NHS
National Institute for Health and Clinical Excellence

Issue date: May 2010

Neonatal jaundice

NICE clinical guideline 98
Developed by the National Collaborating Centre for Women's and Children's Health

NICE clinical guideline 98
Neonatal jaundice

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You can download the following documents from
www.nice.org.uk/guidance/CG98

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- 'Understanding NICE guidance' – a summary for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and reviews of the evidence they were based on.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N2143 (quick reference guide)
- N2144 ('Understanding NICE guidance').

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

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

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Contents

Introduction 3
Patient-centred care 5
Key priorities for implementation 7
Guidance 10
1.1 Information for parents or carers 11
1.2 Care for all babies 11
1.3 Management and treatment of hyperbilirubinaemia 14
1.4 Measuring and monitoring bilirubin thresholds during phototherapy 15
1.5 Factors that influence the risk of kernicterus 20
1.6 Formal assessment for underlying disease 20
1.7 Care of babies with prolonged jaundice 21
1.8 Intravenous immunoglobulin 21
1.9 Exchange transfusion 22
1.10 Other therapies 23
2 Notes on the scope of the guidance 24
3 Implementation 24
4 Research recommendations 25
5 Other versions of this guideline 28
6 Related NICE guidance 29
7 Updating the guideline 30
Appendix A: The Guideline Development Group and acknowledgements 31
Appendix B: The Guideline Review Panel 35
Appendix C: The algorithms 36
Appendix D: The treatment threshold graphs 37

Introduction

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. Jaundice 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 generally 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 these babies. Prolonged jaundice is generally harmless, but can 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. This is particularly so 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.

Treatment and care should take into account parents' preferences. Parents of babies with neonatal jaundice should have the opportunity to make informed decisions about their babies' care and treatment, in partnership with their healthcare professionals. If parents do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent (available from www.dh.gov.uk/consent) and the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk/). In Wales, healthcare professionals should follow advice on consent from the Welsh Assembly Government *(*available from www.wales.nhs.uk/consent).

Healthcare professionals should follow the guidelines in 'Seeking consent: working with children' (available from www.dh.gov.uk/consent).

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

Families and carers should also be given the information and support they need.

Key terms used in this guideline

Conventional phototherapy Phototherapy given using a single light source (not fibreoptic) that is positioned above the baby

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

Fibreoptic phototherapy Phototherapy given using a single light source that comprises a light generator, a fibreoptic cable through which the light is carried and a flexible light pad, on which the baby is placed or that is wrapped around the baby

Multiple phototherapy Phototherapy that is given using more than one light source simultaneously; for example two or more conventional units, or a combination of conventional and fibreoptic units

Near-term 35 to 36 weeks gestational age

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

Key priorities for implementation

Information

- 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.

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.

- 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.

- 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.

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.

Measuring bilirubin in all babies with jaundice

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

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.

How to manage hyperbilirubinaemia

- Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see threshold table[1] and treatment threshold graphs[2]).

[1] The threshold table is on page 10 of this guideline.
[2] The treatment threshold graphs are in appendix D on page 37 of this guideline.

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.

Guidance

The following guidance is based on the best available evidence. The full guideline (www.nice.org.uk/guidance/CG98/Guidance) gives details of the methods and the evidence used to develop the guidance.

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.

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.

1.2.2 Ensure that adequate support is offered to all women who intend to breastfeed exclusively[3].

[3] Refer to 'Routine postnatal care of women and their babies' (NICE clinical guideline 37) for information on breastfeeding support.

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.

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

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.

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

1.2.7 Do not measure bilirubin levels routinely in babies who are not visibly jaundiced.

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).

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.

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.

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.

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.

1.2.13 Interpret bilirubin levels according to the baby's postnatal age in hours and manage hyperbilirubinaemia according to the threshold table[4] and treatment threshold graphs[5].

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.

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

[4] The threshold table is on page 10 of this guideline.
[5] The treatment threshold graphs are in appendix D on page 37 of this guideline.

- 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.

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.

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

1.3.3 Provide lactation/feeding support to breastfeeding mothers whose baby is visibly jaundiced.

How to manage hyperbilirubinaemia

1.3.4 Use the bilirubin level to determine the management of hyperbilirubinaemia in all babies (see threshold table[6] and treatment threshold graphs[7]).

[6] The threshold table is on page 10 of this guideline.

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

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[8] and treatment threshold graphs[9]).

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[8] and treatment threshold graphs[9] when considering the use of phototherapy.

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[8] repeat the bilirubin measurement in 6–12 hours.

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[8] repeat the bilirubin measurement in 6 hours regardless of whether or not phototherapy has subsequently been started.

1.4.4 Do not use phototherapy in babies whose bilirubin does not exceed the phototherapy threshold levels in the threshold table[8] and treatment threshold graphs[9].

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.

[7] The treatment threshold graphs are in appendix D on page 37 of this guideline.

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[8] and treatment threshold graphs[9]).

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.

Type of phototherapy to use

1.4.8 Do not use sunlight as treatment for hyperbilirubinaemia.

Single phototherapy treatment for term babies

1.4.9 Use conventional 'blue light' phototherapy as treatment for significant hyperbilirubinaemia in 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[12] and treatment threshold graphs[13]).

1.4.10 Do not use fibreoptic phototherapy as first-line treatment for hyperbilirubinaemia for babies with a gestational age 37 weeks or more.

[8] The threshold table is on page 10 of this guideline.
[9] The treatment threshold graphs are in appendix D on page 37 of this guideline.

Single phototherapy treatment in preterm babies

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[10] and treatment threshold graphs[11]).

Continuous multiple phototherapy treatment for term and preterm babies

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[15] and treatment threshold graphs[16]).
- 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 single phototherapy).

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.

[10] The threshold table is on page 10 of this guideline.
[11] The treatment threshold graphs are in appendix D on page 37 of this guideline.

Information for parents or carers on phototherapy

1.4.14 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
- 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.

General care of the baby during phototherapy

1.4.15 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.

1.4.16 Give the baby eye protection and routine eye care during phototherapy.

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.

Monitoring the baby during phototherapy

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.

1.4.19 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.

Phototherapy equipment

1.4.20 Ensure all phototherapy equipment is maintained and used according to the manufacturers’ guidelines.

1.4.21 Use incubators or bassinets according to clinical need and availability.

1.4.22 Do not use white curtains routinely with phototherapy as they may impair observation of the baby.

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.

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[12] and treatment threshold graphs[13]):

- 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.

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).

[12] The threshold table is on page 10 of this guideline.
[13] The treatment threshold graphs are in appendix D on page 37 of this guideline.

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.

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.

1.8 Intravenous immunoglobulin

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.

1.8.2 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.

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.

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

- whose serum bilirubin level indicates its necessity (see threshold table[14] and treatment threshold graphs[15]) **and/or**
- with clinical features and signs of acute bilirubin encephalopathy.

1.9.3 During exchange transfusion do not :

- stop continuous multiple phototherapy
- perform a single-volume exchange
- use albumin priming
- routinely administer intravenous calcium.

1.9.4 Following exchange transfusion:

- maintain continuous multiple phototherapy
- measure serum bilirubin level within 2 hours and manage according to the threshold table[20] and treatment threshold graphs[21].

[14] The threshold table is on page 10 of this guideline.
[15] The treatment threshold graphs are in appendix D on page 37 of this guideline.

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.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from www.nice.org.uk/guidance/CG98 – click on 'How this guidance was produced'.

This guideline covers all babies with jaundice from birth up to 28 days of age. Special attention was given to the recognition and management of neonatal jaundice in babies with dark skin tones.

It does not cover babies with jaundice that lasts beyond the first 28 days of life, babies with jaundice that requires surgical treatment to correct the underlying cause and babies with conjugated hyperbilirubinaemia.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Women's and Children's Health to develop this guideline. The Centre established a guideline development group (see appendix A), which reviewed the evidence and developed the recommendations. An independent guideline review panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website (www.nice.org.uk/HowWeWork). A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' (fourth edition, published 2009), is available from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1739).

3 Implementation

NICE has developed tools to help organisations implement this guidance (see www.nice.org.uk/guidance/CG98).

4 Research recommendations

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

4.1 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.

4.2 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.

4.3 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.

4.4 Interruptions during phototherapy

How frequently and for how long can conventional 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 conventional 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.

4.5 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.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Neonatal jaundice' contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Women's and Children's Health, and is available from www.ncc-wch.org.uk and our website (www.nice.org.uk/guidance/CG98/FullGuidance).

5.2 Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/guidance/CG98/QuickRefGuide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N2143).

5.3 'Understanding NICE guidance'

A summary for parents and carers ('Understanding NICE guidance') is available from www.nice.org.uk/guidance/CG98/PublicInfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N2144).

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about neonatal jaundice.

