Queensland Clinical Guidelines

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Maternity and Neonatal **Clinical Guideline**

Neonatal jaundice

Queensland Government

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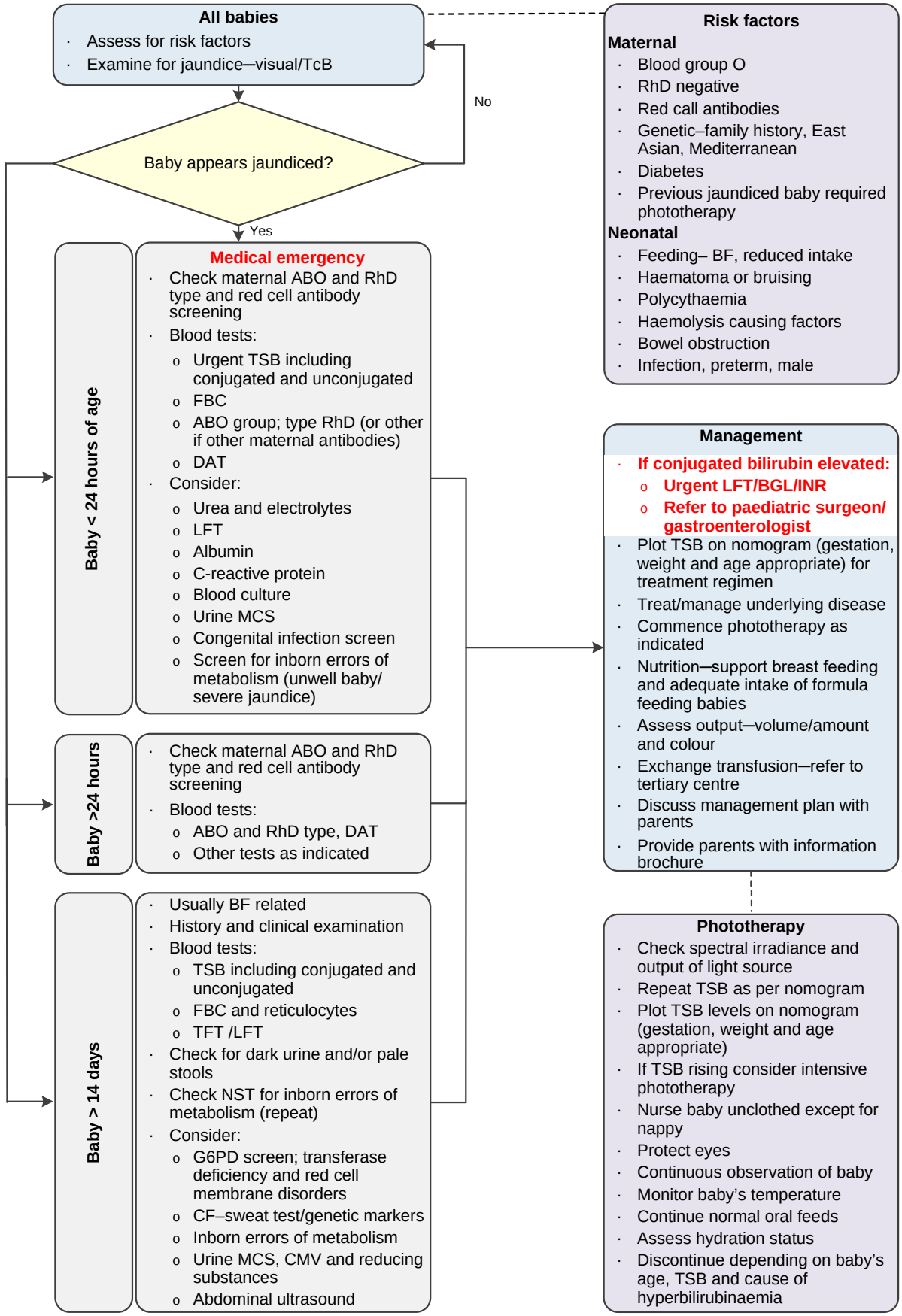
Flow Chart: Management of neonatal jaundice



Abbreviations: BF Breastfeeding**; BGL** Blood glucose level; **CF** Cystic fibrosis**; CMV** Cytomegalovirus**; DAT** Direct antiglobulin test**; FBC** Full blood count**; G6PD** Glucose 6 dehydrogenase deficiency**; INR** International normalised ratio; **LFT** Liver function tests; **MCS** Microscopy, culture and sensitivity; **NST** Neonatal screening test**; Rh** Rhesus**; TcB** Transcutaneous bilirubin**; TFT** Thyroid function tests; **TSB** Total serum bilirubin**; USS** Ultrasound scan; **<** Less than; **>** Greater than

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Abbreviations

ABR	Auditory brainstem-evoked response
ANSD	Auditory neuropathy spectrum disorder
BIND	Bilirubin induced neurologic dysfunction
CMV	Cytomegalovirus
CNS	Central nervous system
DAT	Direct antiglobulin test
G6PD	Glucose-6-phosphate dehydrogenase deficiency
INR	International normalised units
IVIg	Intravenous immunoglobulin
LED	Light emitting diode
LFT	Liver function tests
NST	Newborn screening test
RhD	Rh blood type D
RBC	Red blood cell(s)
SNHL	Sensorineural hearing loss
TcB	Transcutaneous bilirubin
TSB	Total serum bilirubin
USS	Ultrasound scan
UV	Ultraviolet

Definitions

Alagille syndrome	Genetic disorder with absent, narrowed or reduced number of bile ducts and other clinical features.[1]
Athetoid cerebral palsy	Cerebral palsy with abnormal involuntary movements associated with damage to the basal ganglia.[2]
Auditory brainstem-evoked response	Neurologic test of auditory brainstem function in response to auditory stimuli.[3]
β glucuronidase	Enzyme that converts conjugated bilirubin to unconjugated bilirubin form in breastfed babies.[4]
Bilirubin encephalopathy	Acquired metabolic encephalopathy caused by unconjugated hyperbilirubinaemia.[5]
Conjugated hyperbilirubinaemia	Increased levels of conjugated (water soluble) bilirubin caused by obstruction, infection, toxins or metabolic/genetic or alloimune disorders.[1] Measured as greater than 25 micromols/L direct bilirubin of total bilirubin level[4,6]
Coombs test	See Direct Antiglobulin Test.
Direct Antiglobulin Test (DAT)	An agglutination test that detects the presence of antibodies that are bound to red blood cells cause haemolysis. It is also known as a Coombs test.[7]
Extreme hyperbilirubinaemia	TSB approaching exchange transfusion range.[8]
Haemolysis	Destruction of red blood cells in the blood stream.[8]
Haemolytic disease of the newborn	Haemolytic disease of the newborn (HDN) is characterised by a breakdown of red blood cells (RBC) by maternal antibodies. Antibodies to the RhD, Rhc and Kell antigen are the most common causes of severe HDN in Australia.[9]
Hyperbilirubinaemia	Increased level of bilirubin in the blood.[10]
Intensive phototherapy	Phototherapy provided by light source(s) with irradiance of at least 30microW cm^{-2} nm^{-1} over the waveband interval 460–490 nm^{-1}.[11]
Kernicterus	Yellow staining of the brain caused by unbound, unconjugated bilirubin crossing the blood brain barrier.[5]
Minor blood type	Less common blood group associated with causing severe haemolytic disease of the newborn.[12]
Opisthotonus	Severe hyperextension causing backward arching of the head, neck, and spine.[13]
Prolonged jaundice	Jaundice that persists after day 14 in term babies and day 21 in preterm babies and is more common in breast fed babies.[14]
Retrocollis	Spasmodic torticollis (abnormal, asymmetrical head or neck position) where the head is drawn back.[13]
Sensorineural hearing loss	Acquired permanent hearing loss caused by damage to the cochlear nuclei and central auditory pathways.[15]
Severe hyperbilirubinaemia	Hyperbilirubinaemia requiring phototherapy.[16]
Significant hyperbilirubinaemia	Hyperbilirubinaemia requiring treatment.[6]
Spectral irradiance	Amount of spectral energy (microW) delivered per unit area (cm^2) of exposed skin at a particular wavelength (nm) measured as microW/cm^2/nm.[11]
Standard phototherapy	Phototherapy provided by light source(s) with irradiance of 25–30 microW cm^{-2} nm^{-1} over the waveband interval 460–490 nm^{-1}.[4,11]
Total serum bilirubin	The sum value of conjugated and unconjugated bilirubin.[17]
Unconjugated hyperbilirubinaemia	Increased levels of unconjugated (lipid soluble) bilirubin usually caused by haemolysis, immature liver or sepsis.[4]

