

Jaundice (Hyperbilirubinaemia) in Preterm Babies < 35 Weeks Gestation

Key Points

- Hyperbilirubinaemia and jaundice occur in almost all preterm babies, lasting longer and with risk of neurological dysfunction at lower levels than more mature babies
- Assessment of hyperbilirubinaemia in preterm babies is with SBR measurements
- Management is determined by gestation, birth weight, postnatal age in hours, and total SBR level
- Preterm babies routinely have their cord blood tested for group and DAT
- Exchange transfusion is a very high risk procedure in preterm babies
- All preterm babies admitted to NICU/ **SCN** for > 48 hours, regardless of their SBR level, are referred for formal audiology assessment at 8 months of age
- Preterm babies should have an SBR level performed at 12 - 24 hours (timed with planned blood collection), earlier if they are visibly jaundiced, have significant bruising or bleeding, or are DAT positive
- There are 4 hyperbilirubinaemia treatment charts for babies born < 35 weeks' gestation
- SBR should be plotted according to gestation at birth, unless the baby's birthweight is <1000g
- Isoimmunised preterm babies (DAT positive) should be treated at an SBR 20 micromol/L below their usual threshold
- If the SBR remains elevated at day 21, consider investigations for prolonged hyperbilirubinaemia.

1. Purpose

This clinical guideline outlines the management of jaundice (hyperbilirubinaemia) in babies born less than 35 completed weeks gestation in Newborn Intensive Care (NICU), Special Care Nursery (SCN), in Maternity, in Women's Emergency Care (WEC) at The Women's and in the community.

Where processes differ between campuses, those that refer to the Sandringham campus are differentiated by pink text or have the heading **Sandringham campus (W@S)**.

2. Definitions

NICU	Newborn Intensive Care
SCN	Special Care Nursery
RWH	The Royal Women's Hospital
WEC	Women's Emergency Care
RBC	red blood cell
HCT	haematocrit
SBR	total serum bilirubin
G6PD	glucose-6-phosphate dehydrogenase
TcB	transcutaneous bilirubin
DAT	direct antiglobulin titre
IAT	indirect antiglobulin titre
FBE	full blood evaluation
Rh	rhesus
EBM	expressed breast milk
NHITH	neonatal hospital in the home

3. Responsibilities

Medical, nursing and midwifery staff caring for babies at The Women's and in the community.

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4. Guideline

4.1 *Hyperbilirubinaemia in the preterm baby*

Hyperbilirubinaemia and jaundice occur in almost all preterm babies <35 weeks' gestation. Hyperbilirubinaemia lasts longer and can be more severe in preterm babies as their red blood cells, liver and gastrointestinal tract are less mature. In addition, they take longer to establish full enteral feeds, increasing enterohepatic circulation.

Preterm babies are at risk of neurological dysfunction at lower levels of hyperbilirubinaemia than term babies. Signs of acute bilirubin encephalopathy, such as increased tone, irritability and seizures are harder to identify in very preterm babies. Features such as periodic breathing and apnoea may be masked by their respiratory support or by sedative medication.

There is very little evidence available to determine what SBR level requires treatment in preterm babies. Treatment guidelines are based on birth weight or gestational age, although there is no consensus as to which is better.

The relative risks and benefits of phototherapy and exchange transfusion are unclear. It is not established whether early aggressive phototherapy is beneficial or harmful. Phototherapy may cause photo-oxidative injury to cells, but may also provide some antioxidant role.

It remains important to recognise hyperbilirubinaemia in preterm babies in order to avoid:

- Very high hyperbilirubinaemia
- Acute bilirubin encephalopathy and subsequent kernicterus
- Exchange transfusion.

Preterm babies will be at additional risk of developing serious jaundice if there is:

- Isoimmunisation (ABO blood group incompatibility, Rhesus isoimmunisation, other red blood cell antibodies) or a previous sibling treated with phototherapy for haemolytic disease
- Family history of red cell defects e.g. G6PD deficiency, hereditary spherocytosis
- Cephalhaematoma or significant bruising
- Macrosomia in an infant of a diabetic mother.