6 Related NICE guidance

Published

- Diabetes in pregnancy: management of diabetes and its complications from pre-conception to the postnatal period. NICE clinical guideline 63 (2008). Available from www.nice.org.uk/guidance/CG63
- Antenatal care: routine care for the healthy pregnant woman. NICE clinical guideline 62 (2008). Available from www.nice.org.uk/guidance/CG62
- Intrapartum care: care of healthy women and their babies during childbirth. NICE clinical guideline 55 (2007). Available from www.nice.org.uk/guidance/CG55
- Routine postnatal care of women and their babies. NICE clinical guideline 37 (2006). Available from www.nice.org.uk/guidance/CG37

7 Updating the guideline

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

Appendix A: The Guideline Development Group and acknowledgements

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Guidelines Coordinator

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Technical lead

Acknowledgements

The NCC-WCH and the Guideline Development Group (GDG) would like to thank Dr Giles Kendall MBBS, BSc(hons), MRCPCH PhD, Academic Clinical Lecturer Neonatal Medicine, University College London/University College London Hospital NHS Foundation Trust and TJ Cole, Professor of Medical Statistics, MRC Centre of Epidemiology for Child Health, UCL Institute of Child Health for allowing the GDG to adapt their Excel spreadsheet in developing the treatment threshold graphs included in this guideline.

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr John Hyslop (Chair)

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Dr Ash Paul

Medical Director, Bedfordshire Primary Care Trust

Mr Peter Gosling

Lay member

Professor Liam Smeeth

Professor of Clinical Epidemiology, London School of Hygiene and Tropical Medicine

Mr Kieran Murphy

Health Economics and Reimbursement Manager, Johnson & Johnson Medical Devices & Diagnostics, UK

Appendix C: The algorithms

The quick reference guide contains algorithms on investigation, phototherapy and exchange transfusion for babies with neonatal jaundice, available from www.nice.org.uk/guidance/CG98/QuickRefGuide

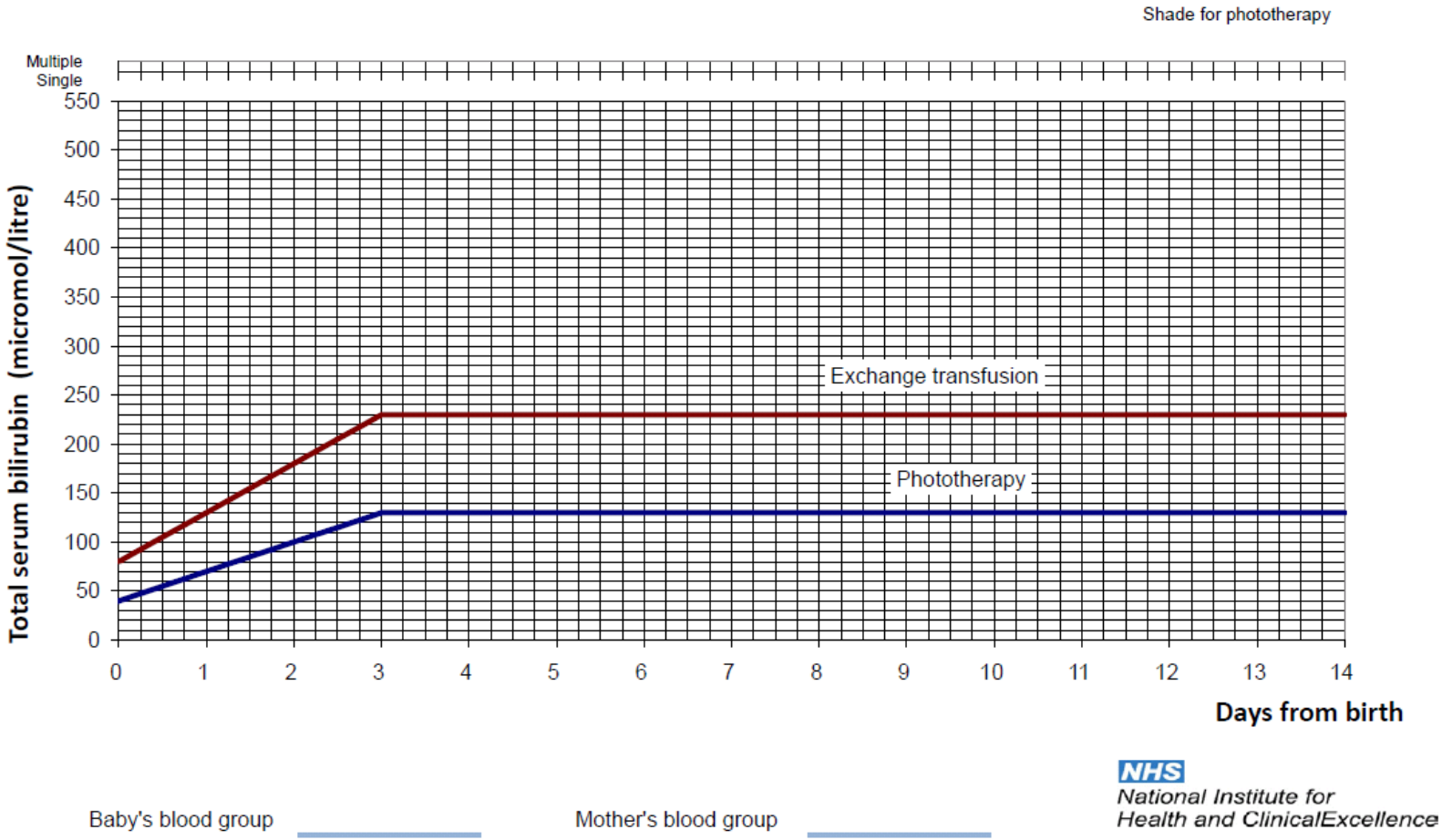
Appendix D: The treatment threshold graphs

See pages 38–53 for treatment threshold graphs for phototherapy and exchange transfusion for babies with gestational ages from 23 weeks to 38 weeks or more. They are also available as an implementation tool (see www.nice.org.uk/guidance/CG98).

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 23 **weeks gestation**



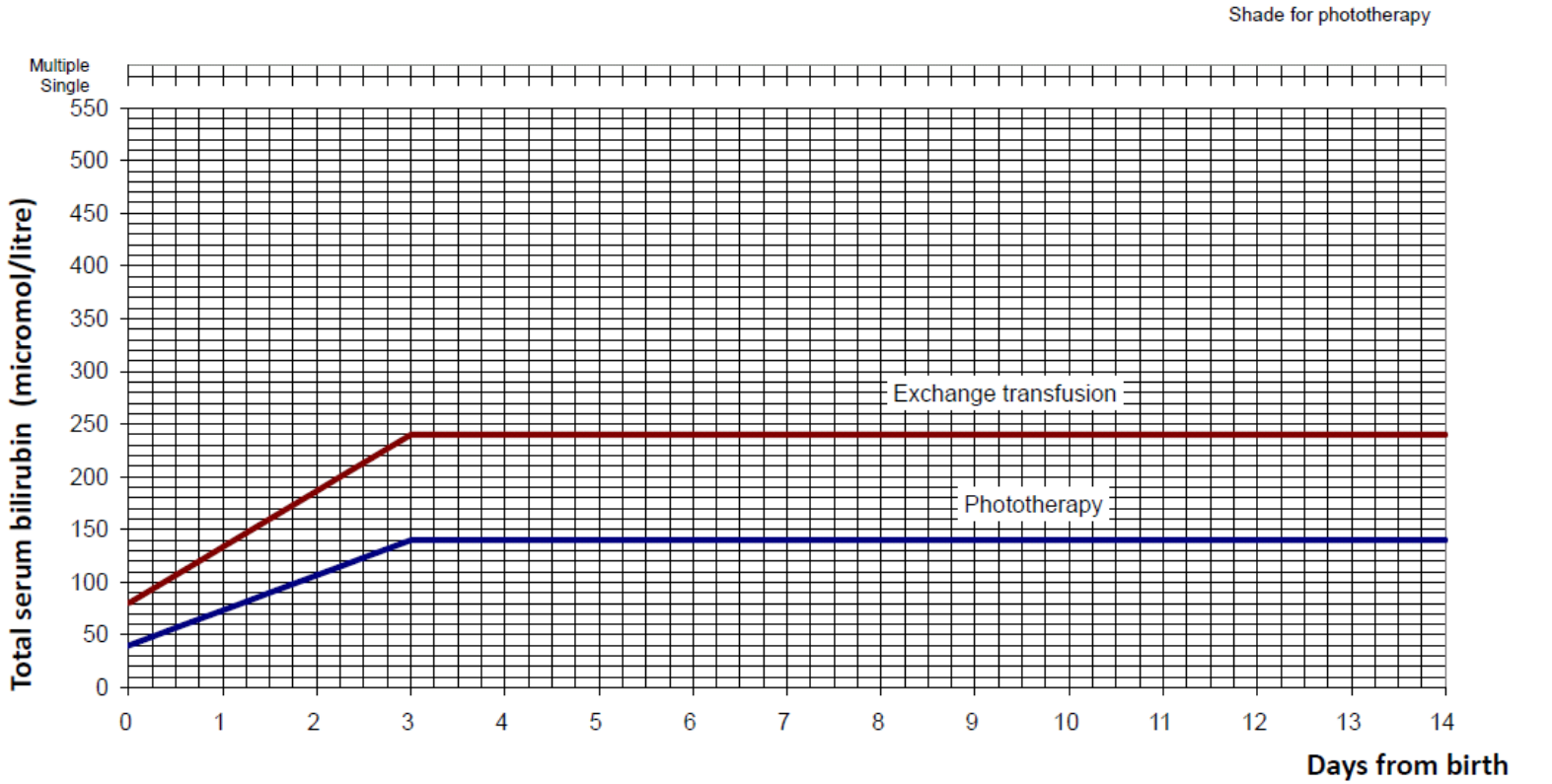
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 24 **weeks gestation**