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1 Introduction

Jaundice is one of the most common conditions requiring medical attention in newborn babies.[18] Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life.[19] In 2015 in Queensland 3.2% of all babies born had jaundice requiring phototherapy.[20]

Jaundice is a sign of elevated levels of bilirubin in the blood.[4] The baby presents with a yellowish appearance resulting from the accumulation of bilirubin in the skin, mucous membranes and conjunctiva.[19]

Hyperbilirubinaemia occurs when there is an imbalance between bilirubin production, conjugation and elimination. The breakdown of red blood cells (RBC) and haemoglobin cause unconjugated bilirubin to accumulate in the blood.[19] Unconjugated bilirubin binds to albumin and is transported to the liver where it is converted to conjugated bilirubin. Conjugated bilirubin is water soluble and able to be eliminated via urine and faeces.[21] Unbound unconjugated bilirubin is lipid soluble and can cross the blood-brain barrier.[4]

In the first week of life, most babies have a bilirubin level that exceeds the upper limit of normal for an adult.[22] Jaundice resulting from a small increase in unconjugated bilirubin after birth is normal and generally does not need to be investigated or treated. Mild jaundice may persist past the first week to 10 days of life without any underlying cause. However, early onset jaundice (detectable clinically before 24 hours of age) is a risk factor for severe hyperbilirubinaemia requiring treatment.

When jaundice has a high peak level regardless of the cause, treatment is required to prevent brain damage. In addition, some underlying causes of hyperbilirubinaemia are serious or even life-threatening illnesses that require urgent treatment. Investigations are warranted to determine the underlying cause of jaundice in any of the following:

- Early onset with a high peak level[21]
- Elevated conjugated bilirubin component[23]
- Persists after the normal time for jaundice to resolve[4]
- Present in a baby with other clinical illness or abnormalities

2 Risk factors for clinically significant hyperbilirubinaemia

2.1 Maternal risk factors

Table 1. Maternal risk factors

Aspect	Comment
Blood group	· Blood group O · Rhesus D (RhD) negative · Red cell antibodies—D,C,c,E,e and K and certain others[24]
Previous jaundiced baby[23]	· Required phototherapy or other treatment
Diabetes[23]	· High red cell mass in baby where maternal diabetes is poorly controlled diabetes (any type).
Genetic	· East Asian[23] · Mediterranean[14] · Family history of inherited haemolytic disorders (e.g. G6PD deficiency, hereditary spherocytosis)[23]

2.2 Neonatal risk factors

Table 2. Neonatal risk factors

Aspect	Comment
Feeding	· Breast milk: o β glucuronidase in breast milk increases the breakdown of conjugated bilirubin to unconjugated bilirubin in the gut[4] o Lipoprotein lipase (a water-soluble enzyme) and nonesterified fatty acids in breast milk may inhibit normal bilirubin metabolism[25,26] · Factors that delay normal colonisation with gut bacteria resulting in high concentration of bilirubin in the gut) · Low breast milk (may be due to delayed milk production) or formula intake leading to dehydration and increased enterohepatic circulation[4,27]
Haematological[18,23,28]	· Factors causing haemolysis (immune or non-immune)[4] · Polycythaemia · Haematoma or bruising
Gastrointestinal[29]	· Bowel obstruction
Other[4,23]	· Infection · Prematurity · Male

3 Causes of jaundice

Jaundice peaking on the third to fifth day of life is likely to be caused by normal newborn physiology. However, a pathological cause of jaundice may coexist with physiological jaundice[24,30]

There are a number of causes of neonatal jaundice. The following information is not exhaustive and includes the more common causes that place the baby at risk of developing hyperbilirubinaemia requiring treatment.

3.1 Jaundice presenting early (before 24 hours of age or with a high peak level)

The early onset of jaundice (detectable clinically before 24 hours of age) is a risk factor for severe hyperbilirubinaemia requiring treatment.[31] Babies who develop jaundice in the first 24 hours of life, particularly due to haemolysis, are at risk of developing acute and chronic bilirubin encephalopathy.[4,32] [refer to Section 7.1 Acute and chronic bilirubin encephalopathy]. Jaundice incidence is higher in the first 24 hours of life in babies between 35 and 36 weeks gestation.[33]

Regardless of the underlying cause, in babies who develop jaundice at any time the following factors increase the level of free bilirubin (bilirubin unbound to albumin) in the circulation and so can increase the risk of bilirubin encephalopathy:

- Acidosis or hypoxia
- Hypothermia
- Hypoalbuminaemia
- Infection
- Certain medications given to the mother or baby [refer to 6.1Medication use]

3.1.1 Common causes of pathological jaundice

Table 3. Common causes of pathological jaundice

Pathogenesis	Cause
Haemolysis [19,33]	· Blood extravasation o Bruising/birth trauma · Haemorrhage e.g. cerebral, pulmonary, intra-abdominal · Isoimmunisation[4,18]: o ABO (low risk) or RhD (high risk) alloantibodies o Other blood group alloantibodies–Kell and Rh c and E are the most common[12]
Decreased conjugation of bilirubin in the liver[28,33]	· Gilbert Syndrome (gluronyltransferase deficiency disorder) · Congenital hypothyroidism
Decreased excretion of bilirubin[4,23,25]	· Abnormal biliary ducts, e.g. intrahepatic biliary atresia or extrahepatic biliary stenosis or atresia · Cystic fibrosis

3.1.2 Less common causes of pathological jaundice

Less common causes of jaundice may present early but can be episodic related to the timing of an insult such as infection or exposure to an oxidant in G6PD deficiency. Others, such as pyloric stenosis are much more likely to cause late onset jaundice.

Table 4. Less common causes of pathological jaundice

Pathogenesis	Cause
Haemolysis [19,33]	· RBC enzyme defects: o G6PD deficiency o Pyruvate kinase deficiency[23] · Hereditary RBC membrane abnormalities: o Spherocytosis o Elliptocytosis · Haemoglobinopathies o Alpha thalassaemia · Infection
Decreased conjugation of bilirubin in the liver[28,33]	· Other gluronyltransferase deficiency disorders o Crigler-Najjar Syndrome[28] o Transient familial neonatal hyperbilirubinaemia/Lucey-Driscoll syndrome (may be severe) · Congenital hypopituitarism
Liver cell damage (may cause combination of decreased bilirubin uptake, conjugation and/or excretion)	· Congenital infections: o *Cytomegalovirus* (CMV), *Herpes simplex* virus o Toxoplasmosis, rubella, syphilis, *varicella zoster*, parvovirus B19 causing hepatitis · Inborn errors of metabolism (e.g. urea cycle defects, galactasaemia, fatty acid oxidation defects)
Decreased excretion of bilirubin[4,23,25]	· Conditions causing abnormal biliary ducts, e.g. Alagille Syndrome, choledochal cyst · Increased enterohepatic bilirubin recirculation o Bowel obstruction, pyloric stenosis o Meconium ileus or plug, cystic fibrosis

3.2 Jaundice presenting after 24 hours and resolving early

In the first week of life, most babies have a total serum bilirubin (TSB) that exceeds the upper limit of normal for an adult.[22] Jaundice resulting from a small increase in unconjugated bilirubin after birth is normal and generally does not need to be investigated or treated.[23,33,34] Mild jaundice may persist past the first week but usually resolves within the first 10 days (term baby) or three weeks (preterm baby) of life without any underlying cause identified.

