NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Neonatal infection: antibiotics for prevention and treatment

Draft for consultation, December 2020

This guideline covers preventing infection within 72 hours of birth in healthy babies, treating pregnant women whose baby is at risk, and caring for babies who have a suspected or confirmed infection. It aims to reduce delays in recognising and treating sick babies and prevent unnecessary use of antibiotics.

For simplicity of language, this guideline will use the term 'woman' or 'mother' throughout, and this should be taken to include people who do not identify as women but who have given birth. Similarly, where the term 'parents' is used, this should be taken to include other people who are the baby's primary caregivers and single parents.

This guideline will update NICE guideline CG149 (published August 2012).

The recommendations on recognising and treating bacterial meningitis in babies up to and including 28 days old will be updated through the update to NICE guideline CG102 on meningitis (bacterial) and meningococcal septicaemia in under 16s, which is currently in development. Once the update of CG102 is completed the updated recommendations will be inserted into the neonatal infection guideline.

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, and the public

What does it include?

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2021 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on the prevention, diagnosis and treatment of neonatal infection. You are invited to comment on the new and updated recommendations. These are marked as **[2021]**.

You are also invited to comment on recommendations that we propose to delete from the 2012 guideline.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See update information for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2021 recommendations are in the evidence reviews. Evidence for the 2012 recommendations is in the full version of the 2012 guideline.

The recommendations in this guideline were developed before the COVID-19 pandemic. Please tell us if there are any particular issues relating to

COVID-19 that we should take into account when finalising the guideline for publication.

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Contents

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 specified otherwise 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 guideline on patient experience in adult NHS services. **[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 explain what neonatal infection is
- discuss the options for management that may be best for their baby (for example, observation, investigations or antibiotic treatment)

- when possible, allow the baby's parents and carers time to think about the information they have been given, and provide further opportunities for discussion if necessary. **[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, carers 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 GBS test in a previous pregnancy
  - her maternity care team will recommend that she has 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 recommend that she has 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 all babies

1.1.12 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 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 developed difficulties with feeding, **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.

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

1.1.13 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 preterm 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 PCR on a rectovaginal swab samples collected between 35 and 37 weeks' gestation in the current pregnancy **or**
- have had a previous baby with an invasive group B streptococcal infection **or**
- have suspected or confirmed chorioamnionitis. **[2021]**

1.2.2 For women without suspected or confirmed chorioamnionitis use intravenous benzylpenicillin to prevent group B streptococcal early-onset neonatal infection. **[2021]**

1.2.3 For women with suspected or confirmed chorioamnionitis, use intravenous benzylpenicillin plus gentamicin to treat the infection and to prevent early-onset neonatal infection. **[2021]**

1.2.4 For women who have a penicillin allergy that is not severe, and so cannot take benzylpenicillin (see recommendations 1.2.2 and 1.2.3), use a cephalosporin with activity against group B streptococcus (for example cefotaxime) alone (additional gentamicin is not needed if the women has suspected or confirmed chorioamnionitis).

In March 2021, this was an off-label use of cephalosporins. See NICE's information on prescribing medicines. **[2021]**

1.2.5 For women who have a severe penicillin allergy, and so cannot take benzylpenicillin (see recommendations 1.2.2 and 1.2.3), consider:

- vancomycin (with gentamicin, if the woman has suspected or confirmed chorioamnionitis), or
- an alternative antibiotic regimen that would be expected to be active against group B streptococcus (with gentamicin, if the woman has suspected or confirmed chorioamnionitis), based on either sensitivity testing performed on the woman's isolate or on local antibiotic susceptibility surveillance data.

In March 2021, this was an off-label use of vancomycin. See NICE's information on prescribing medicines. **[2021]**

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

1.2.7 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]**

1.2.8 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

1.2.9 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: PPROM.

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
- Preterm birth following spontaneous labour before 37 weeks' gestation
- Confirmed rupture of membranes for more than 18 hours before a preterm 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
- Confirmed or suspected chorioamnionitis

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

Red flag clinical indicators:

- Apnoea
- 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
- 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)

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

- In babies with any red flag, or with 2 or more 'non-red-flag' risk factors or clinical indicators:
  - follow recommendations 1.7.1 to 1.7.3 on investigations before starting antibiotics, and
  - start antibiotic treatment according to recommendations 1.8.1 to 1.8.4, 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 up to 8 weeks after birth. **[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 only if it is part of a prospective audit. The audit 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 infection:

- consider starting antibiotic treatment (see recommendations 1.7.1 to 1.7.3 on investigations before starting antibiotics, and recommendations 1.8.1 to 1.8.4 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 1.1.10 and 1.1.11). **[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: risk factors: early onset.

