well as poor educational attainment or the need for special educational assistance
- long-term behavioural problems and problems with adjustment
- psychological distress
- hearing problems, including acute deafness.

Most of the evidence concerned long-term complications for babies over 28 days, children, young people and young adults. However, the committee agreed that it was reasonable to extrapolate much of this evidence to newborn babies, because meningitis can have similar impacts on people regardless of age.

Based on this evidence, the committee agreed that people with bacterial meningitis should not be discharged from hospital until follow-up needs have been identified and planned for, and until certain assessments have been planned or completed. The committee did recognise that certain tests, like an audiological assessment, might not be possible until

after discharge (although testing before discharge would be preferable).

The evidence for epilepsy as a long-term complication was mixed. For example, there was evidence of an increase in children who have had meningitis being admitted as inpatients because of epilepsy, but no evidence of increased use of outpatient epilepsy services in the same population. The committee were also concerned about unnecessary long-term use of anti-epileptic drugs. They recommended a 3-month review to check whether the seizures were a short-term effect of the illness.

The evidence on long-term complications after bacterial meningitis in newborn babies was limited to a single, small study. The committee agreed that quantifying the long-term complications of bacterial meningitis is important, to allow follow-up to be arranged for those at risk and to help with prioritising treatment and prevention strategies. To address this, the committee made a recommendation for research to investigate long-term outcomes after bacterial meningitis in infancy.

How the recommendations might affect practice

It is routine practice to identify possible follow-up needs before discharge and to make referrals when needed.

Return to recommendations

Planning for care after discharge

Recommendation 1.14.17 and recommendations 1.17.1 to 1.17.4

Why the committee made the recommendations

There was evidence on the views and experiences of families and carers of people who have had meningitis. The committee built on this with their own expertise. They recommended coordination with other professionals and services because this will ensure that follow-up care and support meets the person's needs, and will potentially reduce the impact of long-term complications.

Referral for psychosocial support is recommended because of the potential psychological impact of meningitis on family members and carers. It may need to be arranged after

discharge because the impact may not be apparent immediately.

How the recommendations might affect practice

It is routine practice to make referrals and plan for care after discharge, and to inform GPs and other key professionals of any follow up needs.

Return to recommendation 1.14.17

Return to recommendations 1.17.1 to 1.17.4

Care after hospital discharge

Recommendations 1.14.18 to 1.14.24

Why the committee made the recommendations

The committee agreed areas to cover in the post-discharge review based on the evidence of the long-term complications associated with meningitis.

The review should happen at 4 to 6 weeks after discharge so that short-term effects of the illness can be ruled out and long-term issues can be identified early enough to make prompt referrals. The results of hearing tests may not be available at this point (for example, if illness interferes with the timing of the test), but the overall review should not be delayed if this is the case.

The evidence showed particular long-term complications for babies, children and young people. The committee used their own knowledge and experience to make recommendations on further tests and reviews for babies. These tests and reviews are important for identifying late-onset complications and developmental issues as children and young people grow up.

The tests and reviews recommended will involve staff working in multiple services, across health and education. The committee made a recommendation on coordinating follow-up, to avoid situations where professionals assume other services are responsible and people do not receive proper care as a result.

The evidence suggested that meningitis can increase the risk of poor educational outcomes, that the impact of long-term complications may not always be apparent, and that children and younger people who are seen to be underachieving could be achieving more if they had more specific support. This guideline does not cover education settings, so the committee advised parents and carers to discuss educational complications with their child or young person's school.

How the recommendations might affect practice

It is routine practice to review people who have had meningitis for long-term complications after hospital discharge.

Return to recommendations

Recurrent bacterial meningitis

Recommendations 1.14.25 to 1.14.30

Why the committee made the recommendations

Risk factors

Evidence showed that some anatomical factors increased the risk of recurrent bacterial meningitis (such as a cerebrospinal fluid leak). For most immunological factors, there was no evidence that met the review criteria.

The committee had concerns about the reliability of the anatomical and immunological evidence, because the studies only looked at a very small number of people for some risk factors and for recurrent bacterial meningitis in general. Because of this, the committee made recommendations about the risk factors they believed to be most important, based on their knowledge and experience.

Management

There was no evidence, so the committee made recommendations based on their knowledge and experience. They recommended a specialist review to decide which investigations, treatments and immunisations were needed to help prevent further

recurrence.

The committee made recommendations on immunisation, medicine history, and sinus tract examination, in line with the recommendations on assessing for immunodeficiency and recurrence risk (see the explanation of the recommendations on assessing for immunodeficiency and recurrence risk).

The committee also highlighted the possibility of other rare causes of recurrent meningitis.

How the recommendations might affect practice

Risk factors

The recommendations are largely in line with current practice. Healthcare professionals may have to change some of the risk factors they look for, but there should be no resource impact for services.

Management

Specialist review and prophylactic antibiotics are part of routine current practice for babies with recurrent bacterial meningitis.

Return to recommendations

Context

Neonatal bacterial infection 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 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 neonatal infection is managed in healthy babies. The approach taken by the NHS needs to:

- prevent neonatal infection when possible
- 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, when appropriate, reassurance.
- Intrapartum antibiotic prophylaxis should be administered in a timely manner to all eligible women who choose it.
- Babies with suspected neonatal infection should receive treatment as quickly as possible.
- Antibiotic exposure should be minimised in babies who do not have a neonatal infection.
- An integrated system of clinical care is needed to allow full implementation of the guideline recommendations.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on infections.

For full details of the evidence and the guideline committee's discussions, see the evidence reviews. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

Update information

March 2024: The updated NICE guideline on bacterial meningitis and meningococcal disease made new recommendations for newborn babies in the following areas:

- information and support
- lumbar puncture
- cerebrospinal fluid investigations
- fluid restriction
- assessing for immunodeficiency and recurrence risk
- preparing for hospital discharge, including identifying and managing complications
- care after discharge
- recurrent bacterial meningitis.

We have moved these recommendations from the meningitis guideline into this neonatal infection guideline, so that all the recommendations for newborn babies are in one place. These recommendations are marked **[2024]**.

April 2021: We have reviewed the evidence and made new recommendations on the risk factors for infection and clinical indicators of possible infection and on intrapartum antibiotics of neonatal infection. These recommendations are marked **[2021]**.

We have also made some changes without an evidence review:

- what to do if a woman has been identified as having a group B streptococcal infection in relation to future pregnancies
- when to perform a lumbar puncture for babies who are receiving antibiotics who did not have a lumbar puncture on presentation
- early- and late-onset meningitis.

These recommendations are marked **[2012, amended 2021]**.

Recommendations marked **[2012]** last had an evidence review in 2012. In some cases, minor changes have been made to the wording to bring the language and style up to date, without changing the meaning.

Minor changes since publication

January 2024: Various links were updated throughout to point to the newly updated NICE guideline on suspected sepsis.

October 2023: We updated links to the NICE guideline on intrapartum care, which has been updated.

October 2022: We added text to indicate that pulse oximetry may be less reliable in people with dark skin. We also added a link to the NHS patient safety alerton the risk of harm from inappropriate placement of pulse oximeter probes. See recommendation 1.8.3.

October 2021: We added a link to NICE's guidelines on babies, children and young people's experience of healthcare and on shared decision making in recommendation 1.1.1.

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