Table 5. Jaundice presenting after 24 hours

Cause	Comment
Context	· Physiological jaundice is transient, mild unconjugated hyperbilirubinaemia[31] · More common in first born babies[23] · Mostly benign[4]
Causes	· Increased bilirubin levels secondary to an increase in the volume and a decrease in the life span of RBC and an immature liver with reduced enzyme activity [23,33,34] · Normal population variation in maturation of bile metabolism after birth · More common in breastfed baby where there is inadequate milk intake[31] · If baby unwell, has risk factors for underlying disorder or has a TSB above the treatment line consider pathological causes · Refer to Appendix A Nomogram: Jaundice management for baby greater than 38 weeks gestation
Characteristics	· Usually first seen on day two of life[23] and peaks at day three to five · Peaks on day three in term babies and days five to six in preterm babies[34] · Usually resolves in the first week to 10 days of life in a term baby or within three weeks in a preterm baby
Management	· Usually does not require treatment[33,35] but may require phototherapy · Reassure the parents and monitor the baby[33] · Investigate unwell jaundiced baby for underlying disease · Treat any pathological cause if identified

3.3 Prolonged jaundice

Prolonged jaundice begins or persists after day 14 in term babies and day 21 in preterm babies[25], and is more common in breast fed babies. It is present in 15-40% of well, breastfed babies at 2 weeks of age and 9% of well, breast fed babies at 4 weeks of age.[25] Prolonged jaundice is usually harmless but can be an indication of serious disease such as biliary atresia.

Table 6. Prolonged jaundice

Pathogenesis	Common causes	Less common causes
Unconjugated hyperbilirubinaemia	· Inadequate nutrition and hydration more common in exclusively breastfeeding baby o Due to inadequate milk supply · Breast milk jaundice[4,14,36-38] o Commonly presents between days four and seven with a peak at two to three weeks of age and resolves by three months of age[31] o Due to altered gut flora	· Infection · G6PD deficiency · Spherocytosis · Pyloric stenosis[4,14,25] · Crigler-Najjar syndrome[28] · Inherited disorders for e.g. Gilbert's Syndrome[28]
Conjugated hyperbilirubinaemia		· Biliary atresia[4] · Idiopathic neonatal cholestasis[4,39] · Inherited disorders for e.g. Alagille Syndrome · Congenital hypopituitarism
Unconjugated and/or conjugated hyperbilirubinaemia	· Congenital hypothyroidism[33,40] · Haemolysis[41] o RhD or other haemolytic disease ▪ Usually unconjugated initially then conjugated bilirubin levels rise o G6PD[42]deficiency ▪ Can cause episodic or prolonged jaundice depending on oxidant exposure	· Infection · Metabolic disorders · Congenital hypopituitarism[25] · Parenteral nutrition · Inborn errors of metabolism[4]

4 Clinical assessment

Prevention of severe consequences of hyperbilirubinaemia and detection of important underlying disorders requires that for all babies, there is consideration of risk factors[25] and repeated visual assessment for jaundice.[23] In babies with significant risk factors (e.g. unwell babies, preterm babies, babies at risk for haemolytic conditions), screening using transcutaneous bilirubinometry (TcB) and/or TSB is likely to be justified.

All jaundiced babies require an assessment including history and a full clinical examination. Consultation with a tertiary service regarding management may be required.[23,33] Any baby who appears unwell and is jaundiced requires a medical assessment. If there are other signs of conjugated hyperbilirubinaemia present including dark urine and pale stools immediate referral to a tertiary service for urgent investigation and treatment,[14,25,38,43] is required to prevent secondary complications.[17,44]

Table 7. Clinical assessment

Aspect	Comment
Jaundice	· Examine all babies for jaundice[23]: o Every eight to 12 hours in the first 72 hours of life o Prior to discharge · Jaundice appears cephalocaudal depending on severity (only head appears jaundiced in mild cases) and regresses in the reverse order[18] · Do not rely on visual examination alone to assess level of jaundice[10,18] o There is poor correlation of TSB and visual assessment even: ▪ In natural light or a well-lit room ▪ If blanching the skin with a finger[18] o Visual estimation of bilirubin levels can lead to errors in babies who ▪ Have darker skin tones[10,18,23] ▪ Are receiving phototherapy
Potential signs of bilirubin encephalopathy[25,33,43,45]	· Lethargy · Poor feeding · Vomiting · High pitched cry · Hypotonia followed by hypertonia · Opisthotonus · Seizure
Intake/output	· Feeding assessment[4]: [refer to Table 11. Nutritional considerations] o Refer to Queensland Clinical Guideline *Establishing breastfeeding*[46] · Weight: o Assess weight in first week of life[4,47] ▪ Loss of 10% of birth weight is acceptable in first week of life o Return to birth weight by 7–10 days of life o The percentage of weight loss on day three may be predictive of significant hyperbilirubinaemia[47] (low level evidence)
Urine	· Four or more wet nappies per day by 72 hours of age indicates adequate milk intake[47] o Refer to Queensland Clinical Guideline *Establishing breastfeeding*[46] · Dark urine may be indicative of conjugated hyperbilirubinaemia[43] · Urates are commonly present in the urine of newborn babies up to 96 hours of age[38,43]
Stools	· Check there are three to four stools per day by the fourth day of life[47] · Stools change from meconium to mustard yellow by third day of life[47] · Pale stools and jaundice are key indicators of liver disease[43]
Pathology	· Refer to Section 5 Investigations o If conjugated bilirubinaemia is suspected also check liver function tests (LFT), INR and blood glucose level

5 Investigations

The urgency of investigations and treatment depends on the clinical presentation of the baby. An unwell baby requires more urgent investigation and treatment as the underlying aetiology can be associated with a variety of diseases.

5.1 Measurement of bilirubin

A baby's TSB or TcB and gestation are good predictors of hyperbilirubinaemia risk. TSB is interpreted according to the baby's age in hours [18] by plotting on a gestation specific nomogram. Refer to Appendix A Nomogram: Jaundice management for baby greater than 38 weeks gestation.

Table 8. Measurement of bilirubin

Aspect	Good practice point
Context	· Insufficient evidence available to support universal bilirubin screening to prevent chronic bilirubin encephalopathy[23] and some evidence of harm (due to overuse of phototherapy)[48] · If baby has clinically detectable early (first 24 hours), or suspected severe jaundice or significant risk factors use TcB and/or TSB, as visual assessment unreliable[23] [refer to Table 1. Maternal risk factors and Table 2. Neonatal risk factors] · Combine blood testing to reduce number of venepunctures to baby
TcB	· TcB meter: o Screens for unconjugated hyperbilirubinaemia o Measures the reflected light transmitted onto the skin o Estimates the TSB from mathematical algorithm accounting for haemoglobin and skin pigments[49] o Predictive in identifying babies that need phototherapy[50] o Use according to manufacturer's recommendations and local protocols, including confirming correlation with TBR · Decreases the number of invasive blood tests[18] · Measure on either sternum or forehead[49] · Suitable for babies: o Postnatal age greater than 24 hours[45] o Gestation greater than 35 weeks[45]—more reliable in term babies[51] · Not recommended to assess bilirubin if: o Jaundice is prolonged[50] or there is conjugated hyperbilirubinaemia[50] o Baby having phototherapy[49] or has had phototherapy[4,50] o Baby has had an exchange transfusion · Correlation of TcB with TSB on nomogram[52]: o Needs further evaluation and may increase false negative rate · If TcB is greater than 250 micromol/L or less than 50 micromol/L below threshold for phototherapy measure the TSB[32,53] o Clinical decision regarding treatment is based on TcB trend and not one value[54] [refer to Table 13. Phototherapy treatment]
TSB	· Gold standard for diagnosing hyperbilirubinaemia[49] · Point of care (e.g. blood gas analyser) and laboratory testing measure the sum of conjugated and unconjugated bilirubin in serum[14] · May need to measure total, unconjugated and conjugated bilirubin in pathology laboratory to ensure conjugated hyperbilirubinaemia is not missed (especially in unwell baby and /or severe or prolonged jaundice) · Measure if baby visibly jaundiced: o If less than 24 hours of age o Less than 35 weeks gestation · Continue measuring when[30]: o Level is at or above treatment thresholds o Therapeutic intervention is being considered
Nomograms	· Use to: o Identify babies at risk of developing significant hyperbilirubinaemia[55] o Monitor the trend of the TSB or TcB o Plot TSB on nomogram appropriate for baby's age in hours, gestation and birth weight[8] · If TSB is in treatment zone or less than 50 micromol/L below treatment level repeat TSB according to nomogram[8]