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

1.4.1 When assessing or reviewing a baby:

- be aware of, and check for, the possible clinical indicators of late-onset neonatal infection shown in table 1
- 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. **[2021]**

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

Table 1 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
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	Tachycardia: heart rate 160 beats per minute or more Bradycardia: heart rate less than 60 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 3 of the NICE guideline on sepsis.

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: late onset.

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

1.5.1 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.

1.6 Avoiding routine use of antibiotics in babies

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

1.7 Investigations before starting antibiotics in babies who may have early- or late-onset infection

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

1.7.2 Measure baseline C-reactive protein concentration when starting antibiotic treatment in babies who may have neonatal infection. **[2021]**

1.7.3 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]**

1.7.4 Do not routinely perform urine microscopy or culture as part of the investigations for neonatal infection. **[2021]**

1.7.5 Do not perform skin swab microscopy or culture as part of the investigations for 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.

Advice for site-specific infections

1.7.6 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]**

1.7.7 In babies with a purulent eye discharge take swab samples urgently for microbiological investigation, using methods that can detect chlamydia and gonococcus. Start systemic antibiotic treatment for possible gonococcal infection while waiting for the swab microbiology results. **[2012]**

1.7.8 In babies with clinical signs of umbilical infection, such as a purulent discharge or signs of periumbilical cellulitis (for example, redness, increased skin warmth or swelling):

- perform a blood culture and
- take a swab sample for microscopy and culture and
- start antibiotic treatment with intravenous flucloxacillin and gentamicin (see recommendations 1.8.3 and 1.8.4).

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

1.8 Antibiotics for suspected early-onset infection

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

1.8.2 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]**

1.8.3 Give gentamicin in a starting dose of 5 mg/kg (see recommendation 1.8.4). **[2012]**

1.8.4 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]**

1.8.5 If a second dose of gentamicin is given (see recommendation 1.9.3) 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]**

1.8.6 Take account of blood gentamicin concentrations when deciding on subsequent gentamicin dosing regimen (see recommendations 1.12.1 to 1.12.3). **[2012]**

1.8.7 Record the times of:

- gentamicin administration

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

1.8.8 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]**

1.8.9 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]**

1.9 Duration of antibiotic treatment for early-onset neonatal infection

Investigations during antibiotic treatment for early-onset neonatal infection

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

1.9.2 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

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

- the blood culture is negative and
- the initial clinical suspicion of infection was not strong and
- the baby's clinical condition is reassuring, with no clinical indicators of possible infection and
- the levels and trends of C-reactive protein concentration are reassuring. **[2012]**

1.9.4 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]**

1.9.5 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

1.9.6 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]**

1.9.7 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]**

1.10 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 who have been admitted from home, treat according to recommendation 1.7.12 in the NICE guideline on sepsis. **[2021]**

1.10.3 When using gentamicin, see the recommendations on therapeutic drug monitoring for gentamicin (recommendations 1.13.1 – 1.13.8). **[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]**

Treatment duration for late-onset neonatal infection without meningitis

1.11.4 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 osteomyelitis or infection of a central venous catheter). **[2021]**

1.11.5 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]

1.11.6 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]**

1.11.7 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 Meningitis (babies in neonatal units)

1.12.1 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]**

1.12.2 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]**

1.12.3 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]**

1.12.4 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 1.8.3)
  - subsequent doses and intervals adjusted if necessary based on clinical judgement (see recommendation 1.8.5) and blood gentamicin concentrations (see recommendations 1.13.1 to 1.13.3)
  - treatment lasting for 5 days. **[2012]**

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

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

Discharge after antibiotic treatment

1.12.7 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]**

1.13 Therapeutic drug monitoring for babies receiving gentamicin

Trough concentrations

1.13.1 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]**

1.13.2 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]**

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

1.13.4 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]**

1.13.5 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

1.13.6 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]**

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

1.13.8 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]**

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

1.14.1 Give prophylactic 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]**

1.14.2 If oral administration of nystatin is not possible, give intravenous fluconazole.

In March 2021, this was an off-label use of fluconazole. See NICE's information on prescribing medicines. **[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.

