Neonatal jaundice

NICE guideline

Draft for consultation, July 2015

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence for the 2015 recommendations is contained in the addendum of the 2015 guideline.

Evidence for the 2010 recommendations is in the full version of the 2010 guideline.

Contents

Introduction

Recommendations on neonatal jaundice have been updated in section 1.4. The addendum [hyperlink to addendum on the NICE website; update this link to go the guideline evidence tab when preparing for publication] contains details of the methods and evidence used to update these recommendations.

Jaundice is one of the most common conditions needing medical attention in newborn babies. Jaundice refers to the yellow colouration of the skin and the sclerae (whites of the eyes) caused by the accumulation of bilirubin in the skin and mucous membranes. It is caused by a raised level of bilirubin in the body, a condition known as hyperbilirubinaemia.

Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month. For most babies, jaundice is not an indication of an underlying disease, and this early jaundice (termed 'physiological jaundice') is usually harmless.

Breastfed babies are more likely than bottle-fed babies to develop physiological jaundice within the first week of life. Prolonged jaundice – that is, jaundice persisting beyond the first 14 days – is also seen more commonly in breastfed babies. Prolonged jaundice is usually harmless, but can sometimes be an indication of serious liver disease.

Jaundice has many possible causes, including blood group incompatibility (most commonly rhesus or ABO incompatibility), other causes of haemolysis (breaking down of red blood cells), sepsis (infection), liver disease, bruising and metabolic disorders. Deficiency of a particular enzyme, glucose-6-phosphate-dehydrogenase, can cause severe neonatal jaundice. Glucose-6-phosphate-dehydrogenase deficiency is more common in certain ethnic groups and runs in families.

Bilirubin is mainly produced from the breakdown of red blood cells. Red cell breakdown produces unconjugated (or 'indirect') bilirubin, which circulates mostly bound to albumin although some is 'free' and hence able to enter the

brain. Unconjugated bilirubin is metabolised in the liver to produce conjugated (or 'direct') bilirubin which then passes into the gut and is largely excreted in stool. The terms direct and indirect refer to the way the laboratory tests measure the different forms. Some tests measure total bilirubin and do not distinguish between the two forms.

In young babies, unconjugated bilirubin can penetrate the membrane that lies between the brain and the blood (the blood–brain barrier). Unconjugated bilirubin is potentially toxic to neural tissue (brain and spinal cord). Entry of unconjugated bilirubin into the brain can cause both short-term and long-term neurological dysfunction (bilirubin encephalopathy). The term kernicterus is used to denote the clinical features of acute or chronic bilirubin encephalopathy, as well as the yellow staining in the brain associated with the former. The risk of kernicterus is increased in babies with extremely high bilirubin levels. Kernicterus is also known to occur at lower levels of bilirubin in term babies who have risk factors, and in preterm babies.

Clinical recognition and assessment of jaundice can be difficult, particularly in babies with darker skin tones. Once jaundice is recognised, there is uncertainty about when to treat, and there is widespread variation in the use of phototherapy and exchange transfusion. There is a need for more uniform, evidence-based practice and for consensus-based practice where such evidence is lacking. This guideline provides guidance regarding the recognition, assessment and treatment of neonatal jaundice. The advice is based on evidence where this is available and on consensus-based practice where it is not.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

Patient-centred care

This guideline offers best practice advice on the care of babies with neonatal jaundice.

Parents of babies with neonatal jaundice and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Parents should have the opportunity to make informed decisions about the care and treatment of their babies, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If a parent does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.

Key terms used in this guideline

Direct antiglobulin test (DAT) Also known as the direct Coombs' test; this test is used to detect antibodies or complement proteins that are bound to the surface of red blood cells

Intensified phototherapy Phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy may be intensified by adding another light source or by increasing the irradiance of the initial light source used

Near-term 35 to 36 weeks gestational age

Phototherapy Phototherapy given using an artificial light source with an appropriate spectrum and irradiance. This can be delivered using light-emitting diode (LED), fibreoptic or fluorescent lamps, tubes or bulbs

Preterm Less than 37 weeks gestational age

Prolonged jaundice Jaundice lasting more than 14 days in term babies and more than 21 days in preterm babies

Significant hyperbilirubinaemia An elevation of the serum bilirubin to a level requiring treatment

Term 37 weeks or more gestational age

Visible jaundice Jaundice detected by visual inspection

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Committee is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also 'Patient-centred care').

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values

and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation wording in guideline updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations shaded in grey and ending 2010 because these were developed before the implementation of the 2009 version of 'The guidelines manual' (see 'Update information' box below for details about how recommendations are labelled). In particular, for recommendations labelled 2010, the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Update information

This guideline is an update of NICE guideline CG98 (published May 2010) and will replace it.

New recommendations have been added for the types of phototherapy used for babies with neonatal jaundice.

You are invited to comment on the new and updated recommendations in this guideline. These are marked as:

- **[new 2015]** if the evidence has been reviewed and the recommendation has been added or updated
- **[2015]** if the evidence has been reviewed but no change has been made to the recommended action.

You are also invited to comment on recommendations that NICE proposes to delete from the 2010 guideline, because either the evidence has been reviewed and the recommendations have been updated, or NICE has updated other relevant guidance and has replaced the original recommendations. Appendix A sets out these recommendations and includes details of replacement recommendations. Where there is no replacement recommendation, an explanation for the proposed deletion is given.