4.2 *Assessment of hyperbilirubinaemia in the preterm baby*

Assessment of hyperbilirubinaemia in preterm babies born < 35 weeks' gestation is always with SBR measurements.

Visual assessment of jaundice (Kramer's Rule) is inaccurate in both term and preterm infants and is no longer used.

Assessment of hyperbilirubinaemia in a preterm baby should include:

- SBR
- FBE (include HCT and blood film for haemolysis, spherocytes, etc)
- Blood group
- Direct antiglobulin (DAT) titre (Coombs' test)
- Consideration of G6PD deficiency in babies of Mediterranean, African or Asian ethnicity
- Mothers blood group, Rh status and indirect antiglobulin titre (IAT).

4.3 *Management of hyperbilirubinaemia in the preterm baby*

Management is primarily determined by gestation, postnatal age in hours, and by the total SBR level. Birth weight is also used for ALL babies with birthweight <1000g. The investigations and frequency of repeat SBR testing are determined by the baby's condition, the SBR level in relation to the baby's age and their subsequent need for phototherapy or exchange transfusion.

Preterm babies should have group and DAT performed with admission bloods. A visibly jaundiced baby who is DAT positive should have an urgent SBR performed. Women with known alloimmunisation will have an antenatal plan for the baby documented in the maternal history.

The DAT is occasionally negative in ABO incompatibility and other pathologies e.g. G6PD deficiency may coexist with a positive DAT.

Overhead phototherapy is the treatment of choice for the initiation of single unit phototherapy in babies <35 weeks' gestation. When multiple unit phototherapy is required additional units may be either overhead or

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fiberoptic devices.

[Jaundice - Phototherapy](#)

Parents should be made aware of, and provided with, the [Jaundice and your newborn baby information sheet](#).

Intravenous immunoglobulin is no longer used for babies with isoimmunisation (Rhesus or ABO incompatibility).

Exchange transfusion is reserved for babies with very high or rapidly rising SBR levels. It is a very high risk procedure in preterm babies, with significant morbidity and mortality. Most exchange transfusions are performed in babies with Rhesus isoimmunisation, ABO and other blood group incompatibilities and red cell enzyme defects.

[Blood - Exchange Transfusion – Newborn Intensive Care](#)

All preterm babies who are admitted to NICU for >48 hours, regardless of their maximum SBR level, are referred for formal audiology assessment at 8 months of age. This is initiated by the Victorian Infant Hearing Screening Program service when the newborn hearing screen is performed.

SBR treatment thresholds for hyperbilirubinaemia in babies < 35 weeks gestation

Preterm babies should have an SBR level performed, at 12-24 hours (timed with planned blood collection), earlier if they are visibly jaundiced, have significant bruising or bleeding, or are DAT positive.

The levels at which to treat preterm babies with phototherapy and exchange transfusion at the RWH are based on consensus, derived from published guidelines from the UK, USA, Norway and New Zealand, as well as other Australian centres (RPA and RCH).

The SBR level should be plotted on the appropriate treatment chart and placed in the baby's medical history. There are four treatment charts for babies born before 35 week's gestation. Babies should be plotted according to their gestation at birth, unless they are born weighing <1000 grams.

Preterm babies who are isoimmunised (i.e. DAT positive) should be treated, at an SBR 20 micromol/L below their usual threshold.