1.15 Care setting

1.15.1 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]**

1.15.2 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]**

1.16 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 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 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 research recommendations, see the rationale and impact section on risk factors for and clinical indicators of possible early-onset neonatal infection.

Full details of the research recommendation are in evidence review D: risk factors and indicators: early onset.

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 in the baby?

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

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

Full details of the research recommendation are in evidence review E: risk factors and indicators: late onset.

Women with prolonged prelabour rupture of membranes

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 research recommendation, see the rationale and impact section on women with prolonged prelabour rupture of membranes.

Full details of the research recommendation are in evidence review C: PPROM.

Investigations for babies who may have early- or late-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]**

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 research recommendation, see the rationale and impact section on antibiotics for late-onset neonatal infection.
>
> Full details of the research recommendation are in evidence review H: antibiotics.

Other recommendations for research

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 research recommendation, see the rationale and impact section on intrapartum antibiotics.
>
> Full details of the research recommendation are in evidence review B: intrapartum antibiotics.

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 research recommendations, see the rationale and impact section on antibiotic-impregnated intravascular catheters for reducing the risk of late-onset neonatal infection.

Full details of the research recommendation are in evidence review F: intravascular catheters.

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 1.1.13

Why the committee made the recommendations

The committee decided that some of the information and support recommendations in previous 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 previous 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

Intrapartum antibiotics

Recommendations 1.2.1 to 1.2.8

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 (GBS) to cover women who had colonisation in a previous pregnancy. This was because GBS colonisation in a previous pregnancy greatly increases the chance of being colonised in future pregnancies.

For women in preterm labour and women with suspected or confirmed 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 preterm labour. The committee also agreed that preterm 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 is also now recommended for women with chorioamnionitis, because chorioamnionitis can be caused by Gram positive or negative bacteria, so clinicians need to use 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 GBS emerging in 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. 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. The new recommendations on intrapartum antibiotics in women with penicillin allergy are consistent with those recommended in the Royal College of Obstetricians and Gynaecologists guideline on prevention of group B streptococcal infection in neonates.

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 preterm labour without prelabour rupture of membranes, women with chorioamnionitis and women with GBS 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

Recommendation 1.2.9

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 (PPROM) 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 research recommendation 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 PPROM 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 GBS 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 recommendations

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.

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.

As there was only limited new evidence, the framework for assessing and managing risk has been retained from 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.

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 further 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 preterm 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 (preterm birth and confirmed rupture of membranes in a preterm 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

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

Recommendations 1.4.1 and 1.4.2

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 research recommendation. 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 sepsis (section 1.4, table 3) 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.

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 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.

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

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

Recommendation 1.5.1

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 recommendations

Investigations for late-onset neonatal infection

Recommendations 1.7.1 to 1.7.5

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. This allows 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. These tests were also not recommended in the 2012 guideline for babies with early-onset infection.

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 research 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 neonates 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 sepsis recommends treating community-acquired sepsis with ceftriaxone or cefotaxime. 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.

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, based 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 a substantial majority of the affected neonates 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 sepsis guideline.

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

Recommendations 1.14.1 and 1.14.2

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.

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 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 webpage on infections.

For details of the guideline committee see the committee member list.

Update information

March 2021: This guideline is an update of NICE guideline CG149 (published August 2012) and will replace it.

We have reviewed the evidence on prevention, diagnosis and treatment for babies with early-onset or late-onset neonatal infection.

Recommendations are marked **[2021]** if the evidence has been reviewed.

Recommendations that have been deleted, or changed without an evidence review

We propose to delete some recommendations from the 2012 guideline. Table 1 sets out these recommendations and includes details of replacement recommendations. If there is no replacement recommendation, an explanation for the proposed deletion is given.

For recommendations shaded in grey and ending **[2012, amended 2021]**, we have made changes that could affect the intent without reviewing the evidence. Yellow shading is used to highlight these changes, and reasons for the changes are given in table 2.

For recommendations shaded in grey and ending **[2012]**, we have not reviewed the evidence. In some cases minor changes have been made – for example, to update links, or bring the language and style up to date – without changing the intent of the recommendation. Minor changes are listed in table 3.

See also the previous NICE guideline and supporting documents.

Table 1 Recommendations that have been deleted

Recommendation in 2012 guideline	Comment
1.1.1.1 If clinical concerns about possible early-onset neonatal infection arise during pregnancy or in the first 72 hours after birth (for example, in relation to risk factors [see table 1] or clinical indicators [see table 2]):	Replaced by: New recommendation (1.1.2).