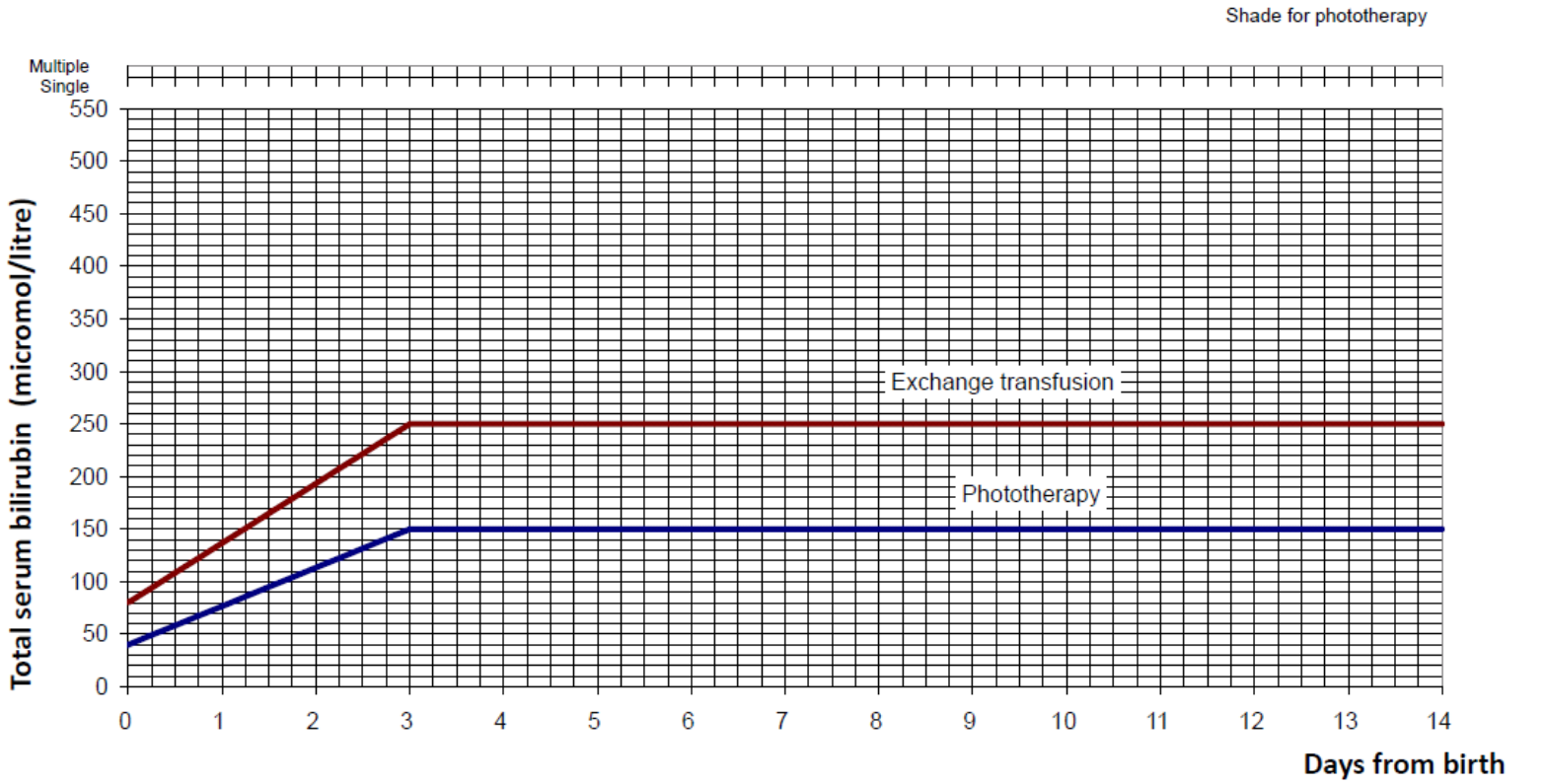
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 25 **weeks gestation**



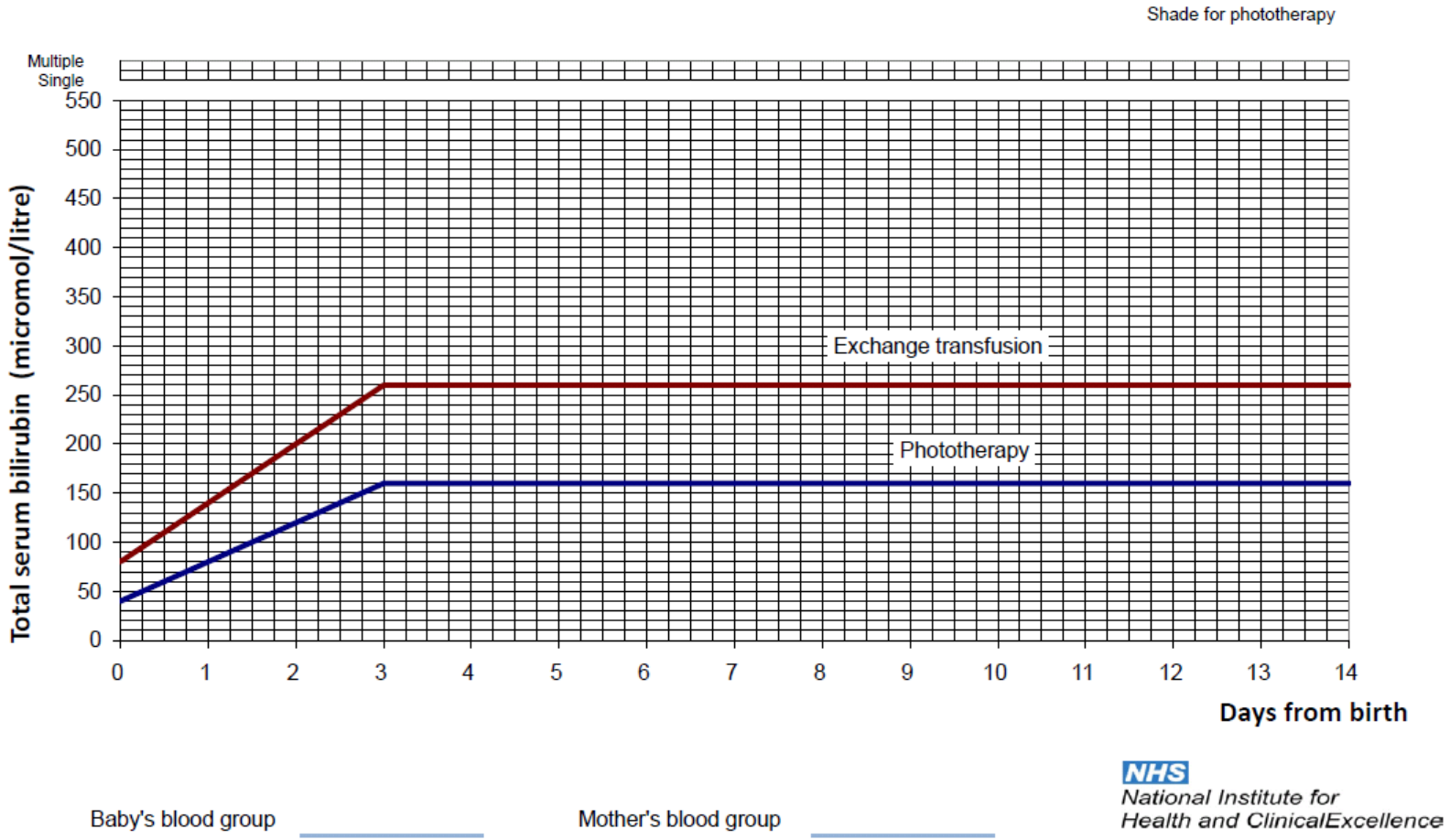
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 26 **weeks gestation**