5.2 Jaundice within first 24 hours

Jaundice within 24 hours of birth always requires urgent investigation (especially to rule out haemolysis) and treatment.[19,23] If the onset is between 24 and 48 hours some investigations may be required but treatment may not be necessary. A baby who is thriving and feeding well requires fewer investigations than an unwell baby who is not thriving. A clinically well looking baby without risk factors for an underlying disease, and whose jaundice is below the exchange transfusion threshold only requires[23]:

- TSB to identify if they require treatment
- Full blood count (FBC) to identify haemolysis and /or infection
- Direct antiglobulin test (DAT) to identify blood group alloimmunisation
  - A weak positive DAT can occur in RhD positive baby of RhD negative mother who had antenatal immunoprophylaxis–usually of no significance if maternal antenatal antibody screen was negative

Table 9. Initial investigations for jaundice (first 24 hours of age)

Aspect	Comment
History	· Check maternal antenatal screening for: o Blood group o RhD type o Red cell antibodies
TSB	· Refer to Table 8. Measurement of bilirubin · Measure total, conjugated and unconjugated bilirubin levels
Haematology[4,23]	· Full blood count[4,23]–important and may need to be repeated if baby: o Looks unwell o Is less than 24 hours of age o Looks pale o Is at risk for polycythaemia– ▪ Appears excessively ruddy ▪ Has risk factors (e.g. heavy maternal smoking, significant fetal growth restriction, maternal diabetes) o High TSB especially if refractory to phototherapy · Blood group compatibility: o If maternal antibodies positive test baby's cord blood or if not available test baby's blood for: ▪ ABO and RhD blood RhD type–extended typing may be indicated if there are other maternal antibodies, e.g. Rhc/C e/E) ▪ Direct antiglobulin test (DAT) · Ensure neonatal screening test (NST) is collected
Other	· Consider checking the electrolytes and urea if concerns regarding hydration · Infection[4,23]: o C-reactive protein–indicative of infection/inflammatory process (note: may be false negative near onset of infection) o Blood culture–unwell baby of any age o Urine–microscopy and culture ▪ Urinary tract infection is a potential cause of prolonged jaundice o Investigate for congenital infections if there are other indications, e.g. clinical signs of suggestive history, severe jaundice, elevated conjugated bilirubin, thrombocytopenia ▪ Toxoplasmosis ▪ Rubella ▪ Cytomegalovirus (CMV) ▪ Herpes simplex virus ▪ Syphilis · Investigate for inborn errors of metabolism if baby looks unwell and the jaundice is severe, e.g. galactosaemia, tyrosinaemia · Liver disease[4,23]: o Albumin ▪ Decreased levels result in poor bilirubin binding capacity and risk of bilirubin toxicity o Liver function tests (LFT) as liver enzymes may be increased, e.g. in congenital infections, inborn errors of metabolism

5.3 Prolonged jaundice

Clinical judgement is needed when considering the investigations required for a baby who continues to be jaundiced after 10–14 days for a term baby or after three weeks for a preterm baby.

The most common cause of prolonged jaundice is breast milk jaundice. It occurs in up to 30% well breast feeding babies.[52] Do not advise to stop breast feeding[4] as the risk of breast milk jaundice does not outweigh the benefits.[36,56]

- Diagnosis is based on history and clinical examination[14,36]
- Occurs in well babies with good weight gain[37]
- TSB peaks between days 5 and 6[57] and does not exceed 200 micromol/L[36]
- Self-limiting[14,36]
- Resolves by 12 weeks of age[37]

Table 10. Jaundice after first week

Aspect	Comment
Progression of early jaundice	· History · Weight gain · Feeding · Blood tests–TSB including conjugated bilirubin, FBC, LFT · Thyroid function tests[4,25]–free thyroxine (T4), thyroid stimulating hormone
Recurrent or new presentation of jaundice	· Urine[4,25]: o Microscopy and culture–urinary tract infection is a potential cause of prolonged jaundice o CMV o Reducing substances–present in galactosaemia · Blood: o FBC and reticulocyte count o Repeat NST o CMV (may be requested on NST) o Targeted investigations, e.g. G6PD screen particularly if baby is a male with at risk genetic history
Unwell baby	· Urine–CMV · Check if stools are pale · Abdominal ultrasound scan (USS) to assess possibility of[23,39]: o Extrahepatic biliary disease o Hepatocellular disease (e.g. hepatitis) secondary to infection · Sweat test and genetic markers for cystic fibrosis · Inborn errors of metabolism[23] o May be detected on neonatal screening test (NST)–galactosaemia, primary hypothyroidism, cystic fibrosis o May need testing for rare inborn errors of metabolism–amino acid organic acid, fatty acid
Genetic[4,25]	· Family history · RBC metabolism disorders[4,18] o G6PD serum level ▪ Reduced or normal enzyme level ▪ Take serum when baby is older than two weeks to avoid false-negative results (high enzyme level in immature RBC)[23] · Test for glucuronyl transferase deficiency disorders · Test for red cell membrane disorders, e.g. hereditary spherocytosis or elliptocytosis o May have anaemia[58] or significant fall in haemoglobin and a high reticulocyte count with a negative DAT o Haemolysis o Increased level of lactate dehydrogenase
Percutaneous liver biopsy	· Rarely needed · After consultation with tertiary centre consider to exclude[23,39]: o Metabolic and storage disorders o Congenital viral infection

6 Management

The core principles of jaundice management include prevention, identification and assessment of babies at risk of developing hyperbilirubinaemia and treatment with phototherapy or if indicated.[18,23] Management of hyperbilirubinemia involves interpretation of TSB or TcB levels on a nomogram based on the baby's gestation, age and birth weight.[21] Refer to Appendix A Nomogram: Jaundice management for guidance with developing an individualised management and follow up plan.[8]

In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line, except for babies less than 1000 g

- If baby is greater than 12 hours old with TSB level 1–50 micromol/L below the line repeat the TSB within 6–24 hours
- Babies under phototherapy:
  - Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly
  - Stop phototherapy if TSB greater than 50 micromol/L below line and recheck in 12–24 hours
- If baby presents with TSB above threshold an exchange transfusion is indicated if the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy
- An immediate exchange transfusion is recommended if there are signs of bilirubin encephalopathy[8,59,60]

6.1 Medication use

Use the following medications with caution in a baby with hyperbilirubinaemia as they may cause bilirubin to be displaced from albumin binding sites.[33,61] Refer to an Australian pharmacopoeia for complete drug information.

- Digoxin
- Diazepam
- Salicylates
- Diuretics e.g. frusemide and hydrochlorothiazide
- Ceftriaxone[4,14]
- Ibuprofen[62]
- Sulfamethoxazole such as in trimethoprim/sulfamethoxazole (cotrimoxazole) or other sulphur medications is **contraindicated** in a jaundiced or at risk of jaundice baby[63]
  - Potentially interfere with several steps of bilirubin metabolism and can markedly increase the risk of bilirubin encephalopathy

6.2 Nutrition

Poor feeding leads to reduced caloric intake and dehydration resulting in elevated TSB.