• tell the baby's parents and carers • explain the reason for concern (including the nature of early-onset neonatal infection) • discuss the preferred options for management (for example, observation, investigations or antibiotic treatment) give the baby's parents and carers time to consider the information provided, and offer further opportunities for discussion if necessary.	
1.1.1.2 If considering antibiotic treatment because of clinical concerns about possible early-onset neonatal infection, discuss: • the rationale for the treatment • the risks and benefits in the individual circumstances • the observations and investigations that may be needed to guide clinical management (for example, when to stop treatment) • the preferred antibiotic regimen and likely duration of treatment • the impact, if any, on where the woman or her baby will be cared for.	Replaced by: New recommendation (1.1.3).
1.1.1.6 If the woman had group B streptococcal colonisation in a previous pregnancy but without infection in the baby, reassure her that this will not affect the management of the birth in the current pregnancy.	This recommendation has been deleted because it is contradicted by new recommendation 1.2.1
1.1.1.8 If there have been any concerns about early-onset neonatal infection before a baby is discharged, advise the parents and carers verbally and in writing that they should seek medical advice (for example, from NHS Direct, their general practice, or an accident and emergency department) if they are concerned that the baby: • is showing abnormal behaviour (for example, inconsolable crying or listlessness), or • is unusually floppy, or	Replaced by: New recommendation (1.1.11).

• has developed difficulties with feeding or with tolerating feeds, or • has an abnormal temperature unexplained by environmental factors (lower than 36°C or higher than 38°C), or • has rapid breathing, or • has a change in skin colour.	
1.1.1.10 If a baby has been treated for suspected or confirmed early-onset neonatal infection: • inform the parents and carers about potential long-term effects of the baby's illness and likely patterns of recovery, and reassure them if no problems are anticipated • take account of parents' and carers' concerns when providing information and planning follow-up.	Replaced by: New recommendation (1.1.10).
1.1.1.12 If the woman has had group B streptococcal colonisation in the pregnancy but without infection in the baby, inform her that if she becomes pregnant again, this will not affect the management of the birth in the next pregnancy.	This recommendation has been deleted because it is contradicted by new recommendation 1.2.1
1.2.1.1 Use table 1 to identify risk factors for early-onset neonatal infection and table 2 to identify clinical indicators of early-onset neonatal infection.	Replaced by: New recommendation (1.3.5).
1.2.1.2 Use tables 1 and 2 to identify red flags (risk factors and clinical indicators that should prompt a high level of concern regarding early-onset neonatal infection).	Replaced by: New recommendation (1.3.5).
1.2.2.1 For women in labour identify and assess any risk factors for early-onset neonatal infection (see table 1). Throughout labour monitor for the emergence of new risk factors, such as intrapartum fever higher than 38°C, or the development of chorioamnionitis.	Replaced by: New recommendation (1.3.1).
1.2.2.2 Manage prelabour rupture of membranes at term according to the recommendations in Intrapartum care (NICE clinical guideline 55).	Replaced by: New recommendation (1.3.2).
1.2.3.1 If there are any risk factors for early-onset neonatal infection (see table 1) or if there are clinical indicators of	Replaced by: New recommendation (1.3.3).

possible early-onset neonatal infection (see table 2) perform a careful clinical assessment without delay. Review the maternal and neonatal history and carry out a physical examination of the baby including an assessment of the vital signs.	

1.2.3.2 Use the following framework based on risk factors and clinical indicators, including red flags (see tables 1 and 2), to direct antibiotic management decisions:
• In babies with any red flags, or with two or more 'non-red flag' risk factors or clinical indicators (see tables 1 and 2), perform investigations (see recommendations 1.5.1.1–1.5.1.3) and start antibiotic treatment. Do not delay starting antibiotics pending the test results (see recommendations 1.6.1.1–1.6.1.3).
• In babies without red flags and only one risk factor or one clinical indicator, using clinical judgement, consider:
  • whether it is safe to withhold antibiotics, and
  • whether it is necessary to monitor the baby's vital signs and clinical condition – if monitoring is required continue it for at least 12 hours (at 0, 1 and 2 hours and then 2-hourly for 10 hours).
	Replaced by:
	New recommendation (1.3.5).