Where recommendations are shaded in grey and end **[2010]**, the evidence has not been reviewed since the original guideline. We will not be able to accept comments on these recommendations. Yellow shading in these recommendations indicates wording changes that have been made for the purposes of clarification only.

The original NICE guideline and supporting documents are available here.

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Key priorities for implementation

The following recommendations were identified as priorities for implementation in the 2010 guideline and have not been changed in the 2015 update.

Information for parents or carers

- Offer parents or carers information about neonatal jaundice that is tailored to their needs and expressed concerns. This information should be provided through verbal discussion backed up by written information. Care should be taken to avoid causing unnecessary anxiety to parents or carers. Information should include:
  - factors that influence the development of significant hyperbilirubinaemia
  - how to check the baby for jaundice
  - what to do if they suspect jaundice
  - the importance of recognising jaundice in the first 24 hours and of seeking urgent medical advice
  - the importance of checking the baby's nappies for dark urine or pale chalky stools
  - the fact that neonatal jaundice is common, and reassurance that it is usually transient and harmless
  - reassurance that breastfeeding can usually continue. [**1.1.1]**

Care for all babies

- Identify babies as being more likely to develop significant hyperbilirubinaemia if they have any of the following factors:
  - gestational age under 38 weeks
  - a previous sibling with neonatal jaundice requiring phototherapy
  - mother's intention to breastfeed exclusively
  - visible jaundice in the first 24 hours of life. **[1.2.1]**

- In all babies:
  - check whether there are factors associated with an increased likelihood of developing significant hyperbilirubinaemia soon after birth

  - examine the baby for jaundice at every opportunity especially in the first 72 hours. **[1.2.3]**

- When looking for jaundice (visual inspection):
  - check the naked baby in bright and preferably natural light
  - examination of the sclerae, gums and blanched skin is useful across all skin tones. **[1.2.5]**

- Do not rely on visual inspection alone to estimate the bilirubin level in a baby with jaundice. **[1.2.6]**

Additional care

- Ensure babies with factors associated with an increased likelihood of developing significant hyperbilirubinaemia receive an additional visual inspection by a healthcare professional during the first 48 hours of life. **[1.2.9]**

How to measure the bilirubin level

- When measuring the bilirubin level:
  - use a transcutaneous bilirubinometer in babies with a gestational age of 35 weeks or more and postnatal age of more than 24 hours
  - if a transcutaneous bilirubinometer is not available, measure the serum bilirubin
  - if a transcutaneous bilirubinometer measurement indicates a bilirubin level greater than 250 micromol/litre check the result by measuring the serum bilirubin
  - always use serum bilirubin measurement to determine the bilirubin level in babies with jaundice in the first 24 hours of life
  - always use serum bilirubin measurement to determine the bilirubin level in babies less than 35 weeks gestational age
  - always use serum bilirubin measurement for babies at or above the relevant treatment threshold for their postnatal age, and for all subsequent measurements
  - do not use an icterometer. **[1.2.15]**

How to manage hyperbilirubinaemia

- Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see threshold table and the full version for the treatment threshold graphs). **[1.3.4]**

Care of babies with prolonged jaundice

- Follow expert advice about care for babies with a conjugated bilirubin level greater than 25 micromol/litre because this may indicate serious liver disease. **[1.7.2]**

1 Recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the 2010 recommendations. The guideline addendum gives details of the methods and the evidence used to develop the 2015 recommendations.

Threshold table

Consensus-based bilirubin thresholds for management of babies 38 weeks or more gestational age with hyperbilirubinaemia

Age (hours)	Bilirubin measurement (micromol/litre)			
0	–	–	> 100	> 100
6	> 100	> 112	> 125	> 150
12	> 100	> 125	> 150	> 200
18	> 100	> 137	> 175	> 250
24	> 100	> 150	> 200	> 300
30	> 112	> 162	> 212	> 350
36	> 125	> 175	> 225	> 400
42	> 137	> 187	> 237	> 450
48	> 150	> 200	> 250	> 450
54	> 162	> 212	> 262	> 450
60	> 175	> 225	> 275	> 450
66	> 187	> 237	> 287	> 450
72	> 200	> 250	> 300	> 450
78	–	> 262	> 312	> 450
84	–	> 275	> 325	> 450
90	–	> 287	> 337	> 450
96+	–	> 300	> 350	> 450

Action	Repeat bilirubin measurement in 6–12 hours	Consider phototherapy and repeat bilirubin measurement in 6 hours	Start phototherapy	Perform an exchange transfusion unless the bilirubin level falls below threshold while the treatment is being prepared

1.1 Information for parents or carers

1.1.1 Offer parents or carers information about neonatal jaundice that is tailored to their needs and expressed concerns. This information should be provided through verbal discussion backed up by written information. Care should be taken to avoid causing unnecessary anxiety to parents or carers. Information should include:

- factors that influence the development of significant hyperbilirubinaemia
- how to check the baby for jaundice
- what to do if they suspect jaundice
- the importance of recognising jaundice in the first 24 hours and of seeking urgent medical advice
- the importance of checking the baby's nappies for dark urine or pale chalky stools
- the fact that neonatal jaundice is common, and reassurance that it is usually transient and harmless
- reassurance that breastfeeding can usually continue. **[2010]**

1.2 Care for all babies

1.2.1 Identify babies as being more likely to develop significant hyperbilirubinaemia if they have any of the following factors:

- gestational age under 38 weeks
- a previous sibling with neonatal jaundice requiring phototherapy
- mother's intention to breastfeed exclusively
- visible jaundice in the first 24 hours of life. **[2010]**

1.2.2 Ensure that adequate support is offered to all women who intend to breastfeed exclusively. See the NICE guideline on postnatal care for information on breastfeeding support. **[2010]**

1.2.3 In all babies:

- check whether there are factors associated with an increased likelihood of developing significant hyperbilirubinaemia soon after birth
- examine the baby for jaundice at every opportunity especially in the first 72 hours. **[2010]**

1.2.4 Parents, carers and healthcare professionals should all look for jaundice (visual inspection). **[2010]**

1.2.5 When looking for jaundice (visual inspection):

- check the naked baby in bright and preferably natural light
- examination of the sclerae, gums and blanched skin is useful across all skin tones. **[2010]**

1.2.6 Do not rely on visual inspection alone to estimate the bilirubin level in a baby with jaundice. **[2010]**

1.2.7 Do not measure bilirubin levels routinely in babies who are not visibly jaundiced. **[2010]**

1.2.8 Do not use any of the following to predict significant hyperbilirubinaemia:

- umbilical cord blood bilirubin level
- end-tidal carbon monoxide (ETCOc) measurement
- umbilical cord blood direct antiglobulin test (DAT) (Coombs' test). **[2010]**

Additional care

1.2.9 Ensure babies with factors associated with an increased likelihood of developing significant hyperbilirubinaemia receive an additional visual inspection by a healthcare professional during the first 48 hours of life. **[2010]**

Urgent additional care for babies with visible jaundice in the first 24 hours

1.2.10 Measure and record the serum bilirubin level urgently (within 2 hours) in all babies with suspected or obvious jaundice in the first 24 hours of life. **[2010]**

1.2.11 Continue to measure the serum bilirubin level every 6 hours for all babies with suspected or obvious jaundice in the first 24 hours of life until the level is both:

- below the treatment threshold
- stable and/or falling. **[2010]**

1.2.12 Arrange a referral to ensure that an urgent medical review is conducted (as soon as possible and within 6 hours) for babies with suspected or obvious jaundice in the first 24 hours of life to exclude pathological causes of jaundice. **[2010]**

1.2.13 Interpret bilirubin levels according to the baby's postnatal age in hours and manage hyperbilirubinaemia according to the threshold

table and the treatment threshold graphs in the full guideline. **[2010]**

Care for babies more than 24 hours old

1.2.14 Measure and record the bilirubin level urgently (within 6 hours) in all babies more than 24 hours old with suspected or obvious jaundice. **[2010]**

How to measure the bilirubin level

1.2.15 When measuring the bilirubin level:

- use a transcutaneous bilirubinometer in babies with a gestational age of 35 weeks or more and postnatal age of more than 24 hours
- if a transcutaneous bilirubinometer is not available, measure the serum bilirubin
- if a transcutaneous bilirubinometer measurement indicates a bilirubin level greater than 250 micromol/litre check the result by measuring the serum bilirubin
- always use serum bilirubin measurement to determine the bilirubin level in babies with jaundice in the first 24 hours of life
- always use serum bilirubin measurement to determine the bilirubin level in babies less than 35 weeks gestational age
- always use serum bilirubin measurement for babies at or above the relevant treatment thresholds for their postnatal age, and for all subsequent measurements
- do not use an icterometer. **[2010]**

1.3 Management and treatment of hyperbilirubinaemia

Information for parents or carers on treatment

1.3.1 Offer parents or carers information about treatment for hyperbilirubinaemia, including:

- anticipated duration of treatment
- reassurance that breastfeeding, nappy-changing and cuddles can usually continue. **[2010]**

1.3.2 Encourage mothers of breastfed babies with jaundice to breastfeed frequently, and to wake the baby for feeds if necessary. **[2010]**

1.3.3 Provide lactation/feeding support to breastfeeding mothers whose baby is visibly jaundiced. **[2010]**

How to manage hyperbilirubinaemia

1.3.4 Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see threshold table and the full guideline for treatment threshold graphs). **[2010]**

1.3.5 Do not use the albumin/bilirubin ratio when making decisions about the management of hyperbilirubinaemia. **[2010]**

1.3.6 Do not subtract conjugated bilirubin from total serum bilirubin when making decisions about the management of hyperbilirubinaemia (see management thresholds in the threshold table and the treatment threshold graphs in the full guideline). **[2010]**

1.4 Measuring and monitoring bilirubin thresholds during phototherapy

Starting phototherapy

1.4.1 Use serum bilirubin measurement and the treatment thresholds in the threshold table and the treatment threshold graphs in the full guideline when considering the use of phototherapy. **[2010]**

1.4.2 In babies with a gestational age of 38 weeks or more whose bilirubin is in the 'repeat bilirubin measurement' category in the threshold table, repeat the bilirubin measurement in 6–12 hours. **[2010]**

1.4.3 In babies with a gestational age of 38 weeks or more whose bilirubin is in the 'consider phototherapy' category in the threshold table repeat the bilirubin measurement in 6 hours regardless of whether or not phototherapy has subsequently been started. **[2010]**

1.4.4 Do not use phototherapy in babies whose bilirubin does not exceed the phototherapy threshold levels in the threshold table and the treatment threshold graphs in the full guideline. **[2010]**