The 4 treatment groups are as described below, the corresponding treatment graphs are shown in Appendices 1-4:

- Treatment of hyperbilirubinaemia in babies born <27 weeks' gestation OR any baby with birth weight <1000g
- Treatment of hyperbilirubinaemia in babies born 27– 30⁺⁶ weeks' gestation (if birth weight <1000g - go to <27 week chart)
- Treatment of hyperbilirubinaemia in babies born 31 – 32⁺⁶ weeks' gestation (if birth weight <1000g - go to <27 week chart)
- Treatment of hyperbilirubinaemia in babies born at 33 – 34⁺⁶ weeks' gestation (if birth weight <1000g - go to <27 week chart)

4.4 Monitoring hyperbilirubinaemia and treatment with phototherapy in premature babies

Preterm babies with rising SBR levels should have their SBR checked 12 -24 hourly. Single overhead phototherapy should be commenced according to the appropriate hyperbilirubinaemia treatment graphs. The SBR should be rechecked daily whilst on phototherapy.

Babies with rapidly rising SBR levels:

- rate of rise >8.5 micromol/L per hour (~50 micromol/L in 6 hrs) *prior* to phototherapy or
- rise of >50 micromol/L in 24 hrs (or equivalent) *during* single unit phototherapy and
- babies with very high SBR levels (within 50 micromol/L of exchange level)

should have the number of phototherapy units increased and be considered for exchange transfusion.

When the SBR is more than 50 micromol/L below the exchange level, the number of phototherapy units can be reduced.

Consider stopping phototherapy when the SBR is below the treatment level, definitely stop phototherapy when the SBR is 50 micromol/L below the treatment level. Repeat SBR should be done 12-24 hours after ceasing phototherapy. Some rebound is expected (about a 10% rise).

If the repeat SBR is static or falling, repeat SBR only if clinically indicated. If the repeat SBR is rising then repeat

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SBR in a further 24 hours. If the repeat SBR has risen to above the treatment threshold restart phototherapy.

If treatment for jaundice with single unit phototherapy is the only indication for ongoing NICU admission, and the baby cannot be readmitted to the maternity wards, then consider referral to NHITH for [Phototherapy at Home](#).

If the SBR remains elevated at 21 days of age, consider investigations for prolonged unconjugated hyperbilirubinaemia.

[Jaundice \(Hyperbilirubinaemia\) in Newborn Babies Greater Than 35 Weeks Gestation](#)

5. Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be monitored by incidences reported to VHIMs and the annual number of exchange transfusions performed. It will be evaluated by annual audit of documentation on treatment charts in patient histories.

6. References

1. Neonatal Jaundice: A Clinical Guideline, NHS National Institute for Health and Clinical Excellence, May 2010, Clinical Guideline 98; www.nice.org.au
2. American Academy of Pediatrics Subcommittee on Hyperbilirubinaemia. Management of hyperbilirubinaemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297
3. RPA Newborn Care Guidelines: <http://www.sswahs.nsw.gov.au/rpa/neonatal/>
4. Up to Date: Hyperbilirubinaemia in the premature infant (less than 35 weeks gestation), www.uptodate.com, 2012
5. The Royal Children's Hospital, Melbourne, Clinical Practice Guidelines; Jaundice in Early Infancy http://www.rch.org.au/clinicalguide/cpg.cfm?doc_id=5217
6. National Women's Health Guidelines, Auckland City Hospital, New Zealand <http://www.adhb.govt.nz/newborn/Guidelines/GI/Jaundice.htm>
7. An approach to the management of hyperbilirubinaemia in the preterm infant less than 35 weeks of gestation. MJ Maisels. Journal of Perinatology 2012; Sep;32(9):660-4
8. Uniform treatment thresholds for hyperbilirubinaemia in preterm infants: Background and synopsis of a national guideline. van Imhoff DE. Early Human Development 2011;(87):521-5

7. Legislation/Regulations related to this guideline

Not applicable.