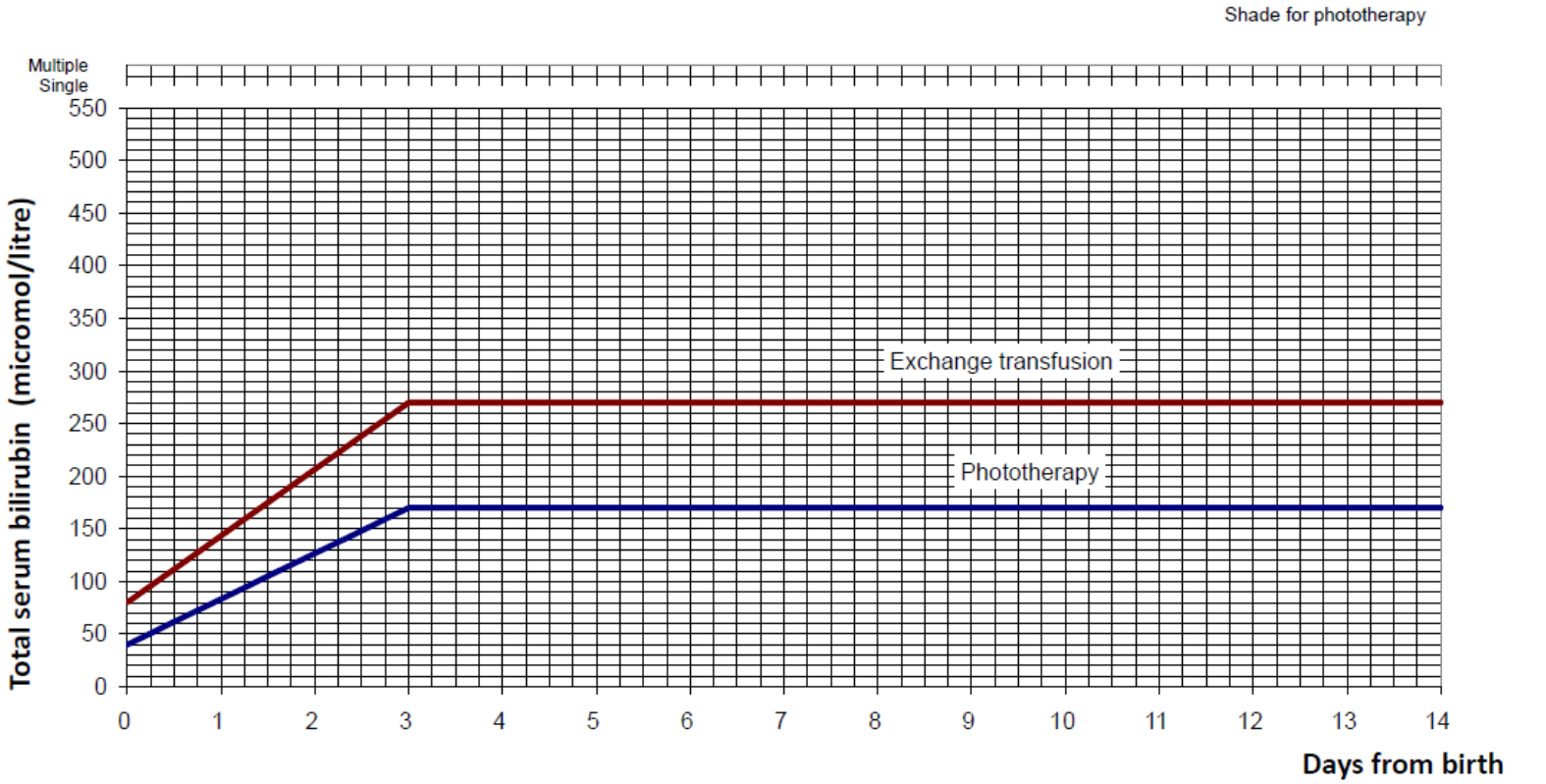
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **27 weeks gestation**



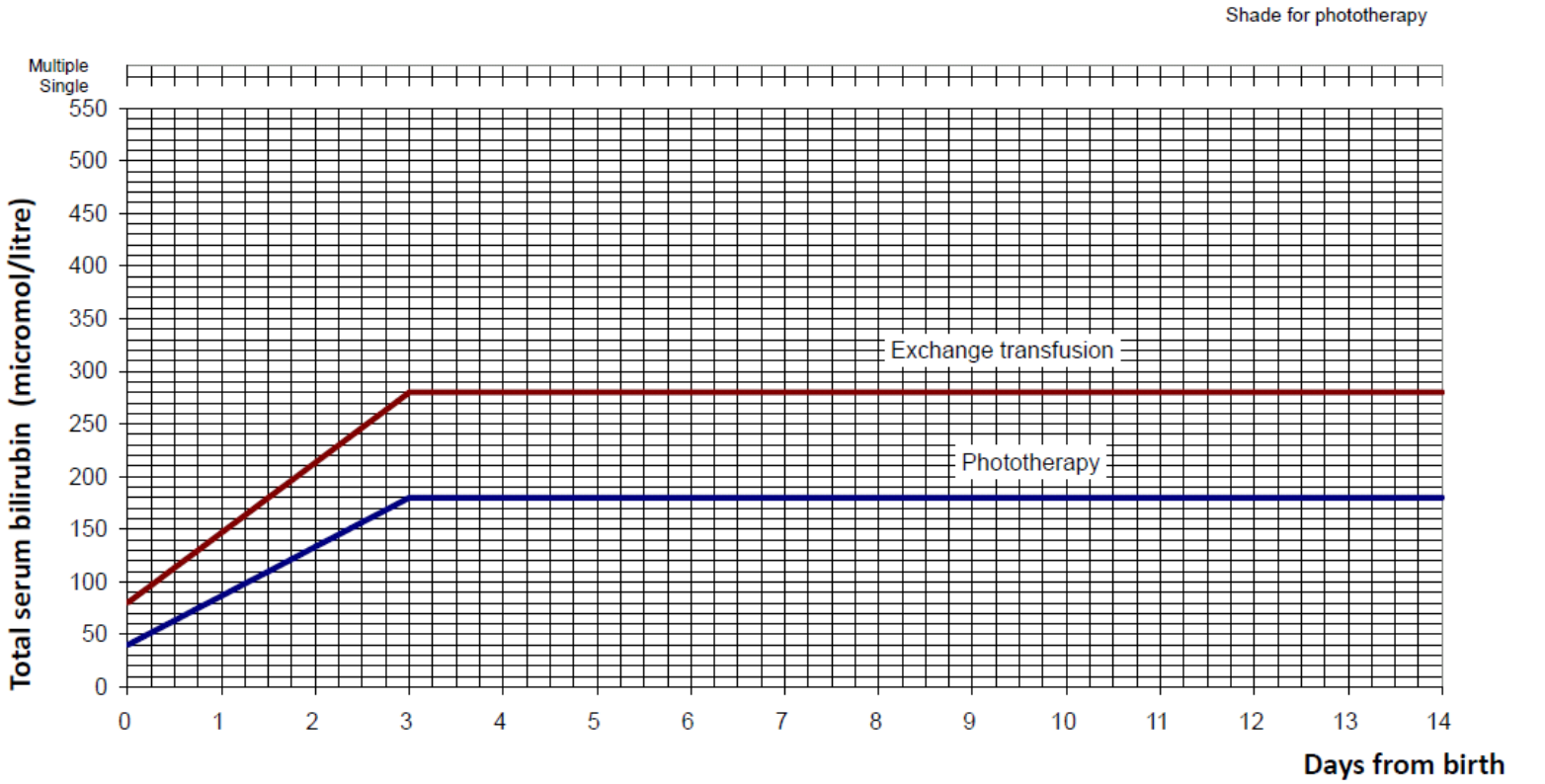
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **28 weeks gestation**



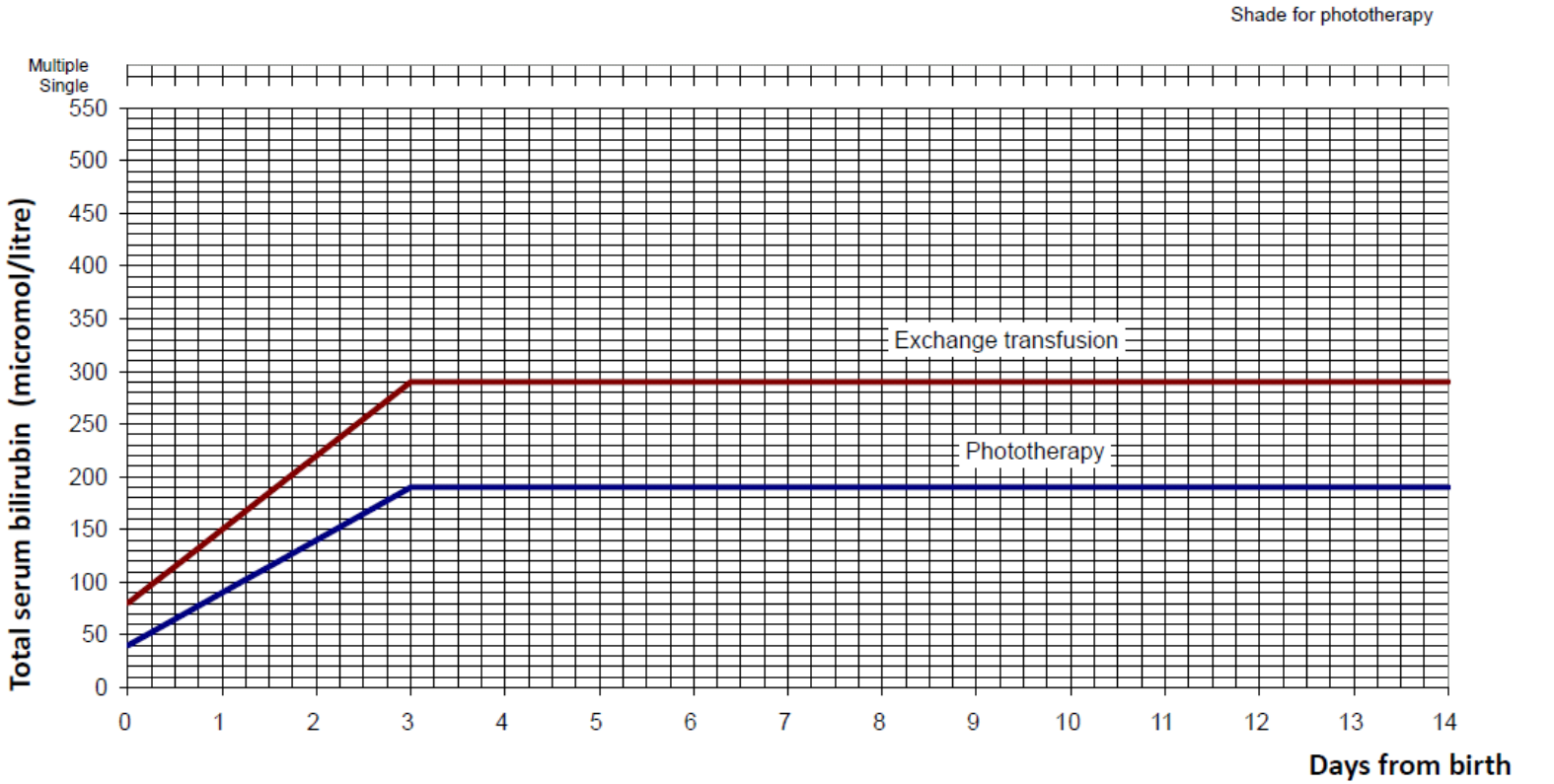
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **29 weeks gestation**