During phototherapy

1.4.5 During phototherapy:

- repeat serum bilirubin measurement 4–6 hours after initiating phototherapy
- repeat serum bilirubin measurement every 6–12 hours when the serum bilirubin level is stable or falling. **[2010]**

Stopping phototherapy

1.4.6 Stop phototherapy once serum bilirubin has fallen to a level at least 50 micromol/litre below the phototherapy threshold (see threshold table and the full guideline for treatment threshold graphs). **[2010]**

1.4.7 Check for rebound of significant hyperbilirubinaemia with a repeat serum bilirubin measurement 12–18 hours after stopping phototherapy. Babies do not necessarily have to remain in hospital for this to be done. **[2010]**

Type of phototherapy to use

1.4.8 Do not use sunlight as treatment for hyperbilirubinaemia. **[2010]**

1.4.9 Use phototherapy[1] to treat significant hyperbilirubinaemia (see the threshold table and the full guideline for treatment threshold graphs) in babies. **[new 2015]**

1.4.10 Consider intensified phototherapy[2] to treat significant hyperbilirubinaemia in babies if any of the following apply **[new 2015]**:

- the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour)
- the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and the full guideline for treatment threshold graphs)
- the bilirubin level fails to respond to initial phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting phototherapy). **[2010]**

1.4.11 If the serum bilirubin level falls during intensified phototherapy to a level 50 micromol/litre below the threshold for which exchange transfusion is indicated reduce the intensity of phototherapy. **[2010]**

Information for parents or carers on phototherapy

1.4.12 Offer parents or carers verbal and written information on phototherapy including all of the following:

- why phototherapy is being considered
- why phototherapy may be needed to treat significant hyperbilirubinaemia
- the possible adverse effects of phototherapy
- the need for eye protection and routine eye care

[1] Phototherapy given using an artificial light source with an appropriate spectrum and irradiance. This can be delivered using light-emitting diode (LED), fibreoptic or fluorescent lamps, tubes or bulbs.

[2] Phototherapy that is given with an increased level of irradiance with an appropriate spectrum. Phototherapy can be intensified by adding another light source or increasing the irradiance of the initial light source used.

- reassurance that short breaks for feeding, nappy changing and cuddles will be encouraged
- what might happen if phototherapy fails
- rebound jaundice
- potential long-term adverse effects of phototherapy
- potential impact on breastfeeding and how to minimise this. **[2010]**

General care of the baby during phototherapy

1.4.13 During phototherapy:

- place the baby in a supine position unless other clinical conditions prevent this
- ensure treatment is applied to the maximum area of skin
- monitor the baby's temperature and ensure the baby is kept in an environment that will minimise energy expenditure (thermoneutral environment)
- monitor hydration by daily weighing of the baby and assessing wet nappies
- support parents and carers and encourage them to interact with the baby. **[2010]**

1.4.14 Give the baby eye protection and routine eye care during phototherapy. **[2010]**

1.4.15 Use tinted headboxes as an alternative to eye protection in babies with a gestational age of 37 weeks or more undergoing phototherapy. **[2010]**

Monitoring the baby during phototherapy

1.4.16 During phototherapy:

- using clinical judgement, encourage short breaks (of up to 30 minutes) for breastfeeding, nappy changing and cuddles

- continue lactation/feeding support
- do not give additional fluids or feeds routinely.

Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. **[2015]**

1.4.17 During intensified phototherapy:

- do not interrupt phototherapy for feeding but continue administering intravenous/enteral feeds
- continue lactation/feeding support so that breastfeeding can start again when treatment stops.

Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. **[2015]**

Phototherapy equipment

1.4.18 Ensure all phototherapy equipment is maintained and used according to the manufacturers' guidelines. **[2010]**

1.4.19 Use incubators or bassinets according to clinical need and availability. **[2010]**

1.4.20 Do not use white curtains routinely with phototherapy as they may impair observation of the baby. **[2010]**

1.5 Factors that influence the risk of kernicterus

1.5.1 Identify babies with hyperbilirubinaemia as being at increased risk of developing kernicterus if they have any of the following:

- a serum bilirubin level greater than 340 micromol/litre in babies with a gestational age of 37 weeks or more
- a rapidly rising bilirubin level of greater than 8.5 micromol/litre per hour
- clinical features of acute bilirubin encephalopathy. **[2010]**

1.6 Formal assessment for underlying disease

1.6.1 In addition to a full clinical examination by a suitably trained healthcare professional, carry out all of the following tests in babies with significant hyperbilirubinaemia as part of an assessment for underlying disease (see threshold table and the full guideline for treatment threshold graphs):

- serum bilirubin (for baseline level to assess response to treatment)
- blood packed cell volume
- blood group (mother and baby)
- DAT (Coombs' test). Interpret the result taking account of the strength of reaction, and whether mother received prophylactic anti-D immunoglobulin during pregnancy. **[2010]**

1.6.2 When assessing the baby for underlying disease, consider whether the following tests are clinically indicated:

- full blood count and examination of blood film
- blood glucose-6-phosphate dehydrogenase levels, taking account of ethnic origin
- microbiological cultures of blood, urine and/or cerebrospinal fluid (if infection is suspected). **[2010]**

1.7 Care of babies with prolonged jaundice

1.7.1 In babies with a gestational age of 37 weeks or more with jaundice lasting more than 14 days, and in babies with a gestational age of less than 37 weeks and jaundice lasting more than 21 days:

- look for pale chalky stools and/or dark urine that stains the nappy
- measure the conjugated bilirubin
- carry out a full blood count
- carry out a blood group determination (mother and baby) and DAT (Coombs' test). Interpret the result taking account of the

strength of reaction, and whether mother received prophylactic anti-D immunoglobulin during pregnancy

- carry out a urine culture
- ensure that routine metabolic screening (including screening for congenital hypothyroidism) has been performed. **[2010]**

1.7.2 Follow expert advice about care for babies with a conjugated bilirubin level greater than 25 micromol/litre because this may indicate serious liver disease. **[2010]**

1.8 Intravenous immunoglobulin

1.8.1 Use intravenous immunoglobulin (IVIG) (500 mg/kg over 4 hours) as an adjunct to continuous intensified phototherapy in cases of rhesus haemolytic disease or ABO haemolytic disease when the serum bilirubin continues to rise by more than 8.5 micromol/litre per hour. **[2010]**

1.8.2 Offer parents or carers information on IVIG including:

- why IVIG is being considered
- why IVIG may be needed to treat significant hyperbilirubinaemia
- the possible adverse effects of IVIG
- when it will be possible for parents or carers to see and hold the baby. **[2010]**

1.9 Exchange transfusion

1.9.1 Offer parents or carers information on exchange transfusion including:

- the fact that exchange transfusion requires that the baby be admitted to an intensive care bed
- why an exchange transfusion is being considered
- why an exchange transfusion may be needed to treat significant hyperbilirubinaemia
- the possible adverse effects of exchange transfusions

- when it will be possible for parents or carers to see and hold the baby after the exchange transfusion. **[2010]**

1.9.2 Use a double-volume exchange transfusion to treat babies:

- whose serum bilirubin level indicates its necessity (see threshold table and the full guideline for treatment threshold graphs) **and/or**
- with clinical features and signs of acute bilirubin encephalopathy. **[2010]**

1.9.3 During exchange transfusion do not:

- stop continuous intensified phototherapy
- perform a single-volume exchange
- use albumin priming
- routinely administer intravenous calcium. **[2010]**

1.9.4 Following exchange transfusion:

- maintain continuous intensified phototherapy
- measure serum bilirubin level within 2 hours and manage according to the threshold table and the treatment threshold graphs in the full guideline. **[2010]**

1.10 Other therapies

1.10.1 Do not use any of the following to treat hyperbilirubinaemia:

- agar
- albumin
- barbiturates
- charcoal
- cholestyramine
- clofibrate
- D-penicillamine
- glycerin

- manna
- metalloporphyrins
- riboflavin
- traditional Chinese medicine
- acupuncture
- homeopathy. **[2010]**

2 Research recommendations

In 2010, the Guideline Committee made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Breastfeeding and hyperbilirubinaemia

What are the factors that underlie the association between breastfeeding and jaundice?

Why this is important

Breastfeeding has been shown to be a factor in significant hyperbilirubinaemia. The reasons for this association have not yet been fully elucidated.

This question should be answered by studying infants in the first 28 days of life receiving different feeding types (breast milk, formula feeds or mixed feeds). Infants who do not develop significant hyperbilirubinaemia should be compared with infants with significant hyperbilirubinaemia. The outcomes chosen should include maternal factors, neonatal factors and blood analyses.

2.2 Trancutaneous bilirubin screening and risk factors

What is the comparative effectiveness and cost-effectiveness of universal pre-discharge transcutaneous bilirubin screening alone or combined with a risk assessment in reducing jaundice-related neonatal morbidity and hospital readmission?

Why this is important

There is good evidence that a risk assessment that combines the result of a timed transcutaneous bilirubin level with risk factors for significant hyperbilirubinaemia is effective at preventing later significant hyperbilirubinaemia.

This question should be answered by studying the effects of timed pre-discharge transcutaneous bilirubin levels and timed pre-discharge transcutaneous bilirubin levels combined with risk assessment. The study population should consist of babies in the first 28 days of life, with subgroups including near-term babies and babies with dark skin tones. The interventions should be compared with standard care (discharge without timed transcutaneous bilirubin level), and the outcomes chosen should include significant hyperbilirubinaemia, cost-effectiveness and parental anxiety.

2.3 Transcutaneous bilirubinometers

What is the comparative accuracy of the Minolta JM-103 and the BiliChek when compared to serum bilirubin levels in all babies?

Why this is important

The accuracy of transcutaneous bilirubinometers (Minolta JM-103 and BiliChek) has been adequately demonstrated in term babies below treatment levels (bilirubin less than 250 micromol/litre). New research is needed to evaluate the accuracy of different transcutaneous bilirubinometers in comparison to serum bilirubin levels in all babies.

This question should be answered by comparing bilirubin levels taken using different transcutaneous bilirubinometers with bilirubin levels assessed using serum (blood) tests. The study population should comprise babies in the first 28 days of life, with subgroups including preterm babies, babies with dark skin tones, babies with high levels of bilirubin and babies after phototherapy. The outcomes chosen should include diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value), parental anxiety, staff and parental satisfaction with test and cost effectiveness.

2.4 Interruptions during phototherapy

How frequently and for how long can phototherapy be interrupted without adversely effecting clinical outcomes?

Why this is important

The effectiveness and tolerability of intermittent phototherapy has been adequately demonstrated in term babies at low treatment levels (bilirubin less than 250 micromol/litre). New research is needed to evaluate the effectiveness and tolerability of different frequencies of interruptions of different durations.