8. Appendices

- Appendix 1: [Treatment of hyperbilirubinaemia in babies born <27 weeks' gestation OR any baby with birth weight <1000 g](#)
- Appendix 2: [Treatment of hyperbilirubinaemia in babies born 27– 30⁺⁶ weeks' gestation \(if birth weight <1000 g - go to <27 week chart\)](#)
- Appendix 3: [Treatment of hyperbilirubinaemia in babies born 31 – 32⁺⁶ weeks' gestation \(if birth weight <1000 g - go to <27 week chart\)](#)
- Appendix 4: [Treatment of hyperbilirubinaemia in babies born at 33 – 34⁺⁶ weeks' gestation \(if birth weight <1000 g - go to <27 week chart\)](#)

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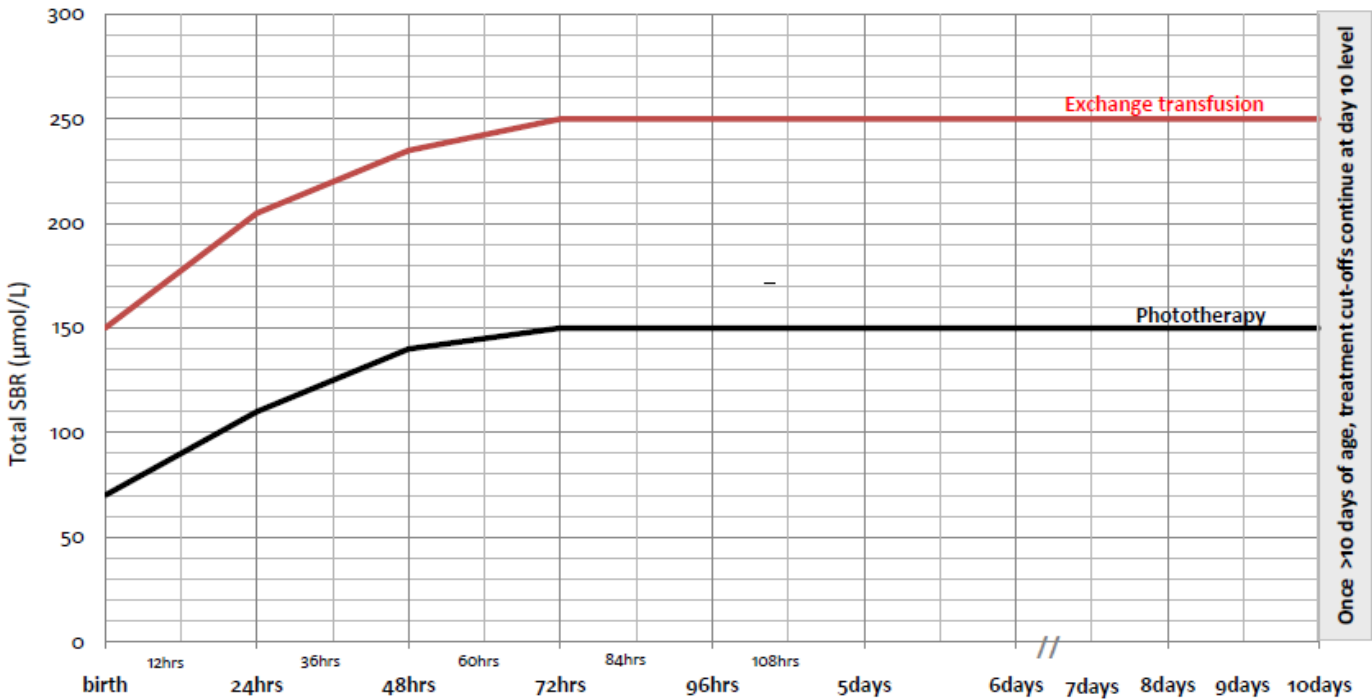
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Treatment of Hyperbilirubinaemia

For isoimmunised preterm babies (DAT positive) treat at SBR 20 $\mu\text{mol/L}$ below their usual threshold level.