Table 11. Nutritional considerations

Aspect	Comment
Breastfeeding	· Breastfed babies are more prone to developing prolonged jaundice than formula fed babies if there is [27,64]: o Inadequate milk production o Insufficient intake of breast milk · Encourage breastfeeding—baby may feed eight to 12 times per day[23] o Offer breastfeeding support[14,37] o Consider referral to lactation consultant o Offer expressed breast milk if extra fluids required o Routine supplementary feeds not recommended[14,37] even if having phototherapy o Refer to Queensland Clinical Guideline *Establishing breastfeeding*[46] o Ensure steps are in place to recognise clinically significant poor nutrition and hydration
Formula	· Encourage feeding to ensure adequate intake of formula[38]
Intravenous fluids	· Not routinely required · Administer according to baby's clinical examination[65] · Consider for babies receiving phototherapy with TSB levels near exchange transfusion level[23]
Probiotics	· Some small studies in term babies have identified they may reduce: o Hyperbilirubinaemia and o Duration of phototherapy[66,67]

6.3 Phototherapy

Contemporary phototherapy was discovered in England when the skin of babies having daily sunshine was seen to be less jaundiced than unexposed skin. It was also noticed that exposure of a blood tube with pre-exchange transfusion blood sample to sunlight resulted in a lower level of bilirubin than the unexposed sample.[18]

Table 12. Background

Aspect	Comment
Context[68]	· Rapid decrease in bilirubin exposed to daylight, sunlight and artificial light · Initial findings published in 1958 and supported by a randomised controlled trial in 1968[69] · 'Phototherapy' first coined in 1960 · Significant reduction in the number of exchange transfusions · Between 0.5-4% of babies require phototherapy · One of the most frequently used interventions in newborn care[70] · Treatment of choice for jaundiced newborn babies
Science	· Chemical reaction when bilirubin in skin absorbs light: o Converts bilirubin molecule to products that can bypass the liver's conjugating system · Generates yellow stereo-isomers of bilirubin (photo-isomerisation) that are less likely to cross the blood-brain barrier and can be excreted in bile or urine or produces colourless products of lower molecular weight (photo-oxidation)[71] · Unidirectional (conventional) phototherapy with blue-green light from above in a narrow emission spectrum of 430–490 nanometres (nm) is most effective[71,72] · Absorption peak of bilirubin is at 460 nm[72] · A linear dose response relationship shows a highly significant correlation between light irradiance and total SBR[72] · Clinical response of baby depends on: o Efficacy of the phototherapy unit o Balance between rate of bilirubin production and elimination[11]
Factors affecting phototherapy	· Irradiance of light: o Higher spectral irradiance results in more rapid decline in bilirubin o Different devices deliver significantly different levels of irradiance ▪ Standard treatment: 25–30 microwatts per square centimetre per manometer (microW/cm^2/nm) (430–490 nm) ▪ Intensive treatment: 30 microW/cm^2/nm or more (430–490 nm) o Spectral power increases as the amount of skin exposure increases[71] ▪ There is no evidence of a saturation point for phototherapy (i.e. an irradiation level above which there is no further decrease in TSB[72]) · Light source: o Use additional light source under baby for intensive phototherapy ▪ May be fibre-optic pad, light emitting diode (LED) mattress or bank of special blue lights · Distance: o Maximise irradiance by minimising the distance between the baby and the light source ▪ Usually 10–15 cm for term and near term babies ▪ For halogen or tungsten lights follow manufacturer's recommendations to avoid overheating or burning baby[11] · Treat preterm babies in incubator ensuring light rays are perpendicular to incubator surface to minimise light reflectance[71]

6.3.1 Phototherapy treatment

Table 13. Phototherapy treatment

Aspect	Comment
Indications	· Consider: o TSB level [refer to Appendix A Nomogram: Jaundice management] o Gestation of baby o Age in hours of baby at time of testing[11] o Individual neurotoxicity risk factors[11,18] [refer to Section 7.2 Bilirubin induced neurologic dysfunction] · If facility access to TSB result is delayed: o Test TSB when bilirubin level on TcB is 70% of the treatment line (based on the baby's gestational age, weight and age) o Commence phototherapy when the TcB plots on the treatment line for phototherapy for baby with risk factors o Review indication and need for phototherapy based on TSB when available o Cease phototherapy using clinical judgement considering suitable duration of phototherapy for underlying cause and severity of jaundice ▪ Continue TcB monitoring at intervals several hours after ceasing [refer to Table 15. Phototherapy care]
Contraindications	· Congenital erythropoietin porphyria (or family history)[71] o Very rare disorder o Porphyrins are photosensitisers causing injury to tissue (severe blistering and photosensitivity) when exposed to light[73]
Side effects/ complications	· Separation of mother and baby potentially resulting in: o Impaired parent-baby attachment o Breast feeding interruption ▪ Use fibreoptic or LED blanket or timed interruptions for breast feeding if jaundice is not severe o Baby and parent distress[18] · Small increased risk for seizures (approximately 1-2 infants per 10,000 treated)[48] · Babies with cholestatic jaundice and conjugated hyperbilirubinaemia receiving phototherapy may: o Develop dark grey-brown discoloration of the skin[8,71] ▪ Known as 'bronze baby syndrome' ▪ Gradually disappears after discontinuation of phototherapy ▪ Not a contraindication to phototherapy[71]–consider need for continued phototherapy when the conjugated bilirubin reaches between one third and one half of the total bilirubin o Develop damage to retina of exposed eyes[71] o Increase cutaneous blood flow (photorelaxation) and increase insensible water loss through skin[71,72] o Loose stools[23] o Develop purpura and bullous eruptions[8] o Transient rashes (usually of no clinical significance) · Blue light phototherapy—potential risk factor for melanocytic nevus development[74]
Precautions	· Medications: o Refer to Section 6 Medication use o Refer to an Australian pharmacopoeia for complete drug information regarding the use of medications and topical skin preparations during phototherapy o Concomitant use of photosensitising medications: ▪ Usually only of concern after exposure to light in ultraviolet-A(UV-A) (320–400 nm) or UV-B (290–302nm) ranges ▪ Insignificant UV-A and UV-B light produced by phototherapy[71] as plastic covers or optical filters remove potentially harmful ultraviolet light[11] · Do not use white lights painted blue or covered with blue plastic sheaths[11] · TcB unreliable during and after phototherapy[45]

6.3.2 Phototherapy lights

Table 14. Phototherapy lights

Aspect	Comment
Equipment	· Phototherapy light sources include: o Fluorescent tubes: ▪ Different colours—cool white daylight, blue, special blue, turquoise and green ▪ Different shapes—straight, spiral, U-shaped o Metal halide bulbs: ▪ Used in spotlights and incubator lights o LED or metal halide bulbs: ▪ Used with fibreoptic light guides in pads, blankets and spotlights o High intensity LEDs: ▪ Used over or under the body[11] · LEDs containing high-intensity gallium nitride with emission within 460–490 nm range: o Have longer lifetime o Lower heat output o Low infrared emission o No ultraviolet emission[11] · LEDs, fluorescent tubes and halogen light sources reduce TSB levels at similar rates in both term and preterm babies[75] o Generally fluorescent tubes are suitable for term babies and halogen for preterm o Fibreoptic lights may be used to complement or supplement (e.g. during feeding) other light sources · Follow manufacturer's recommendation regarding the lifetime estimate of the phototherapy lights[11] · Periodically check spectral irradiance of phototherapy[8] · Undertake electrical and fire hazard safety checks on phototherapy units to reduce risks in an environment with high humidity and oxygen[11]
Dose	· Effectiveness depends on phototherapy ability to convert bilirubin to isomers and oxidations products · Bilirubin absorbs visible light most strongly in blue region of spectrum[11] · Dose depends on: o Spectral wavelength of light o Spectral irradiance delivered to the baby's skin o Total spectral power (i.e. average spectral irradiance delivered across the surface area of the baby[71]) · Reduce the distance of the phototherapy lights from the baby as much as possible[72] following manufacturer's instructions o Visual estimations of brightness or use of photometric or colourmetric light meters are not appropriate[72] o LEDs can be positioned closer to the baby · Measure dose during phototherapy using radiometer[11,71] that measure in the 425–475 nm or 400–480 nm band wavelength o Make several measures in different locations on baby and average these ▪ Strength of phototherapy over the surface of the baby may vary and spectral irradiance may differ on different areas of the baby[71] o Achieve average irradiance reading over 80% of baby's body surface: ▪ Standard phototherapy: 25–30 microW/cm^2/nm ▪ Intensive phototherapy:30 microW/cm^2/nm [4,11] ▪ No additional efficacy after 35 microW/cm^2/nm [4] · Clinical effect of phototherapy evident within four to six hours of initiation[11] · Estimated decrease of SBR is 34 micromol/L[11] o Depends on: ▪ Rates of bilirubin production ▪ Enterohepatic circulation ▪ Bilirubin elimination ▪ Degree of bilirubin deposition in the tissues ▪ Rates of photochemical reactions of bilirubin