The study population should comprise babies in the first 28 days of life in phototherapy. Interruptions of 45 or 60 minutes would be made either on demand, every hour or every 2 hours, and compared with interruptions of up to 30 minutes every 3 hours. The outcomes chosen should include effectiveness in terms of the mean decrease in bilirubin levels and the mean duration of phototherapy. Extra outcomes could include adverse effects, parental bonding and parental anxiety, staff and parental satisfaction with treatment and cost effectiveness.

2.5 National registries

National registries are needed of cases of significant hyperbilirubinaemia, kernicterus and exchange transfusions.

Why this is important

There is good evidence that prospective surveys in the UK and data from a national kernicterus register in the US can help to identify root causes of kernicterus and acute bilirubin encephalopathy.

The study population should comprise all children with a peak bilirubin level greater than 450 micromol/litre, which is the threshold for an exchange transfusion recommended by NICE. The intervention would be maternal, prenatal, perinatal and neonatal factors. The outcomes chosen should be

shortcomings in clinical and service provision to prevent recurring themes in kernicterus cases.

3 Other information

3.1 Scope and how this guideline was developed

The scope for the 2010 guideline covers the recommendations labelled **[2010]**. The recommendations labelled **[new 2015]** have been produced during the update.

How this guideline was developed

The 2010 guideline was developed by the National Collaborating Centre for Women's and Children's Health, which is based at the Royal College of Obstetricians and Gynaecologists. The Collaborating Centre worked with a Guideline Committee, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

NICE's Clinical Guidelines Update Programme updated this guideline in 2015. This guideline was updated using a Standing Committee of healthcare professionals, methodologists and lay members from a range of disciplines and localities, as well as topic experts.

The methods and processes for developing NICE clinical guidelines can be found here.

4 Standing Committee and NICE staff

4.1 Standing Committee

Members of Standing Committee A and the topic experts for the 2015 update are listed on the NICE website.

For the composition the previous Guideline Committee see the full guideline.

4.2 Clinical Guidelines Update Team

Philip Alderson
Clinical Adviser

Nicole Elliott
Associate Director

Jennifer Craven
Information Scientist

Nitara Prasannan
Technical Analyst

Toni Tan
Technical Advisor

Rebecca Parsons
Project Manager

Emma Banks
Co-ordinator

Charlotte Purves
Administrator

4.3 NICE project team

Mark Baker
Clinical Lead

Christine Carson

Guideline Lead

Louise Shires

Guideline Commissioning Manager

Joy Carvill (until June 2015) and Trudie Willingham (from June 2015)

Guideline Coordinator

Beth Shaw (until May 2015) and Steven Barnes (from May 2015)

Technical Lead

Catharine Baden-Daintree

Editor

4.4 Declarations of interests

The following members of the Standing Committee made declarations of interest. All other members of the Committee stated that they had no interests to declare.

Committee member	Interest declared	Type of interest	Decision taken
Damien Longson	Family member employee of NICE.	Personal family non-specific	Declare and participate
Damien Longson	Director of Research & Innovation, Manchester Mental Health & Social Care NHS Trust.	Personal non-specific financial	Declare and participate
Catherine Briggs	Husband is a consultant anaesthetist at the University Hospital of South Manchester.	Personal family non-specific	Declare and participate
Catherine Briggs	Member of the Royal College of Surgeons, the Royal College of General Practitioners, the Faculty of Sexual and Reproductive	Personal non-specific financial	Declare and participate

	Health and the BMA.		
Catherine Briggs	Chaired a discussion panel on urinary tract infections in women for Amco.	Personal non-specific financial	Declare and participate
John Cape	Trustee of the Anna Freud Centre, a child and family mental health charity which applies for and receives grants from the department of health and the national institute for health research.	Personal non-specific non-financial	Declare and participate
John Cape	Member of British Psychological Society & British Association for Behaviour & Cognitive Psychotherapists who seek to influence policy towards psychology & psychological therapies.	Personal non-specific non-financial	Declare and participate
John Cape	Clinical Services Lead half-day a week to Big Health, a digital health company that has one commercial product; an online CBT self-help programme for insomnia with online support	Personal non-specific financial	Declare and participate
Alun Davies	Research grant funding – commercial: Vascular Insights; Acergy Ltd; Firstkind; URGO laboratoire; Sapheon Inc (terminated 2013). All administered by Imperial College London as Sponsor and Professor Davies	Personal non-specific financial	Declare and participate

	as CI.		
Alun Davies	Research grant funding – non-commercial: National Institute for Health Research, British Heart Foundation, Royal College of Surgeons, Circulation Foundation, European Venous Forum.	Personal non-specific financial	Declare and participate
Alun Davies	Non-commercial: Attendance at numerous national & international meetings as an invited guest to lecture where the organising groups receive funding from numerous sources including device and pharmaceutical manufacturers. Organising groups pay expenses and occasionally honoraria - the exact source of funding is often not known.	Personal non-specific financial	Declare and participate
Alison Eastwood	Member of an independent academic team at Centre for Review & Dissemination, University of York commissioned by NICE through NIHR to undertake technology assessment reviews.	Non-personal non-specific financial	Declare and participate
Sarah Fishburn	Organises workshops for physiotherapists treating pelvic girdle pain. Paid for this work.	Personal non-specific financial	Declare and participate