Baby's blood group _____ Mother's blood group _____

NHS
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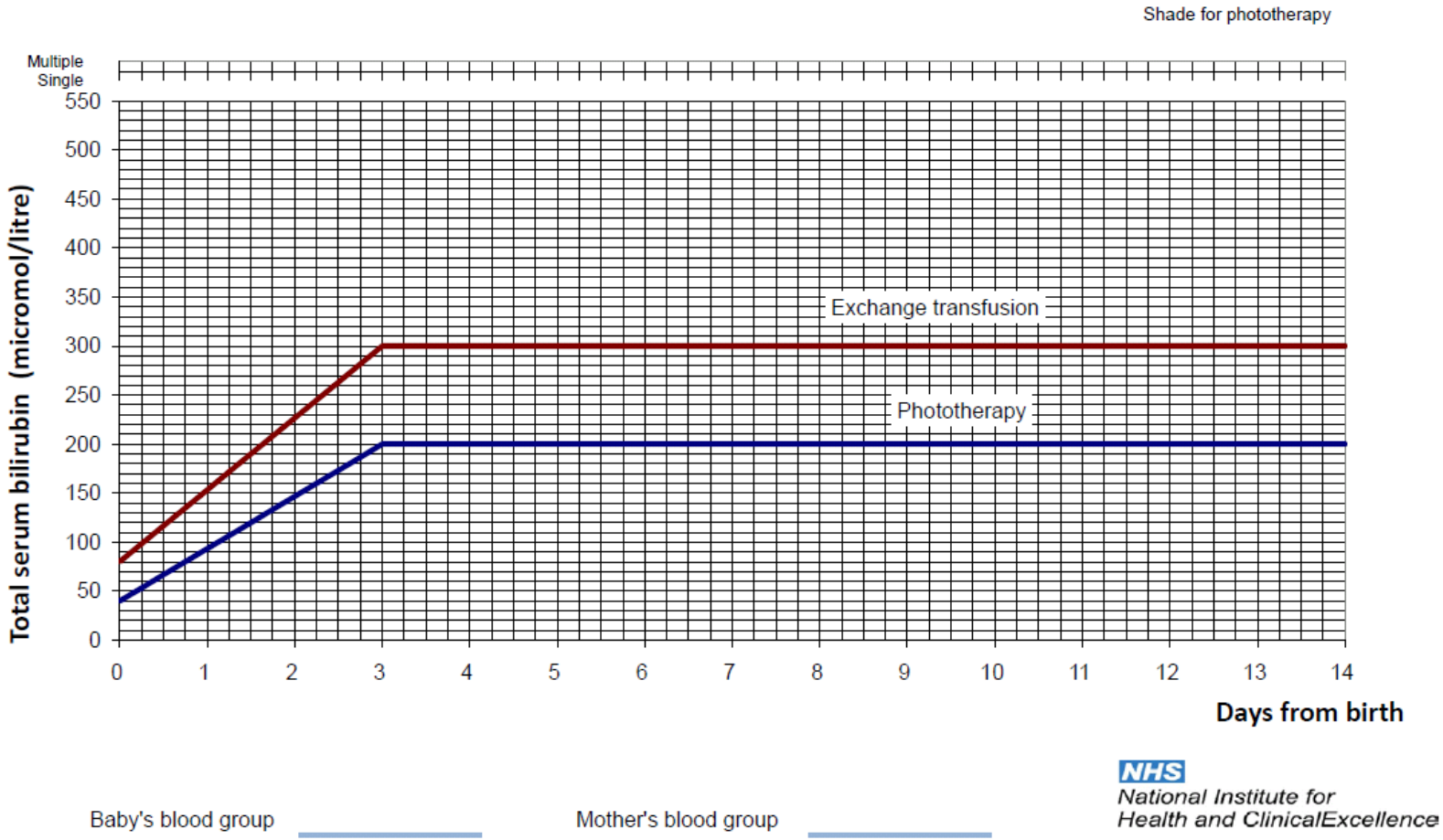
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 30 **weeks gestation**



Baby's blood group _____ Mother's blood group _____

NHS
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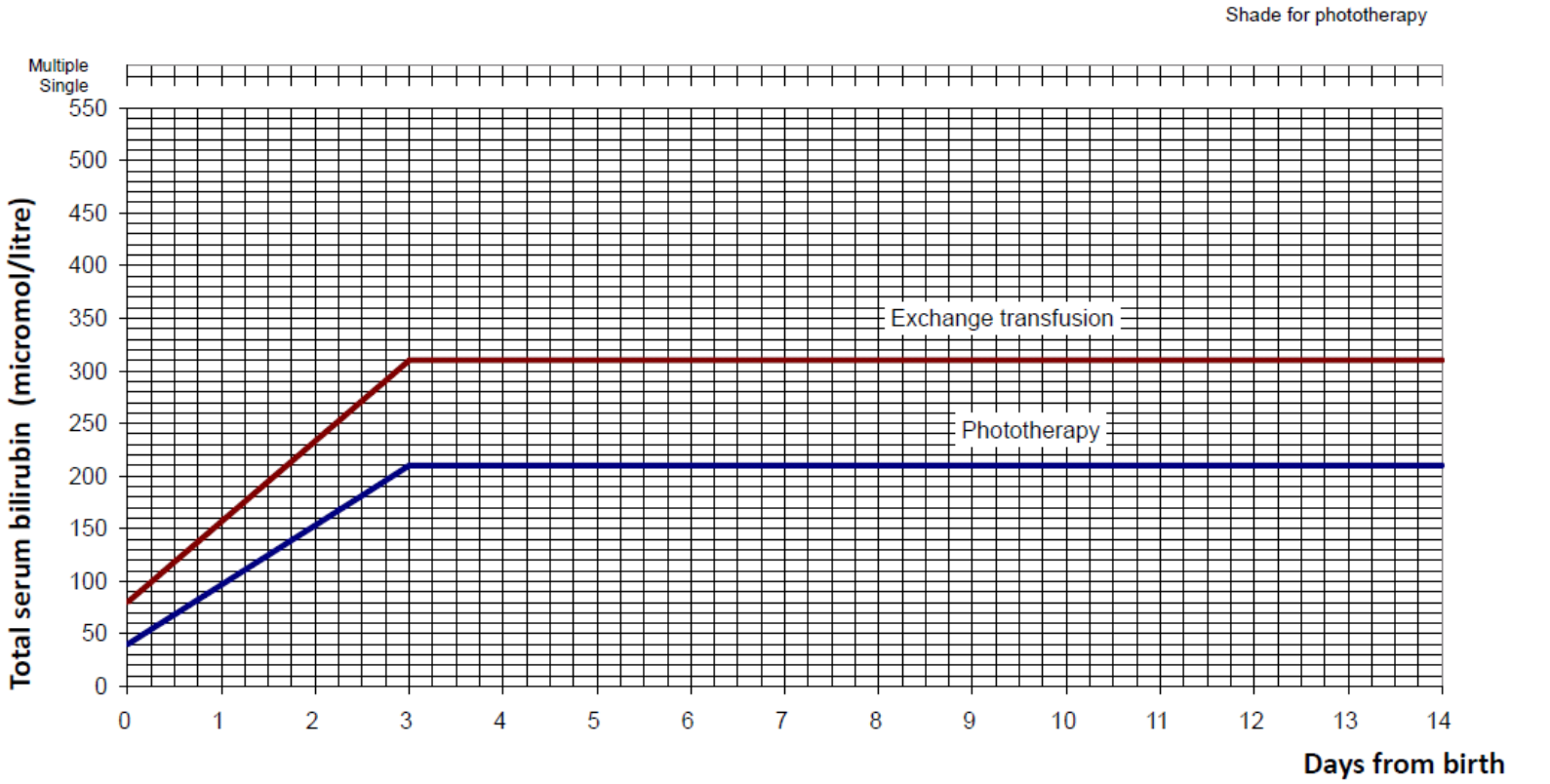
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 31 **weeks gestation**