6.3.3 Care during phototherapy

Table 15. Phototherapy care

Aspect	Comment
Care	· If possible do not separate mother and baby during phototherapy · Nurse baby with only a nappy[11,71] o Use protective barrier creams on buttocks if baby has loose stools · Use eye protection o Lubricating eye drops may be indicated o Monitor for eye discharge and conjunctivitis · Provide continuous observation of baby · Monitor baby's temperature: o Risk of hyperthermia if halogen lights are used o Risk of hypothermia if unclothed baby nursed in bassinette/cot under LED or fluorescent lights where there is cool ambient temperature o Nurse preterm baby in incubator or under radiant warmer · Maintain normal oral feeds in term babies[71] · Clinically assess all babies hydration status[23]
Practice points	· Check spectral output of light source is within acceptable parameters · Check irradiance level is uniform over exposed surface of baby · Expose the maximum amount of baby's skin and avoid blocking light · Disrupt continuity of phototherapy for feeding, parental attachment and nursing care when there has been an adequate bilirubin decrease o Briefly disrupt phototherapy during eye care and blood collection if bilirubin levels have not reduced adequately · Re-check TSB during treatment to measure the rate of response in bilirubin load reduction · Discontinue phototherapy when TSB reduces below treatment threshold o Be aware of possible re-bound increase in TSB[56]
Ceasing phototherapy	· Criteria for discontinuing phototherapy depends on: o Age of baby when phototherapy initiated o Cause of hyperbilirubinaemia · Risk of rebound hyperbilirubinaemia depends on baby's gestation, age when phototherapy started and TSB relative to treatment thresholds when the phototherapy ceased[76] · If baby had haemolytic jaundice or other early onset jaundice and is discharged before 3–4 days organise follow up TSB 24 hours after discharge[8]

6.3.4 Phototherapy in the home

Some facilities provide the option for phototherapy in the home for babies with mild to moderate jaundice. Manage the baby's care and follow up according to local protocols.

Table 16. Home phototherapy

Aspect	Comment
Evidence	· Evidence base is increasing[77] · No current high-quality evidence to recommend or oppose home phototherapy in healthy term babies[77,78]
Criteria/inclusion	· Unconjugated hyperbilirubinaemia o TSB not greater than 50micromols/L above the treatment line o Conjugated bilirubin not greater than 10% of TSB · Baby is: o Feeding well o Greater than 24 hours of age o Greater than 37 weeks gestation o Birth weight greater than 2500 grams · Parents able to transport baby to pathology service for TSB or a home pathology collection service is available · Parental ability to follow written and verbal instructions
Exclusion	· Jaundice in first 24 hours of age · Poor feeding · Temperature instability · Lethargy · Alloimmune haemolytic disease · Asphyxia/acidosis · Infection · Abnormal liver function tests
Parent information	· Verbal instructions and written documentation on: o Temperature monitoring and management o Assessment of hydration ▪ Written feeding plan o Signs of increasing hyperbilirubinaemia o Manufacturer's instructions on use of phototherapy equipment · Equipment o Phototherapy unit o Phototherapy disposable covers o Eye covers o Digital thermometer · Observation chart o Phototherapy o Feeding/output o Temperature · Contact information for any concerns

6.4 Exchange transfusion

If the baby's TSB is at exchange transfusion level it is a medical emergency and requires urgent management. [8,30] The aim of an exchange transfusion is to rapidly reduce the TSB by removing small aliquots of blood from the baby and replacing it with donor blood components.[10] Phototherapy especially intensive for a high risk baby can decrease the need for an exchange transfusion.[11]

Table 17. Exchange transfusion

Aspect	Comment
Indications	· TSB continues to rise despite intense phototherapy[79] · Refer to nomogram appropriate for baby's gestation, weight and age [refer to Appendix A Nomogram: Jaundice management for baby greater than 38 weeks gestation · · Baby showing signs of acute bilirubin encephalopathy[79,80]
Context	· Perform in a Neonatal Intensive Care Unit following comprehensive local work instructions · Contact local retrieval services for: o Advice and discussion of management with neonatologist o Transfer or retrieval of the baby to a tertiary service
Exchange transfusion[23]	· Lowers TSB and may prevent unconjugated bilirubin crossing the blood-brain barrier · Removes RBC that are vulnerable to haemolysis from maternal antibodies and reduces total antibody level · Corrects anaemia if present · Use plasma that is[9]: o Type O RhD negative or for the baby with non-A, B or D antibodies, negative for the relevant antigen o CMV negative (if available) o Irradiated[4] · Exchange double the baby's blood volume (160 mL/kg)[4]
Risks	· Fluid overload · Infection · Thrombocytopenia · Metabolic imbalance o Hypoglycaemia o Hypocalcaemia o Hypokalaemia · Coagulopathy · Air embolism[4] · Thrombosis[23] · Necrotising enterocolitis[21,23]
Post exchange transfusion	· Continue intensive phototherapy · Measure TSB within 2 hours of exchange transfusion[10]

6.5 Supplementation

Babies who develop anaemia due to haemolysis may require supplementation of folic acid and iron. Folic acid aids in the maturation of RBC[81], babies who are low in folic acid are anaemic and fail to thrive.[81] Iron is critical for growth and CNS development[82] and iron deficiency is associated with impaired neurological and behavioural development.[83] However, iron supplementation is rarely required. Most babies with significant haemolysis recycle iron from their own red cells, so there may be a greater risk of iron overload than iron deficiency.

Discuss folic acid and ferrous sulfate supplementation with paediatrician or neonatologist before baby's discharge.

Table 18. Folic acid and ferrous sulphate

Aspect	Consideration
Folic acid*	· Does not reduce incidence or severity of anaemia in babies with a positive DAT[84] · Indicated for use in babies with anaemia caused by haemolytic disease where there has been an high red cell turnover · Dose: 50–100 micrograms/kg/day · Commence from 7 days of age · Adverse effects are rare but may include: o Rash o High temperature o Diarrhoea · May reduce phenytoin levels
Ferrous sulphate*	· Use with caution in any baby who has a haemolytic condition (endogenous iron stores may be high not low) o Well term babies usually have adequate iron stores for 4–6 months · Undertake iron studies before commencing treatment to confirm iron deficiency[85,86] and absence of iron overload · Dose: 4–6 mg/kg/day elemental iron (equivalent to 30 mg/kg/day ferrous sulphate) if treating diagnosed iron deficiency · Administration: o Best absorbed on empty stomach o Administer two hours apart from feeds and medications · Incompatibility o Milk–give between feeds if possible o Medications—proton pump inhibitors (e.g. omeprazole) reduce absorption and antacids (e.g. gaviscon) bind to ferrous sulphate inhibiting absorption · Adverse effects: o Gastric irritation o Constipation

*Refer to an Australian pharmacopoeia for complete drug information

7 Complications of unconjugated hyperbilirubinaemia

7.1 Acute and chronic bilirubin encephalopathy

In hyperbilirubinaemia unconjugated bilirubin is deposited in and stains the auditory pathways, basal ganglia and oculomotor nucleus, resulting in acute and then chronic bilirubin encephalopathy or kernicterus.[18] Kernicterus is seen on autopsy and is the yellow staining of the brain tissue due to the accumulation of unconjugated bilirubin. There is necrosis of neurons in the basal ganglia resulting in irreversible neuro-disabilities.[4,10,23,45,79] The Australian incidence of extreme hyperbilirubinaemia is 9.4/100 000 live births.[45]