Sarah Fishburn	Payment and expenses from the Nursing and Midwifery Council as a lay panellist of the Fitness to Practise Investigating Committee.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Lay reviewer with the Local Supervising Authority auditing supervision of midwives - payment and expenses for this work.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Lay reviewer for the National Institute for Health Research; has reviewed a number of research proposals being considered for funding. Paid for carrying out these reviews.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Chair of the Pelvic Partnership, a support group for women with pregnancy-related pelvic girdle pain (voluntary position).	Personal non-specific financial	Declare and participate
Sarah Fishburn	Trained as a chartered physiotherapist and qualified in 1988 but have not been in clinical practice since 1997. Remains a non-practicing member of the Chartered Society of Physiotherapy.	Personal non-specific financial	Declare and participate
Sarah Fishburn	Appointed by Mott MacDonald to carry out reviews as a lay reviewer on behalf to the Nursing and Midwifery Council of	Personal non-specific financial	Declare and participate

	Local Supervising Authorities and Universities providing courses for nurses and midwives. This is paid work.		
Jim Gray	Deputy Editor, Journal of Hospital Infection, funded by the Healthcare Infection Society (HIS pay the hospital for my time)	Personal financial non-specific	Declare and participate
Jim Gray	Co-investigator in four major trials (3 HTA-funded; 1 British Council funded. Two trials are about antibiotic prophylaxis on obstetrics and gynaecology to prevent pelvic infections, one is comparing different suture materials and the fourth is a diagnostic test accuracy study for use in woman in labour).	Non-personal financial non-specific	Declare and participate
Jim Gray	Associate Editor, International Journal of Antimicrobial Agents.	Non-personal financial non-specific	Declare and participate
Jim Gray	Associate Editor Journal of Pediatric Infectious Diseases.	Non-personal financial non-specific	Declare and participate
Jim Gray	Expert Advisor, British National Formulary for Children.	Non-personal financial non-specific	Declare and participate
Jim Gray	My Department is in receipt of an Educational Grant from Pfizer Ltd to develop improved diagnosis of invasive fungal infections in immunocompromised	Non-personal financial non-specific	Declare and participate

	children		
Kath Nuttall	None		Declare and participate
Tilly Pillay	None		Declare and participate
Nick Screaton	Attended Thorax meeting – travel expenses paid.	Non-specific personal financial	Declare and participate
Nick Screaton	Clinical Commissioning Group stakeholder member	Non-specific personal non-financial	Declare and participate
Nick Screaton	Senior Editor British Journal of Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Advisory Editor Clinical Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Chair East of England British Institute of Radiology	Non-specific personal non-financial	Declare and participate
Nick Screaton	Director – Cambridge Clinical Imaging LTD	Non-specific personal financial	Declare and participate
Nick Screaton	British Thoracic Society Bronchiectasis Guidelines Group	Non-specific personal non-financial	Declare and participate
Nick Screaton	Specialised Imaging Clinical Commissioning Group stakeholder member	Non-specific personal non-financial	Declare and participate
Nick Screaton	Member of the Faculty Board for the Royal College of Radiologists	Non-specific personal non-financial	Declare and participate
Nick Screaton	Member of the Editorial Board of Pulmonary Circulation	Non-specific personal non-financial	Declare and participate
Lindsay Smith	None		Declare and

			participate
Philippa Williams	None		Declare and participate
Sophie Wilne	Recipient of NHS Innovation Challenge Award for clinical awareness campaign to reduce delays in diagnosis of brain tumours in children & young adults. Award will be used to develop the campaign.	Personal non-specific non-financial	Declare and participate
Sophie Wilne	Co-investigator for RFPB grant to undertake systematic reviews in childhood brain tumours.	Personal non-specific non-financial	Declare and participate
Sophie Wilne	Co-investigator for grant awards from charity to evaluate impact of brain tumour awareness campaign.	Personal non-specific non-financial	Declare and participate
Sophie Wilne	Funding for travel and accommodation from Novartis to attend a conference on the management of tuberous sclerosis	Personal non-specific financial	Declare and participate
Christopher Chaloner	None	n/a	Declare and participate
Julia Thomson	None	n/a	Declare and participate
Jane Coyne	None	n/a	Declare and participate
Maria Jenkins	None	n/a	Declare and participate
Aung Soe	None	n/a	Declare and participate

Chris Edwards	None	n/a	Declare and participate

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Appendix A: Recommendations from NICE clinical guideline CG98 (2010) that have been deleted or amended

The table shows recommendations from 2010 that NICE proposes deleting or amending in the 2015 update. The right-hand column explains the reason for the deletion or amendment.