Once >10 days of age, treatment cut-offs continue at day 10 level

UR number: _____
 Surname: _____
 Given name/s: _____
 Date of birth: _____ Gender: _____
 (AFFIX PATIENT LABEL)

Date	of birth																		
Time	of birth																		
Age (hours)																			
SBR ($\mu\text{mol/L}$)																			
Phototherapy	Start time																		
	Stop time																		
No. of phototherapy units																			

Treatment of Hyperbilirubinaemia in Newborn Babies born < 27 weeks gestation (and any baby with birth weight < 1000g)

Treatment of Hyperbilirubinaemia in Newborn Babies born 27 – 30⁺⁶ weeks gestation (If birth weight < 1000g, use < 27 weeks chart MR/1813A)

UR number: _____

Surname: _____

Given name/s: _____

Date of birth: _____ Gender: _____

(AFFIX PATIENT LABEL)

Age in hours	SBR measurement (micromol/L)	
ACTION if total SBR is above this value	Commence single unit phototherapy	Increase to maximum phototherapy and consider exchange transfusion
Birth	80	170
12 hours	110	200
24 hours	140	230
36 hours	160	250
48 hours	175	270
60 hours	185	280
≥ 72 hours	190	290
> 21 days	Consider investigations for prolonged hyperbilirubinaemia	

Monitor SBR
Measure SBR 12-24 hourly whilst SBR rising, then once daily as SBR stabilises during phototherapy.

Increase phototherapy
Increase to multiple phototherapy if:

1. Rate of rise > 8.5 micromol/L per hour prior to phototherapy
2. SBR rises by > 50 micromol/L in 24 hours (or equivalent) during single unit phototherapy
3. SBR is within 50 micromol/L of exchange level

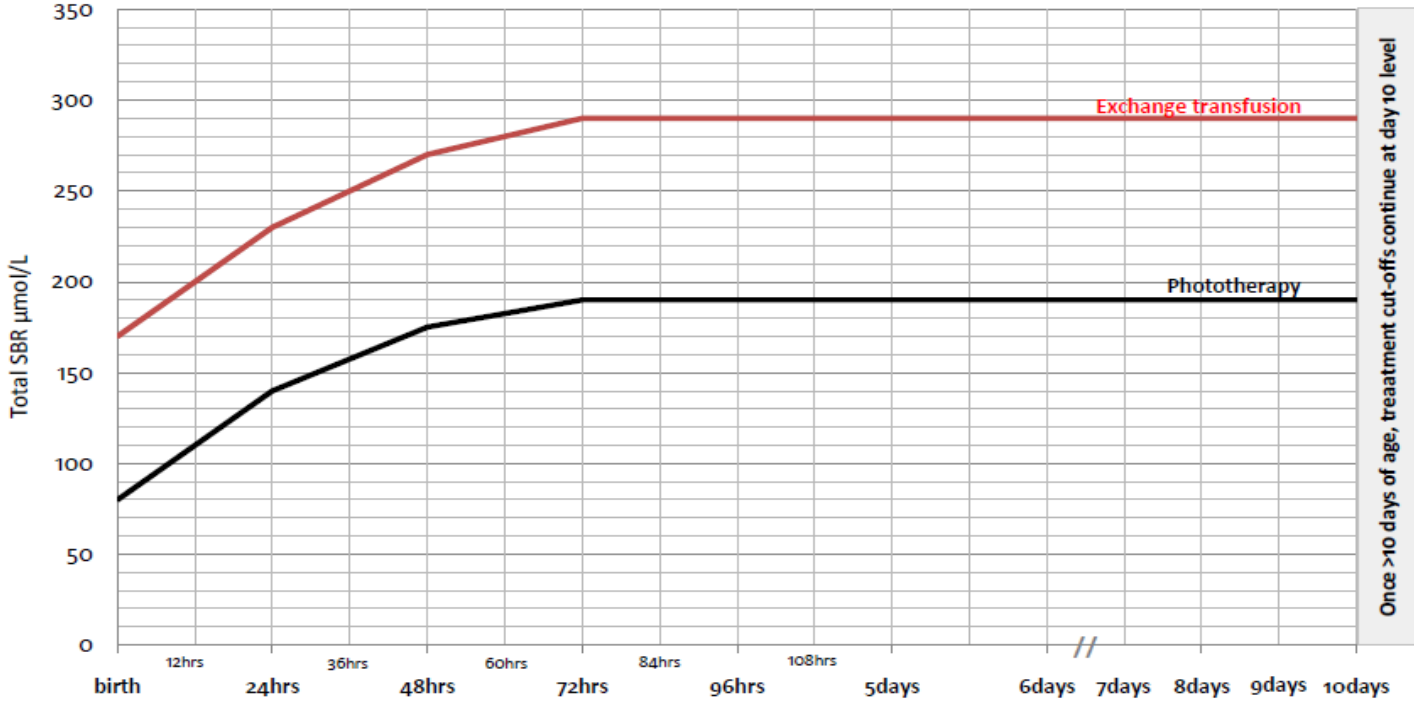
Reduce phototherapy
When SBR is more than 50 micromol/L below exchange level, reduce the number of phototherapy units.