7.1.1 Acute bilirubin encephalopathy

Table 19. Acute bilirubin encephalopathy

Aspect	Comment
Context	· Occurs in the first days of life and causes a temporary alteration in neurologic state[79,80] · Early treatment of hyperbilirubinaemia reduces poor neurological outcomes[4]
Risk factors[79]	· ABO incompatibility · RhD isoimmunisation · G6PD deficiency · Prematurity · Infection · Exclusively breastfeeding
Signs	· Initially subtle and non-specific[79,80]: o Poor feeding o High pitched cry o High temperature o Lethargy · Increase in severity as bilirubin levels increase · Subsequently progressive disturbance in neurobehaviour[80]–hypertonia, retrocollis, opisthotonus
Disease progression	· May lead to: o Athetoid cerebral palsy o Deafness o Blindness due to paralysis of ocular muscles[79]
Preterm babies	· Recognition of signs may be challenging[79,80]: o Apnoea and oxygen desaturations may be the only sign[80] · Higher risk due to immature central nervous system (CNS) and neuronal pathways

7.1.2 Chronic bilirubin encephalopathy

Table 20. Chronic bilirubin encephalopathy

Aspect	Comment
Context	· Permanent sequel of bilirubin toxicity · Becomes evident in the first year of life[80] · History of severe and prolonged hyperbilirubinaemia[79,80]
Risk factors include[23]	· Prematurity · Infection · Asphyxia
Common signs[79,80]	· Athetoid cerebral palsy · Gaze paralysis · Hearing loss
Magnetic resonance imaging	· Damage to basal ganglia, central and peripheral auditory pathways, hippocampus, subthalamic nuclei or midbrain[79,80] and globus pallidus[87] · Cerebral cortex mostly undamaged[23]
Sensorineural hearing loss (SNHL)[88]	· History of extremely high TSB levels (greater or equal to 450 micromol/L) increase the risk · Timely exchange transfusion may reduce risk[88]

7.2 Bilirubin induced neurologic dysfunction

Bilirubin induced neurologic dysfunction (BIND) is a syndrome of subtle bilirubin neurotoxic disorders that can occur in the absence of kernicterus.[56,89] BIND is diagnosed on clinical manifestations in infancy and early childhood together with a history of neonatal hyperbilirubinaemia.[56] The incidence of BIND is unknown.[90]

Table 21. Bilirubin induced neurologic dysfunction

Aspect	Comment
Context	· Based on clinical observation as there are no specific biomarkers[56] · Severe and irreversible[56] · No defined dose-dependent association between moderate or extreme hyperbilirubinemia and neurologic outcomes[56] · History of bilirubin levels lower than those associated with acute and chronic bilirubin encephalopathy[89] o May result from prolonged jaundice with moderate hyperbilirubinaemia below treatment threshold[56]
Risk factors	· Prematurity[56] · Duration and level of serum unconjugated bilirubin[89] · Capacity of bilirubin to bind to albumin[79] · Individual vulnerability of CNS making bilirubin toxicity inherent in each baby[56]
Clinical manifestations	· Clinical signs not completely categorised in term and preterm babies[79] · Neuromotor signs[56] o Muscle tone abnormalities o Hyperexcitable neonatal reflexes · Speech and language difficulties · Central processing abnormalities o SNHL o Visuomotor dysfunction

7.3 Bilirubin-induced auditory toxicity

The risk of bilirubin induced auditory toxicity resulting in hearing loss is increased in babies who have had unbound unconjugated hyperbilirubinaemia.[91]

Table 22. Auditory toxicity

Aspect	Comment
Context	· Relationship between TSB and sensoneural hearing loss (SNHL)[91] · Non-linear–there is a probable threshold effect · Likely to be influenced by causes other than TSB e.g. bilirubin binding, prematurity · Maximum TSB level alone is not indicative of bilirubin-induced auditory toxicity
Hearing assessment	· Screen babies according to local protocols usually after completion of phototherapy · Evaluate auditory brainstem-evoked response (ABR) to identify bilirubin toxicity in babies who have had significant hyperbilirubinaemia · Elevated ABR thresholds may indicate SNHL[91] due to hyperbilirubinaemia or other cause

8 Other treatments

8.1 Treatments of no benefit

There are treatments which do not reduce neonatal hyperbilirubinaemia. For these, is no evidence of benefit and but possible harm to the baby.

Table 23. Treatments of no benefit

Aspect	Comment
Intravenous immunoglobulin (IVIg)[9,92-94]	· Fractionated blood product · Early studies (at high risk of bias) suggest benefits · Two more recent high quality studies found that when used with intensive phototherapy in high risk (RhD haemolytic disease) babies administration of IVIg did not reduce the incidence of exchange transfusion[95,96] · Possible risks of harm include transfusion-related lung injury and necrotising enterocolitis
Medications	· Laxatives to assist passing of meconium includes[97]: o Agar[8,10] o Manna[98] o Glycerine[8,10] · Oral zinc to reduce hyperbilirubinaemia or need for phototherapy[99] · Antenatal phenobarbital in red cell isoimmunised pregnant women[100] · Activated charcoal[10] · Metalloporphyrin[23]: o Inhibits haem oxygenase and production of bilirubin o Treatment of unconjugated hyperbilirubinaemia with a metalloporphyrin is experimental[10] o Not approved in many countries[10,101]
Other therapies	· Acupuncture · Homeopathy · Traditional Chinese medicine[10]

8.2 Emerging research

The following topics have been identified as emerging research but are not recommended or suggested for treatment or prevention of jaundice outside research studies.

Table 24. Emerging research

Aspect	Comment
Prophylactic phototherapy[102]	· Lowers serum bilirubin · May have an effect on the rate of exchange transfusion o Note: Commence phototherapy early in babies with significant alloimmune haemolytic disease (e.g. RhD), without waiting for postnatal TSB especially if an intrauterine transfusion was not given
Medications	· Albumin infusion o Benefits unknown[101] · Vitamin D supplementation[103] o Low levels of vitamin D may be associated with neonatal jaundice · Ursodiol[23]: o Hydrophobic bile salt o Decreases cholesterol production and then dissolves it in bile o Unknown risks and benefits · Clofibrate[23,104] o A fibric acid derivative o Improves activity of glucuronyl transferase o Increases the conjugation of unconjugated bilirubin in the liver o Insufficient data to make recommendations for use in combination with phototherapy o More studies are required to verify safety and long-term neurodevelopmental outcomes
Filtered sunlight[38]	· One non-inferiority randomised controlled trial: o Canopies filtered out greater than 99% of UV-A light, almost all of the UV-B and C light and some infrared radiation (heat) o Canopies permitted transit of 400 to 520 nm of therapeutic blue light o All babies in the trial: ▪ Were 35 weeks gestation or more ▪ Up to 14 days of age ▪ Weighed more than 2200 grams ▪ Had mild-to-moderate hyperbilirubinaemia o Phototherapy with filtered sunlight was non-inferior in efficacy compared to conventional phototherapy · Not recommended for treatment or prevention of neonatal jaundice in Queensland

9 Discharge planning

Table 25. Parent information

Aspect	Good practice point
Predischarge	· Identify baby at risk of jaundice [refer to Section 2 Risk factors for clinically significant hyperbilirubinaemia] · Assess for jaundice prior to discharge especially if less than 72 hours of age · Review babies who are discharged before 72 hours of age within two days following discharge[18] o Consider pre-discharge measurement of TcB if early follow up not likely to occur
Parent information[10,18,64]	· Provide all parents with both written and verbal information o Refer to QCG parent information regarding normal stools, jaundice, breastfeeding · Advise healthcare professional review is required if: o Jaundice ▪ Less than 24 hours of age requires urgent medical review ▪ Any time in the first week of life ▪ Visible after 12 days (requires investigation) ▪ Increasing since last healthcare professional review o Feeding ▪ Poor ▪ Vomiting ▪ Baby losing weight ▪ Refer to Queensland Clinical Guideline *Establishing breastfeeding*[46] o Output ▪ Fewer than six wet nappies per day ▪ Pale stools ▪ Dark urine
Follow up	· Home visiting midwife · General practitioner · Child health services · Paediatrician/neonatologist if baby treated for extreme hyperbilirubinaemia or exchange transfusion · If baby re-presents with jaundice after discharge o Refer to Section 4 Clinical assessment and investigation and Section 6 Management o Also refer to: ▪ Queensland Clinical Guideline *Newborn assessment*[105] ▪ Queensland Clinical Guideline *Establishing breastfeeding*[46]