1.2.3.3 In babies being monitored for possible infection: • if clinical concern increases, consider performing necessary investigations (see recommendations 1.5.1.1–1.5.1.3) and starting antibiotic treatment (see recommendations 1.6.1.1–1.6.1.3) • if no further concerns arise during the period of observation reassure the family and, if the baby is to be discharged, give advice to the parents and carers (see recommendation 1.1.1.8).	Replaced by: New recommendation (1.3.8).

1.2.3.4 If a baby needs antibiotic treatment it should be given as soon as possible and always within 1 hour of the decision to treat.	Replaced by: New recommendation (1.3.9).
1.2.3.5 Manage suspected bacterial meningitis according to the recommendations in Bacterial meningitis and meningococcal septicaemia (NICE clinical guideline 102) unless the baby is already receiving care in a neonatal unit.	Replaced by: New recommendation (section 1.12 on meningitis).
1.2.3.6 Manage suspected urinary tract infection according to the recommendations in Urinary tract infection in children (NICE clinical guideline 54).	NICE clinical guideline 54 has been updated since the 2012 and now simply recommends that babies under 3 months with suspected UTI should be referred immediately to a paediatric specialist. The committee agreed that cross referral to this guideline was therefore no longer helpful.
1.2.3.7 Continue routine postnatal care (see Postnatal care, NICE clinical guideline 37) for babies without risk factors (see table 1) or clinical indicators of possible infection (see table 2).	Replaced by: New recommendation (1.3.5).
1.2.3.8 If maternal colonisation with group B streptococcus is first identified after the birth but within the first 72 hours of life, ask the person directly involved in the baby's care (for example, a parent, carer or healthcare professional) whether they have any concerns, identify any other risk factors present and look for clinical indicators of infection. Use this assessment to decide on clinical management (see recommendation 1.2.3.2).	Replaced by: New recommendation (1.3.4).
1.3.1.1 Offer intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early-onset neonatal infection for women who have had: • a previous baby with an invasive group B streptococcal infection • group B streptococcal colonisation, bacteriuria or infection in the current pregnancy.	Replaced by: New recommendation (1.2.1).
1.3.1.2 If the woman decides to take intrapartum antibiotic prophylaxis, give the first dose as soon as possible and continue prophylaxis until the birth of the baby.	Replaced by: New recommendation (1.2.6).
1.3.1.3 Consider intrapartum antibiotic prophylaxis using intravenous	Replaced by: New recommendation (1.2.1).

benzylpenicillin to prevent early-onset neonatal infection for women in preterm labour if there is prelabour rupture of membranes of any duration.	
1.3.1.5 Offer benzylpenicillin as the first choice for intrapartum antibiotic prophylaxis. If the woman is allergic to penicillin, offer clindamycin unless individual group B streptococcus sensitivity results or local microbiological surveillance data indicate a different antibiotic.	Replaced by: New recommendations (1.2.1 to 1.2.4).
1.5.1.1 When starting antibiotic treatment in babies with risk factors for infection or clinical indicators of possible infection, perform a blood culture before administering the first dose.	Replaced by: New recommendation (1.7.1).
1.5.1.2 Measure the C-reactive protein concentration at presentation when starting antibiotic treatment in babies with risk factors for infection or clinical indicators of possible infection.	Replaced by: New recommendation (1.7.2).
1.5.1.3 Perform a lumbar puncture to obtain a cerebrospinal fluid sample before starting antibiotics if it is thought safe to do so and: • there is a strong clinical suspicion of infection, or • there are clinical symptoms or signs suggesting meningitis. If performing the lumbar puncture would unduly delay starting antibiotics, perform it as soon as possible after starting antibiotics.	Replaced by: New recommendation (1.7.3).
1.5.1.4 Do not routinely perform urine microscopy or culture as part of the investigation for early-onset neonatal infection.	Replaced by: New recommendation (1.7.4).
1.5.1.5 Do not perform skin swab microscopy or culture as part of the investigation for early-onset neonatal infection in the absence of clinical signs of a localised infection.	Replaced by: New recommendation (1.7.5).