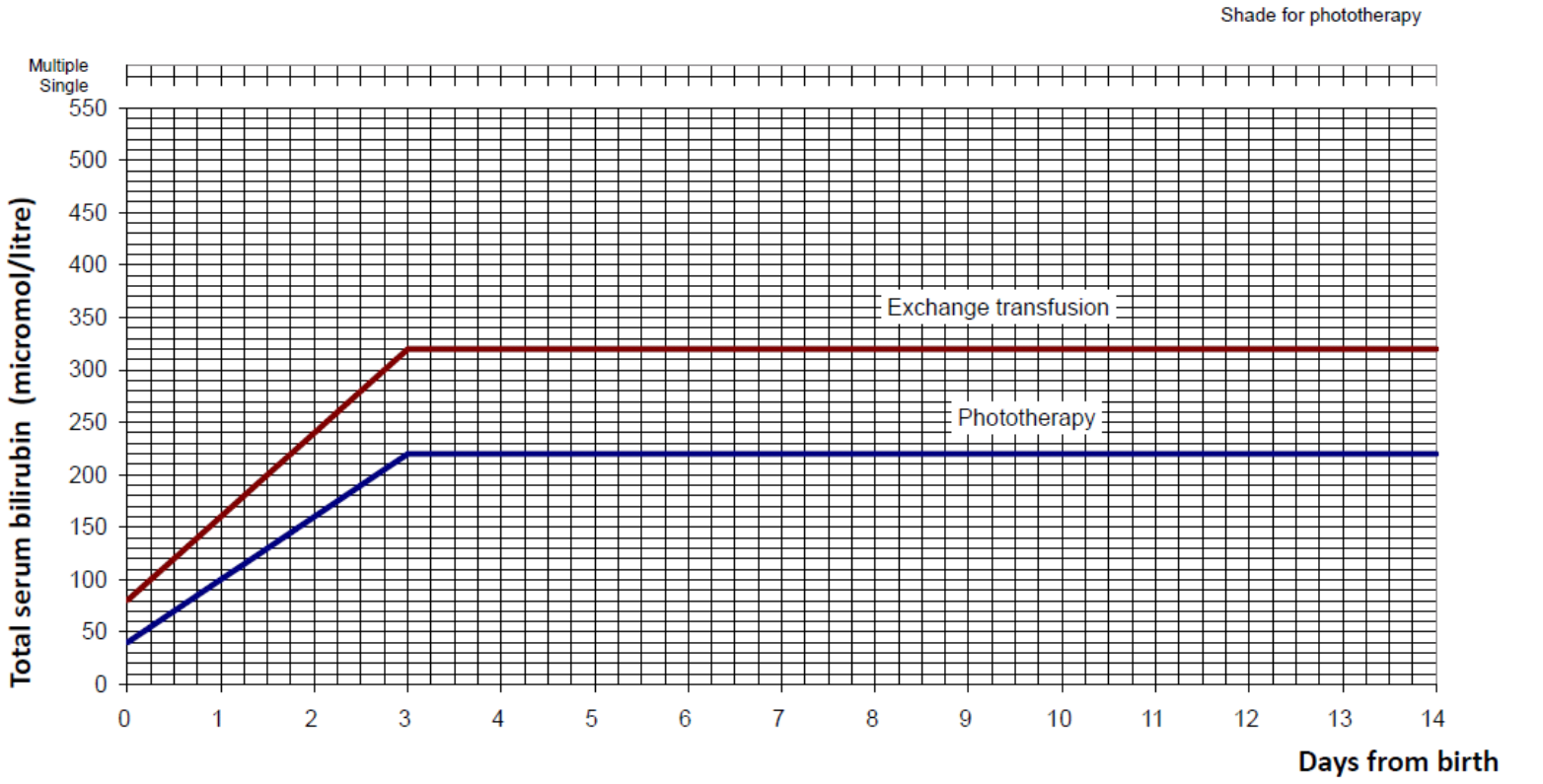
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **32 weeks gestation**



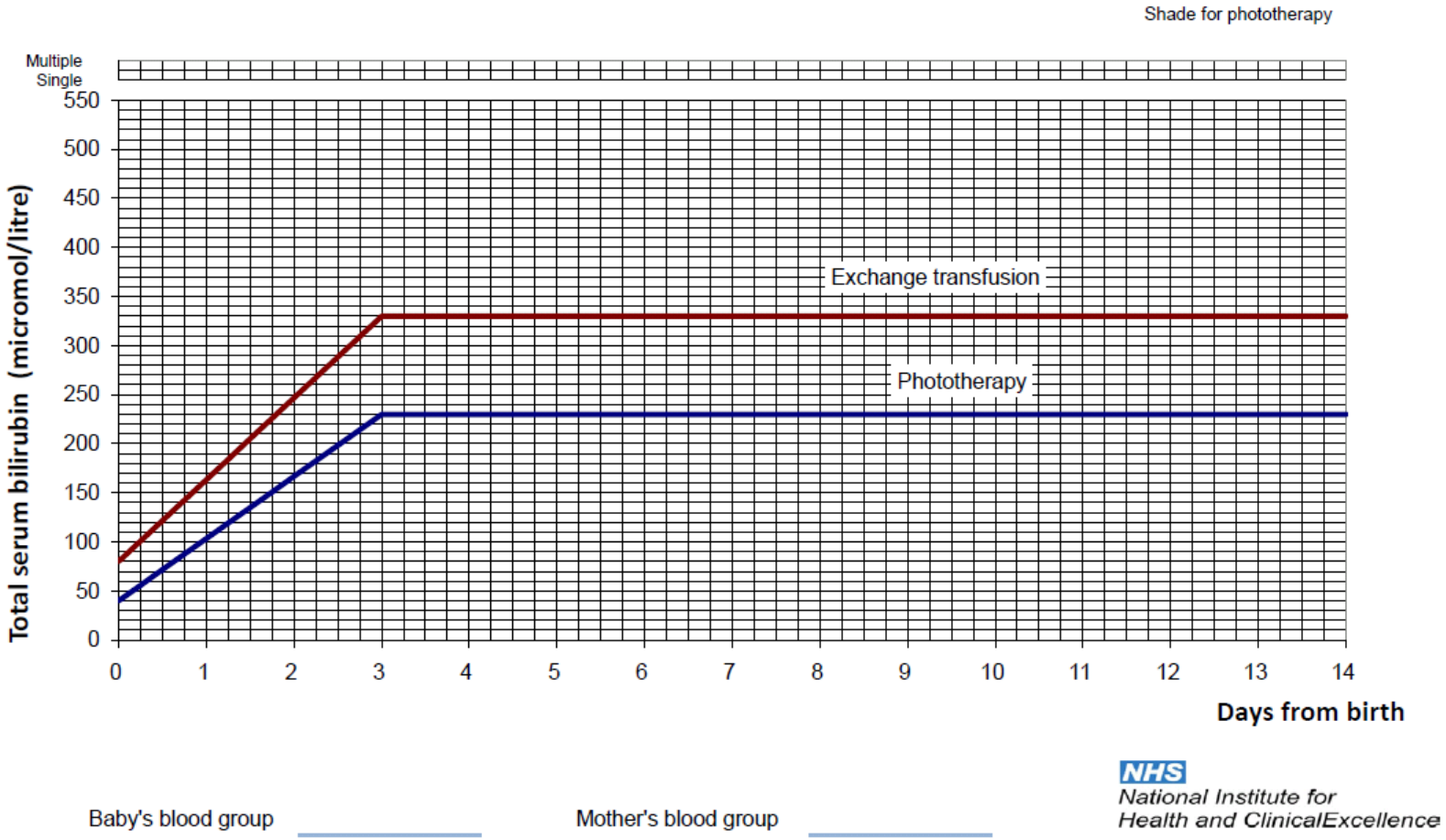
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 33 **weeks gestation**