Stop phototherapy and monitor response

- Consider stopping phototherapy when SBR is below treatment level
- Definitely stop phototherapy when SBR is 50 µmol/L below the treatment level
- Check for rebound (~10% rebound expected) 12-24 hours after ceasing phototherapy. If SBR is static or falling repeat tests only if clinically indicated. If SBR is rising repeat in 24 hours or restart phototherapy if above treatment threshold.

Restart phototherapy
Restart phototherapy if SBR is clearly above treatment threshold (e.g. rebound > 10% or rate of rise is greater than expected for the day of life).

Treatment of Hyperbilirubinaemia in Newborn Babies born 27 – 30⁺⁶ weeks gestation
 (If birth weight < 1000g, use < 27 weeks chart MR/1813A)



For isoimmunised preterm babies (DAT positive) treat at SBR 20 µmol/L below their usual threshold level.

Once >10 days of age, treatment cut-offs continue at day 10 level



Treatment of Hyperbilirubinaemia

UR number: _____
 Surname: _____
 Given name/s: _____
 Date of birth: _____ Gender: _____
 (AFFIX PATIENT LABEL)

Date	of birth																		
Time	of birth																		
Age (hours)																			
SBR (µmol /L)																			
Phototherapy	Start time																		
	Stop time																		
No. of phototherapy units																			



**Treatment of Hyperbilirubinaemia in Newborn Babies born 27 – 30⁺⁶ weeks gestation
(If birth weight < 1000g, use < 27 weeks chart MR/1813A)**

UR number: _____

Surname: _____

Given name/s: _____

Date of birth: _____ Gender: _____

(AFFIX PATIENT LABEL)

Age in hours	SBR measurement (micromol/L)	
ACTION if total SBR is above this value	Commence single unit phototherapy	Increase to maximum phototherapy and consider exchange transfusion
Birth	80	170
12 hours	110	200
24 hours	140	230
36 hours	160	250
48 hours	175	270
60 hours	185	280
≥ 72 hours	190	290
> 21 days	Consider investigations for prolonged hyperbilirubinaemia	

Monitor SBR
Measure SBR 12-24 hourly whilst SBR rising, then once daily as SBR stabilises during phototherapy.

Increase phototherapy
Increase to multiple phototherapy if:

1. Rate of rise > 8.5 micromol/L per hour prior to phototherapy
2. SBR rises by > 50 micromol/L in 24 hours (or equivalent) during single unit phototherapy
3. SBR is within 50 micromol/L of exchange level