Table 2 Amended recommendation wording (change to intent) without an evidence review

Recommendation in 2012 guideline	Recommendation in current guideline	Reason for change

1.1.1.5 Reassure parents and carers that babies at increased risk of, or with, early-onset neonatal infection can usually continue to breastfeed, and that every effort will be made to facilitate this. If a baby is temporarily unable to breastfeed, support the mother to express breast milk if she wishes to do so.	1.1.6 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.	Updated from early-onset neonatal infection to neonatal infection, as this can apply to babies at risk of both early- and late-onset infection
Not applicable	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 GBS test in a previous pregnancy - her maternity care team will recommend that she has 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]	This recommendation has been added for consistency with recommendation 1.2.1 which has been updated.
1.1.1.13 For every baby about whom there has been a clinical concern regarding early-onset neonatal infection, formulate a post-discharge management plan, taking into account factors such as: • the level of the initial clinical concern	1.1.13 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	Updated from early-onset neonatal infection to neonatal infection, as this can apply to babies with clinical concern about both early- and late-onset infection

• the presence of risk factors • parents' and carers' concerns.	• parents' and carers' concerns	
1.6.1.3 Give gentamicin in a starting dosage of 5 mg/kg[1] [1] Gentamicin is licensed for use in newborn babies. The summary of product characteristics recommends a dosage of 4–7 mg/kg/day administered in a single dose. The evidence reviewed for the guideline supports a starting dosage of 5 mg/kg every 36 hours administered in a single dose.	1.8.3 Give gentamicin in a starting dose of 5 mg/kg (see recommendation 1.8.4). [2012] 1.8.4 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]	Footnotes from 2012 guideline have been added as a new recommendation, in line with new accessibility requirements. Information on off label prescribing of gentamicin has been updated according to the current summary of product characteristics.
1.7.1.2 Consider performing a lumbar puncture to obtain a cerebrospinal fluid sample in a baby who did not have a lumbar puncture at presentation who is receiving antibiotics, if it is thought safe to do so and if the baby: • has a C-reactive protein concentration of 10 mg/litre or greater, or • has a positive blood culture, or • does not respond satisfactorily to antibiotic treatment.	1.9.2 Only consider performing a lumbar puncture to obtain a cerebrospinal fluid sample if it would be safe to do so, and only if the baby: • is receiving antibiotics and • did not have a lumbar puncture at presentation and • has any of the following: ○ an unsatisfactory response to antibiotic treatment. ○ a positive blood culture	The recommendation has been restructured to emphasise that lumbar puncture should only be considered if the circumstances in the recommendation are met, following feedback from the committee and stakeholders that lumbar puncture was being carried out too often. This rewording is thought to be in line with the intention of the original committee.

	○ a C-reactive protein concentration of 10 mg/litre or greater	
1.8.1.1 If a second dose of gentamicin is to be given (see recommendation 1.6.1.4) measure the trough blood gentamicin concentration immediately before giving the second dose. Consider the trough concentration before giving a third dose of gentamicin.	1.13.1 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.	The cross reference to a recommendation on the timing of gentamicin dosing in early-onset neonatal infection has been removed because there is no similar recommendation to refer to for late-onset neonatal infection, and the recommendation is relevant to both early and late onset infection. 'Consider' has been replaced with 'Take to trough concentrations into account' to make the recommendation clearer and to avoiding using the word consider in a way that is not consistent with current NICE style. The recommendation has also been edited into the direct style (in line with current NICE style for recommendations in guidelines).
1.8.1.2 Hospital services should make blood gentamicin concentrations available to healthcare professionals in time to inform the next dosage decision (for example, within 30 hours of sampling).	1.13.3 Hospital services should make blood gentamicin concentrations available to healthcare professionals in time to inform the next dosage decision.	The example in brackets has been removed as it relates specifically to early-onset neonatal infection, and the guideline now covers both early and late-onset neonatal infection.
1.7.1.2 Consider performing a lumbar puncture to obtain a cerebrospinal fluid sample in a baby who did not have a lumbar puncture at	1.9.2 Consider performing a lumbar puncture to obtain a cerebrospinal fluid sample in a baby who did not have a lumbar puncture at	During consultation of the scope for this guideline update, stakeholders highlighted that the

presentation who is receiving antibiotics, if it is thought safe to do so and if the baby: • has a C-reactive protein concentration of 10 mg/litre or greater, or • has a positive blood culture, or • does not respond satisfactorily to antibiotic treatment.	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 recommendation was resulting in a lot of lumbar punctures being carried out unnecessarily, especially when a baby had a CRP>10 but was otherwise well. The committee agreed that this was not the intention of the committee that wrote the guideline in 2012. It was therefore agreed that the recommendation should be brought in line with the recommendation formulated by the 2020 guideline committee on use of lumbar puncture when investigating late-onset infection.

1

2 **Table 3 Minor changes to recommendation wording (no change to intent)**

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [2021]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) where possible. Yellow highlighting has not been applied to these changes.