Baby's blood group _____ Mother's blood group _____

NHS
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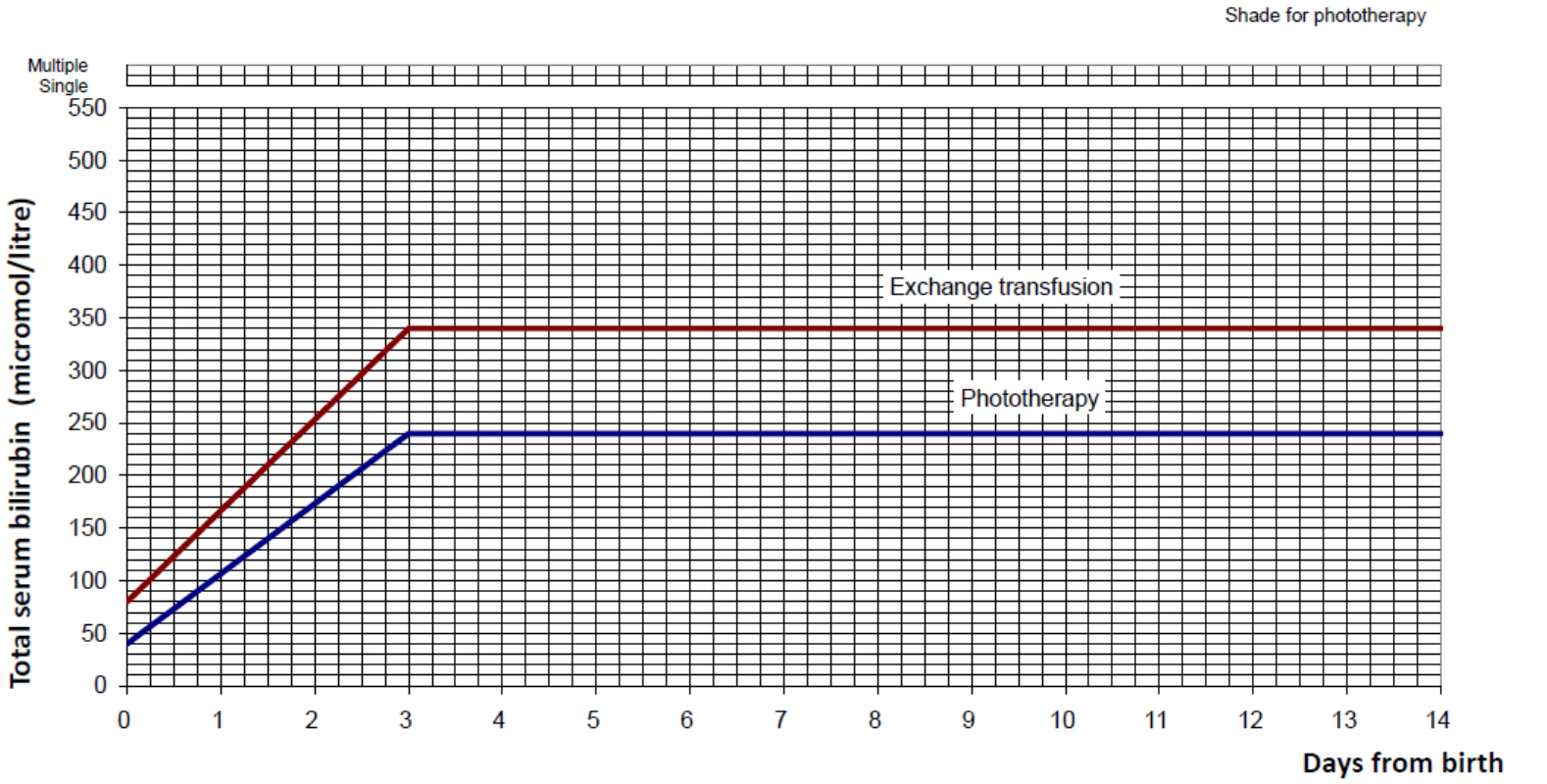
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 34 **weeks gestation**



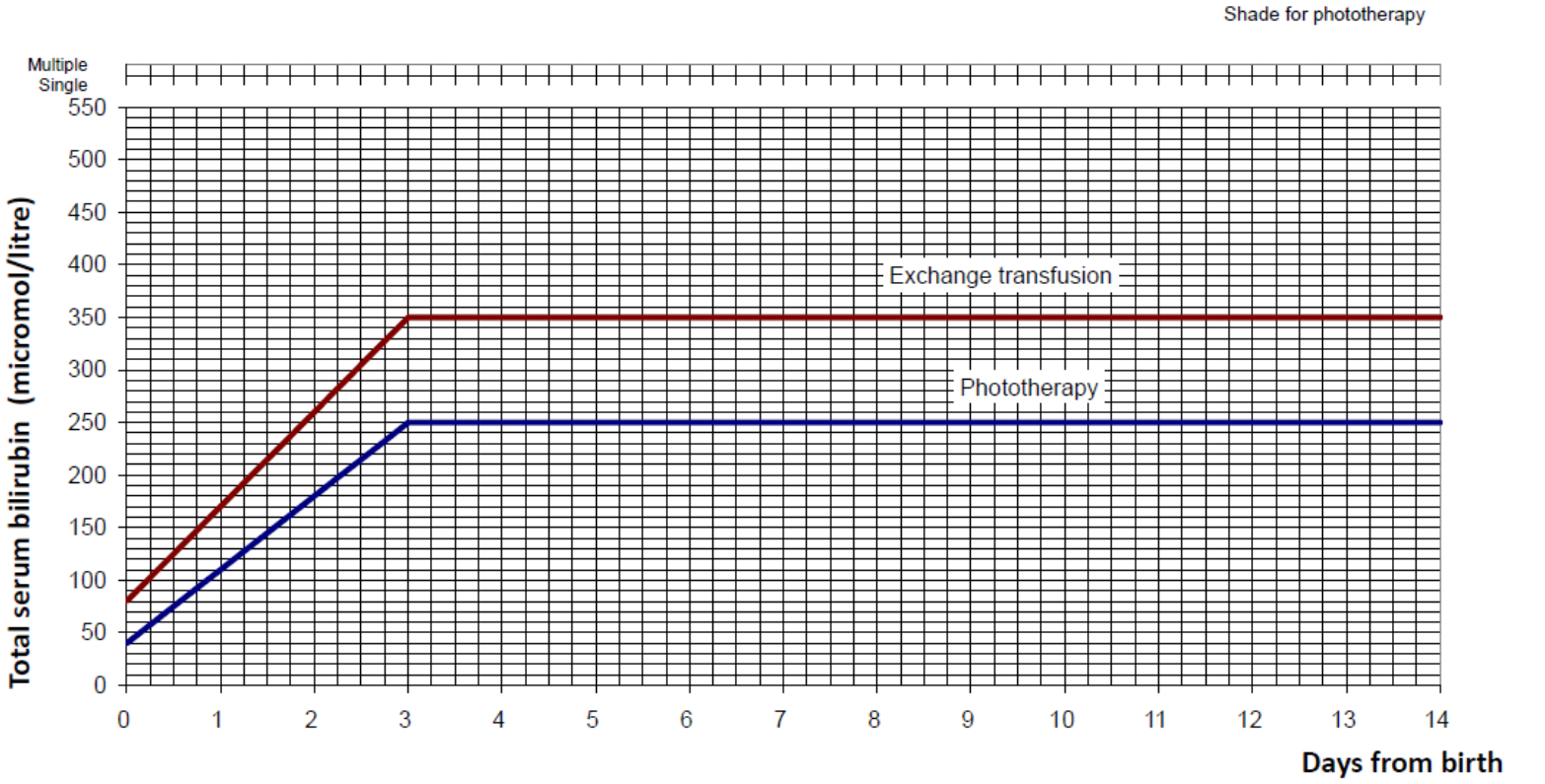
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 35 **weeks gestation**



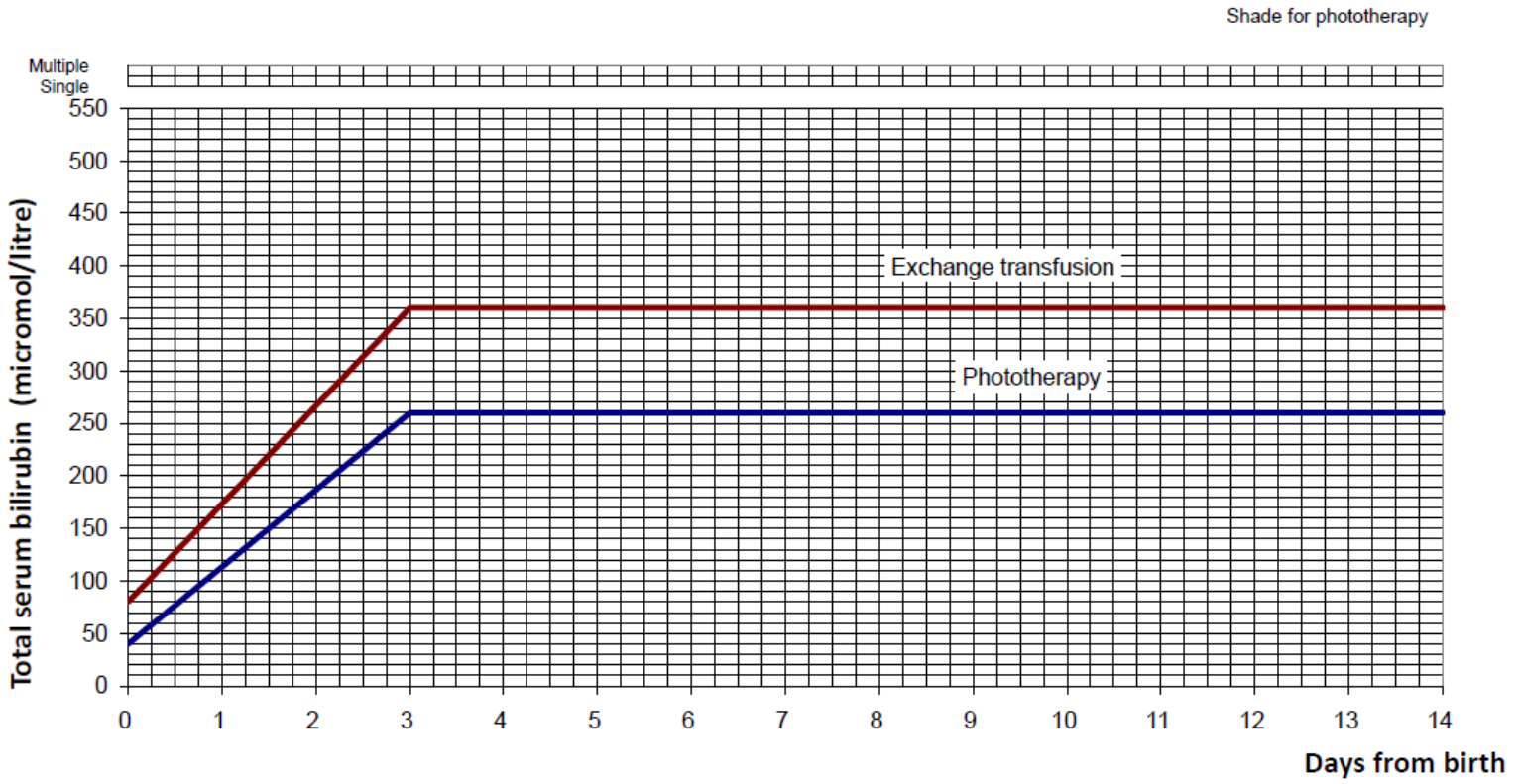
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ 36 **weeks gestation**