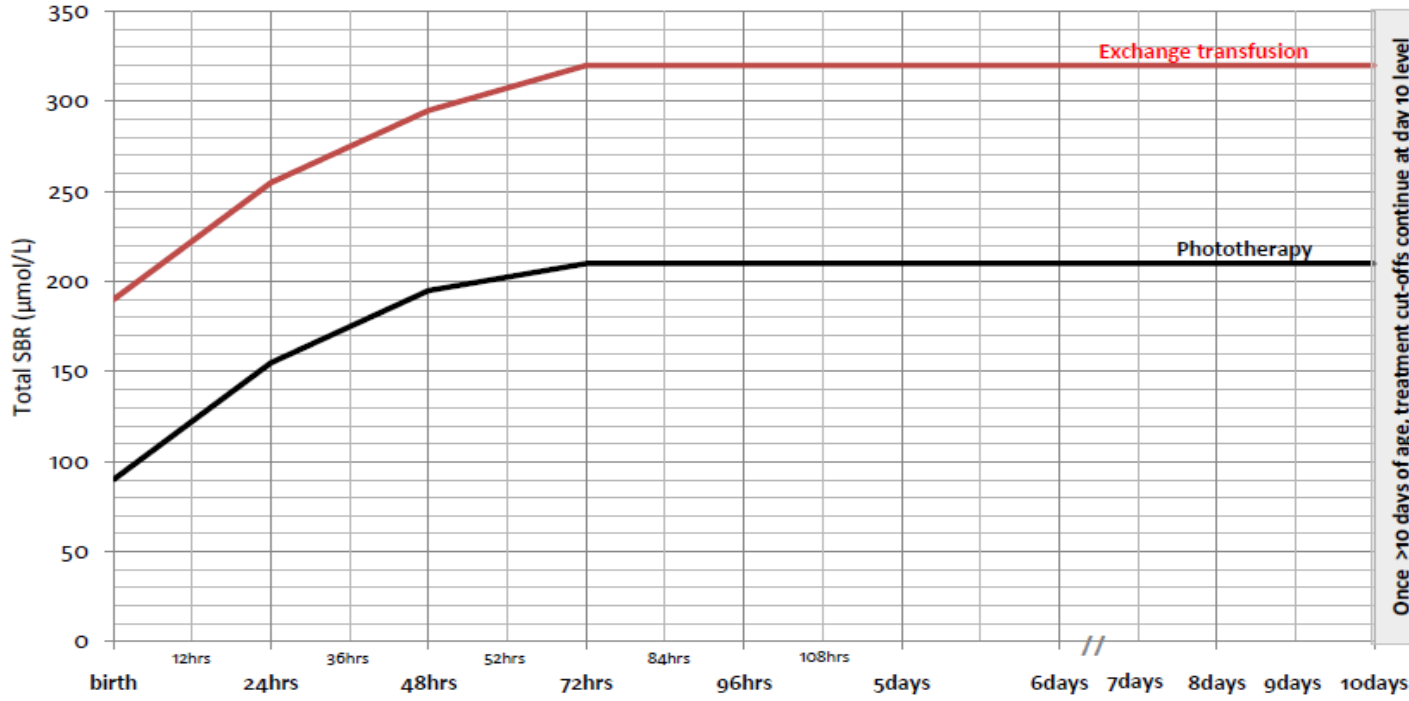
Reduce phototherapy
When SBR is more than 50 micromol/L below exchange level, reduce the number of phototherapy units.

Stop phototherapy and monitor response

- Consider stopping phototherapy when SBR is below treatment level
- Definitely stop phototherapy when SBR is 50 µmol/L below the treatment level
- Check for rebound (~10% rebound expected) 12-24 hours after ceasing phototherapy. If SBR is static or falling repeat tests only if clinically indicated. If SBR is rising repeat in 24 hours or restart phototherapy if above treatment threshold.

Restart phototherapy
Restart phototherapy if SBR is clearly above treatment threshold (e.g. rebound > 10% or rate of rise is greater than expected for the day of life).

Treatment of Hyperbilirubinaemia in Newborn Babies born 31 – 32⁺⁶ weeks gestation (If birth weight < 1000g, use < 27 weeks chart MR/1813A)



For isoimmunised preterm babies (DAT positive) treat at SBR 20 µmol/L below their usual threshold level.