Recommendation in 2010 guideline	Comment
1.4.9 Use conventional 'blue light' phototherapy as treatment for significant hyperbilirubinaemia in all babies with a gestational age of 37 weeks or more unless: • the serum bilirubin levels are rising rapidly (more than 8.5 micromol/litre per hour) • the serum bilirubin is at a level that is within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see the threshold table and treatment threshold graphs[3]).	Replaced with: 1.4.9 Use phototherapy[4] to treat significant hyperbilirubinaemia (see the threshold table and the full guideline for treatment threshold graphs) in babies. **[new 2015]** Changes to this recommendation are based on new evidence. This recommendation is open for consultation.
1.4.10 Do not use fibreoptic phototherapy as first-line treatment for hyperbilirubinaemia for babies with a gestational age 37 weeks or more.	Removed following the review of evidence.
1.4.11 Use either fibreoptic phototherapy or conventional 'blue light' phototherapy as treatment for significant hyperbilirubinaemia in babies less than 37 weeks unless: • the serum bilirubin levels are rising rapidly (more than 8.5 micromol/litre per hour) • the serum bilirubin is at a level that is within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and treatment threshold graphs[4]).	Removed following the review of evidence.
1.4.12 Initiate continuous multiple phototherapy to treat all babies if any of the following apply : • the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour) • the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and treatment threshold graphs[4]) • the bilirubin level fails to respond to single phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting	Replaced with: 1.4.10 Consider intensified phototherapy to treat significant hyperbilirubinaemia in babies if any of the following apply **[new 2015]**: • the serum bilirubin level is rising rapidly (more than 8.5 micromol/litre per hour) • the serum bilirubin is at a level within 50 micromol/litre below the threshold for which exchange transfusion is indicated after 72 hours (see threshold table and the full guideline for treatment threshold graphs) • the bilirubin level fails to respond

[3] The treatment threshold graphs are in appendix D of the full guideline.
[4] Phototherapy given using artificial light sources with appropriate spectrum and irradiance. This can be delivered by light-emitting diode (LED), fibreoptic or fluorescent lamps, tubes or bulbs.

single phototherapy).	to initial phototherapy (that is, the level of serum bilirubin continues to rise, or does not fall, within 6 hours of starting phototherapy). **[2010]** Changes to the stem of this recommendation are based on new evidence. Only the stem of the recommendation is open for consultation. The bullet points are outside the scope of this update, and are not open for consultation.

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Changes to recommendation wording for clarification only (no change to meaning)

Recommendation numbers in current guideline	Comment
1.4.13 If the serum bilirubin level falls during continuous multiple phototherapy to a level 50 micromol/litre below the threshold for which exchange transfusion is indicated step down to single phototherapy.	1.4.11 If the serum bilirubin level falls during continuous intensified phototherapy to a level 50 micromol/litre below the threshold for which exchange transfusion is indicated reduce the intensity of phototherapy. **[2010]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.10 in the updated guideline. This recommendation is not open for consultation.
1.4.17 Use tinted headboxes as an alternative to eye protection in babies with a gestational age of 37 weeks or more undergoing conventional 'blue light' phototherapy.	1.4.15 Use tinted headboxes as an alternative to eye protection in babies with a gestational age of 37 weeks or more undergoing phototherapy. **[2010]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.9 in the updated guideline. This recommendation is not open for consultation.
1.4.18 During conventional 'blue light' phototherapy: • using clinical judgement, encourage short breaks (of up to 30 minutes) for breastfeeding, nappy changing and cuddles • continue lactation/feeding support • do not give additional fluids or feeds routinely. Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated.	1.4.16 During phototherapy: • using clinical judgement, encourage short breaks (of up to 30 minutes) for breastfeeding, nappy changing and cuddles • continue lactation/feeding support • do not give additional fluids or feeds routinely. Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. **[2015]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.9 in the updated guideline. This recommendation is open for consultation.
1.4.19 During multiple phototherapy: • do not interrupt phototherapy for feeding but continue administering intravenous/enteral feeds • continue lactation/feeding support so that breastfeeding can start again when treatment stops. Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated.	1.4.17 During intensified phototherapy: • do not interrupt phototherapy for feeding but continue administering intravenous/enteral feeds • continue lactation/feeding support so that breastfeeding can start again when treatment stops Maternal expressed milk is the additional feed of choice if available, and when additional feeds are indicated. **[2015]** The wording has been amended (highlighted

	in yellow) to be consistent with 1.4.10 in the updated guideline. This recommendation is open for consultation.
1.8.1 Use intravenous immunoglobulin (IVIG) (500 mg/kg over 4 hours) as an adjunct to continuous multiple phototherapy in cases of Rhesus haemolytic disease or ABO haemolytic disease when the serum bilirubin continues to rise by more than 8.5 micromol/litre per hour.	1.8.1 Use intravenous immunoglobulin (IVIG) (500 mg/kg over 4 hours) as an adjunct to continuous intensified phototherapy in cases of rhesus haemolytic disease or ABO haemolytic disease when the serum bilirubin continues to rise by more than 8.5 micromol/litre per hour. **[2010]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.10 in the updated guideline. This recommendation is not open for consultation.
1.9.3 During exchange transfusion do not: • stop continuous multiple phototherapy • perform a single-volume exchange • use albumin priming • routinely administer intravenous calcium.	1.9.3 During exchange transfusion do not : • stop continuous intensified phototherapy • perform a single-volume exchange • use albumin priming • routinely administer intravenous calcium. **[2010]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.10 in the updated guideline. This recommendation is not open for consultation.
1.9.4 Following exchange transfusion: • maintain continuous multiple phototherapy • measure serum bilirubin level within 2 hours and manage according to the threshold table and treatment threshold graphs[5].	1.9.4 Following exchange transfusion: • maintain continuous intensified phototherapy • measure serum bilirubin level within 2 hours and manage according to the threshold table and the treatment threshold graphs in the full guideline. **[2010]** The wording has been amended (highlighted in yellow) to be consistent with 1.4.10 in the updated guideline. This recommendation is not open for consultation.

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[5] The treatment threshold graphs are in appendix D of the guideline.