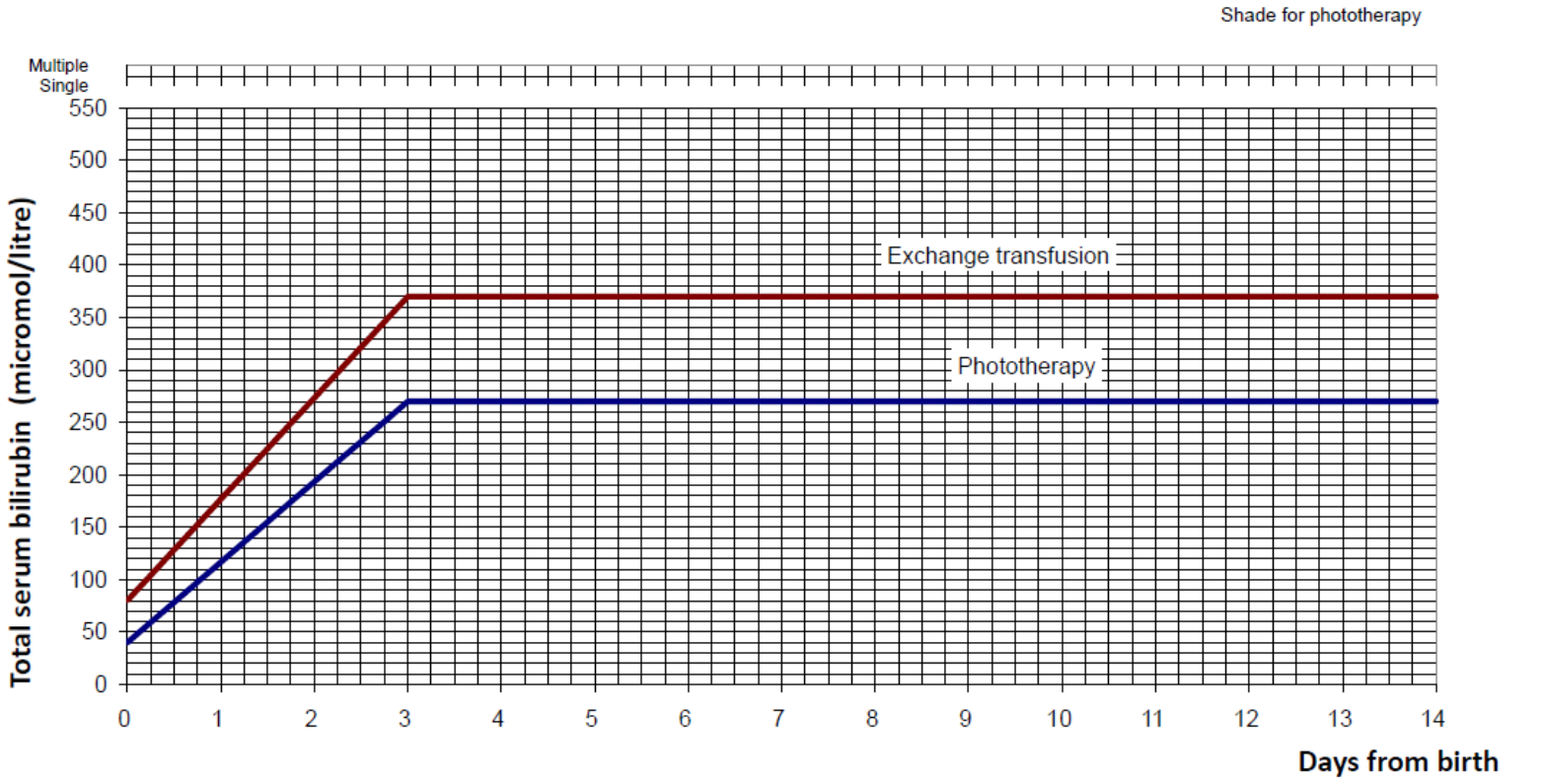
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ **37 weeks gestation**



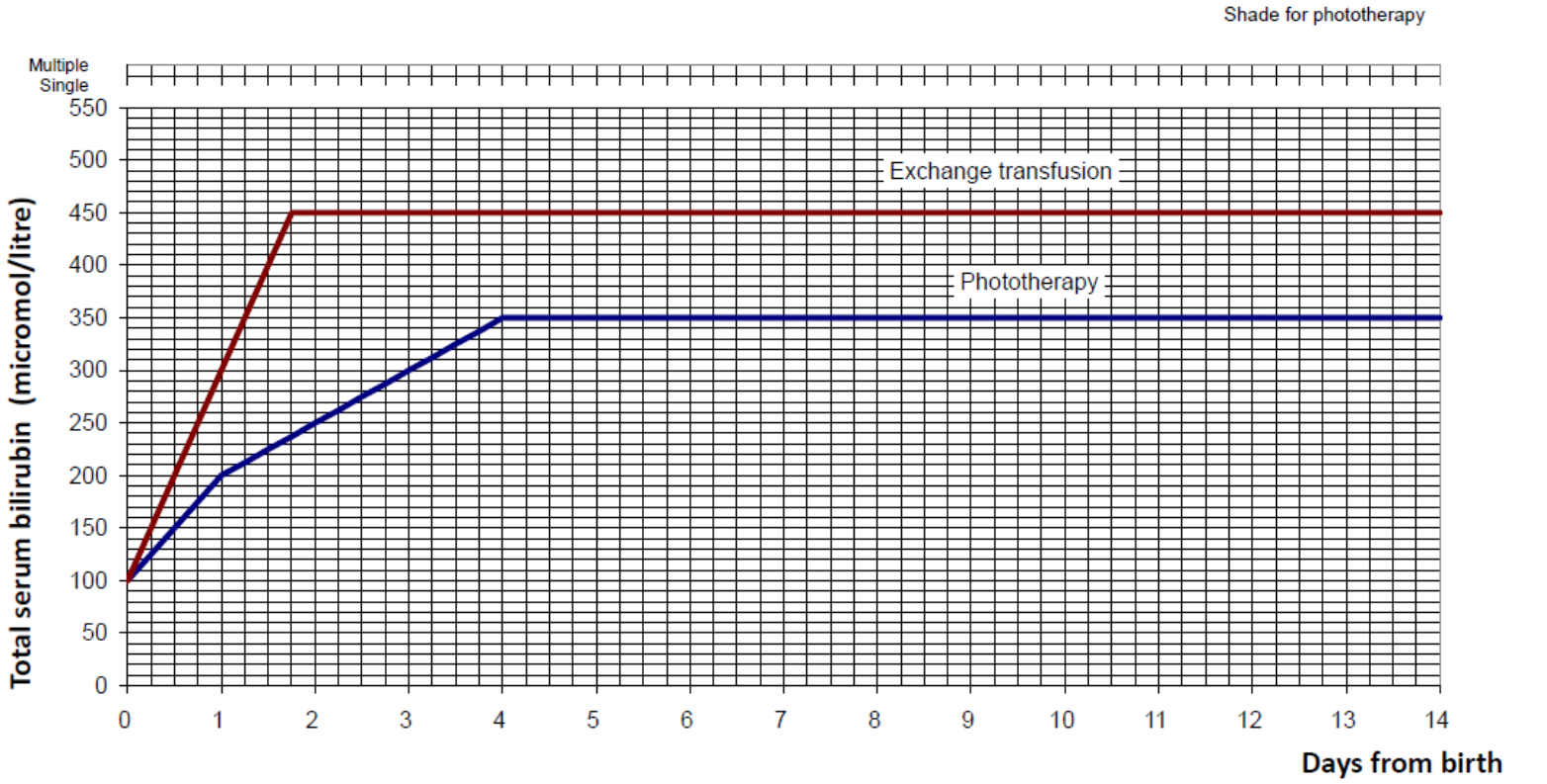
Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence

Bilirubin thresholds for phototherapy and exchange transfusion in babies with hyperbilirubinaemia

Baby's name _____ Date of birth _____

Hospital number _____ Time of birth _____ Direct Antiglobulin Test _____ >=38 **weeks gestation**



Baby's blood group _____ Mother's blood group _____

NHS
National Institute for
Health and ClinicalExcellence