Treatment of Hyperbilirubinaemia

the women's
the royal women's hospital



UR number: _____
 Surname: _____
 Given name/s: _____
 Date of birth: _____ Gender: _____
 (AFFIX PATIENT LABEL)



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the royal women's hospital

Treatment of Hyperbilirubinaemia in Newborn Babies born 31 – 32⁺⁶ weeks gestation (If birth weight < 1000g, use < 27 weeks chart MR/1813A)

UR number: _____

Surname: _____

Given name/s: _____

Date of birth: _____ Gender: _____

(AFFIX PATIENT LABEL)

Age in hours	SBR measurement (micromol/L)	
ACTION if total SBR is above this value	Commence single unit phototherapy	Increase to maximum phototherapy and consider exchange transfusion
Birth	90	190
12 hours	120	225
24 hours	155	255
36 hours	175	275
48 hours	195	295
60 hours	210	310
≥ 72 hours	220	320
> 21 days	Consider investigations for prolonged hyperbilirubinaemia	

Monitor SBR
Measure SBR 12-24 hourly whilst SBR rising, then once daily as SBR stabilises during phototherapy.

Increase phototherapy
Increase to multiple phototherapy if:

1. Rate of rise > 8.5 micromol/L per hour prior to phototherapy
2. SBR rises by > 50 micromol/L in 24 hours (or equivalent) during single unit phototherapy
3. SBR is within 50 micromol/L of exchange level

Reduce phototherapy
When SBR is more than 50 micromol/L below exchange level, reduce the number of phototherapy units.

Stop phototherapy and monitor response

- Consider stopping phototherapy when SBR is below treatment level
- Definitely stop phototherapy when SBR is 50 µmol/L below the treatment level
- Check for rebound (~10% rebound expected) 12-24 hours after ceasing phototherapy. If SBR is static or falling repeat tests only if clinically indicated. If SBR is rising repeat in 24 hours or restart phototherapy if above treatment threshold.

Restart phototherapy
Restart phototherapy if SBR is clearly above treatment threshold (e.g. rebound > 10% or rate of rise is greater than expected for the day of life).



**Treatment of Hyperbilirubinaemia in Newborn Babies born 33 – 34⁺⁶ weeks gestation
(If birth weight > 1000g, use < 27 weeks chart MR/1813A)**

UR number: _____

Surname: _____

Given name/s: _____

Date of birth: _____ Gender: _____

(AFFIX PATIENT LABEL)

Age in hours	SBR measurement (micromol/L)	
ACTION if total SBR is above this value	Commence single unit phototherapy	Increase to maximum phototherapy and consider exchange transfusion
Birth	100	210
12 hours	130	240
24 hours	165	260
36 hours	190	295
48 hours	210	315
60 hours	225	330
≥ 72 hours	240	340
> 21 days	Consider investigations for prolonged hyperbilirubinaemia	

Monitor SBR
Measure SBR 12-24 hourly whilst SBR rising, then once daily as SBR stabilises during phototherapy.

Increase phototherapy
Increase to multiple phototherapy if:

1. Rate of rise > 8.5 micromol/L per hour prior to phototherapy
2. SBR rises by > 50 micromol/L in 24 hours (or equivalent) during single unit phototherapy
3. SBR is within 50 micromol/L of exchange level

Reduce phototherapy
When SBR is more than 50 micromol/L below exchange level, reduce the number of phototherapy units.

Stop phototherapy and monitor response

- Consider stopping phototherapy when SBR is below treatment level
- Definitely stop phototherapy when SBR is 50 µmol/L below the treatment level
- Check for rebound (~10% rebound expected) 12-24 hours after ceasing phototherapy. If SBR is static or falling repeat tests only if clinically indicated. If SBR is rising repeat in 24 hours or restart phototherapy if above treatment threshold.

Restart phototherapy
Restart phototherapy if SBR is clearly above treatment threshold (e.g. rebound > 10% or rate of rise is greater than expected for the day of life).