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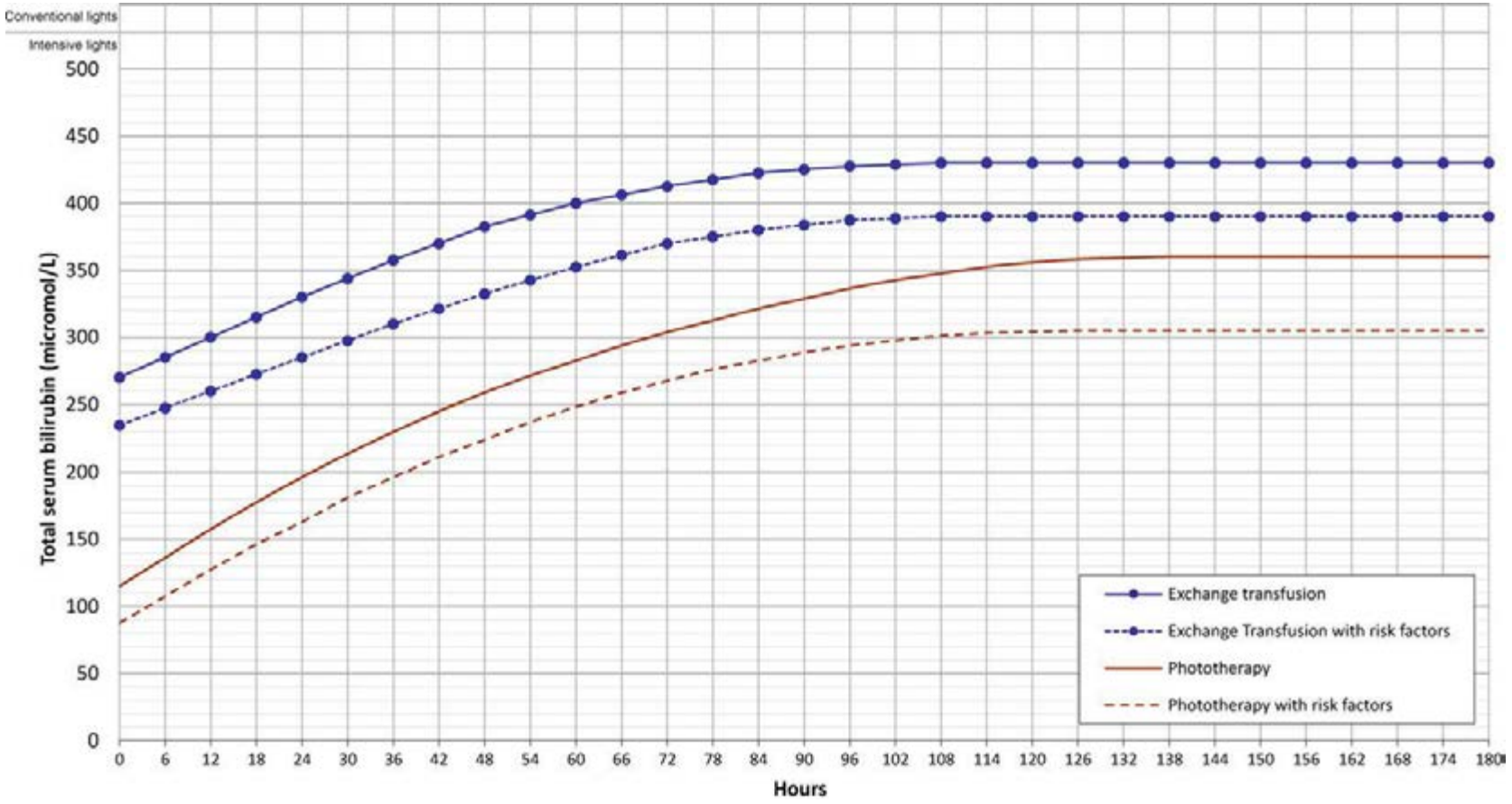
Appendix A Nomogram: Jaundice management for baby greater than 38 weeks gestation

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



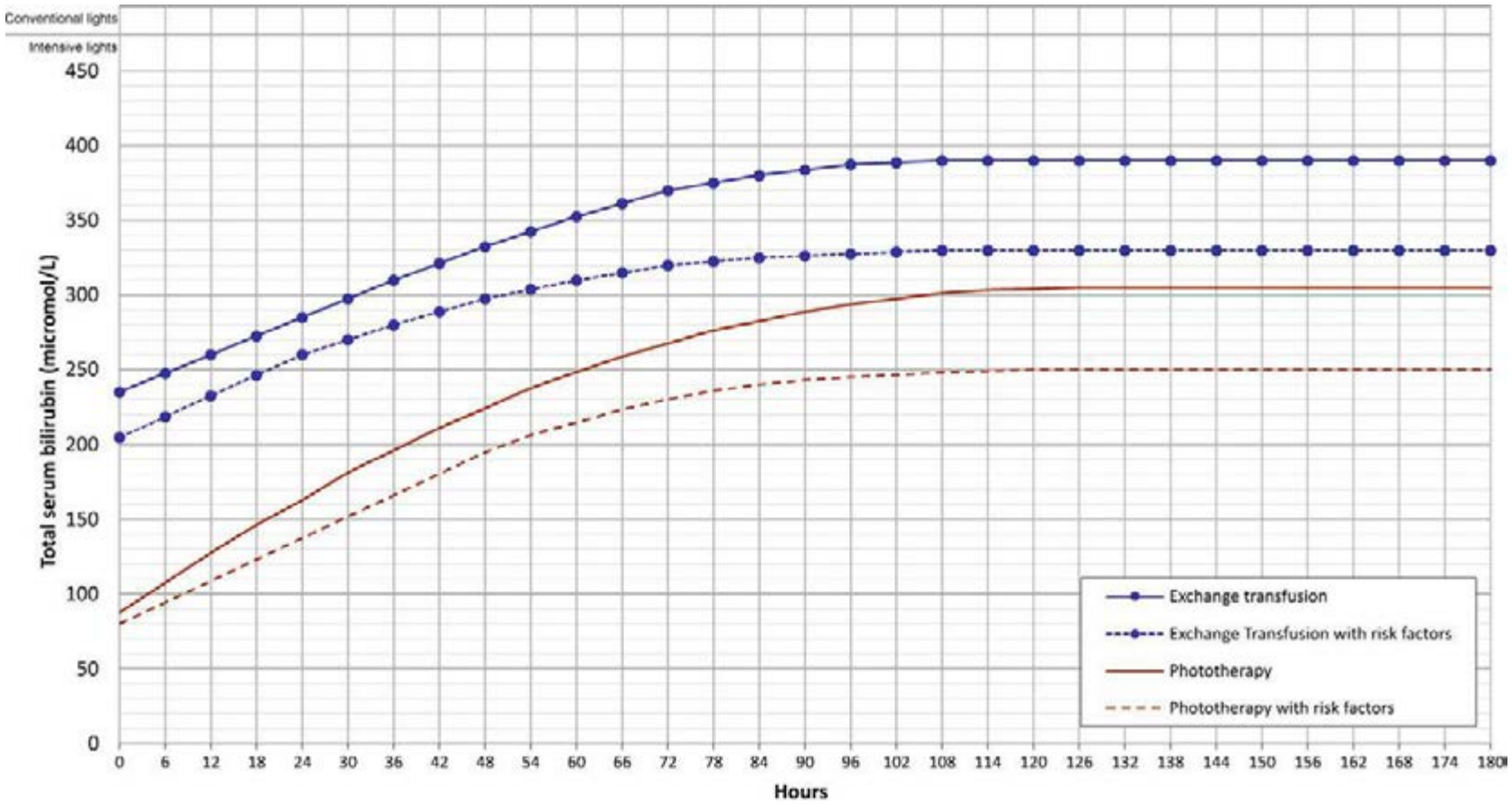
Date and time	Total Serum Bilirubin

Baby greater than 38 weeks gestation

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

Appendix B Nomogram: Jaundice management for baby 35+0 to 37+6 weeks gestation

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



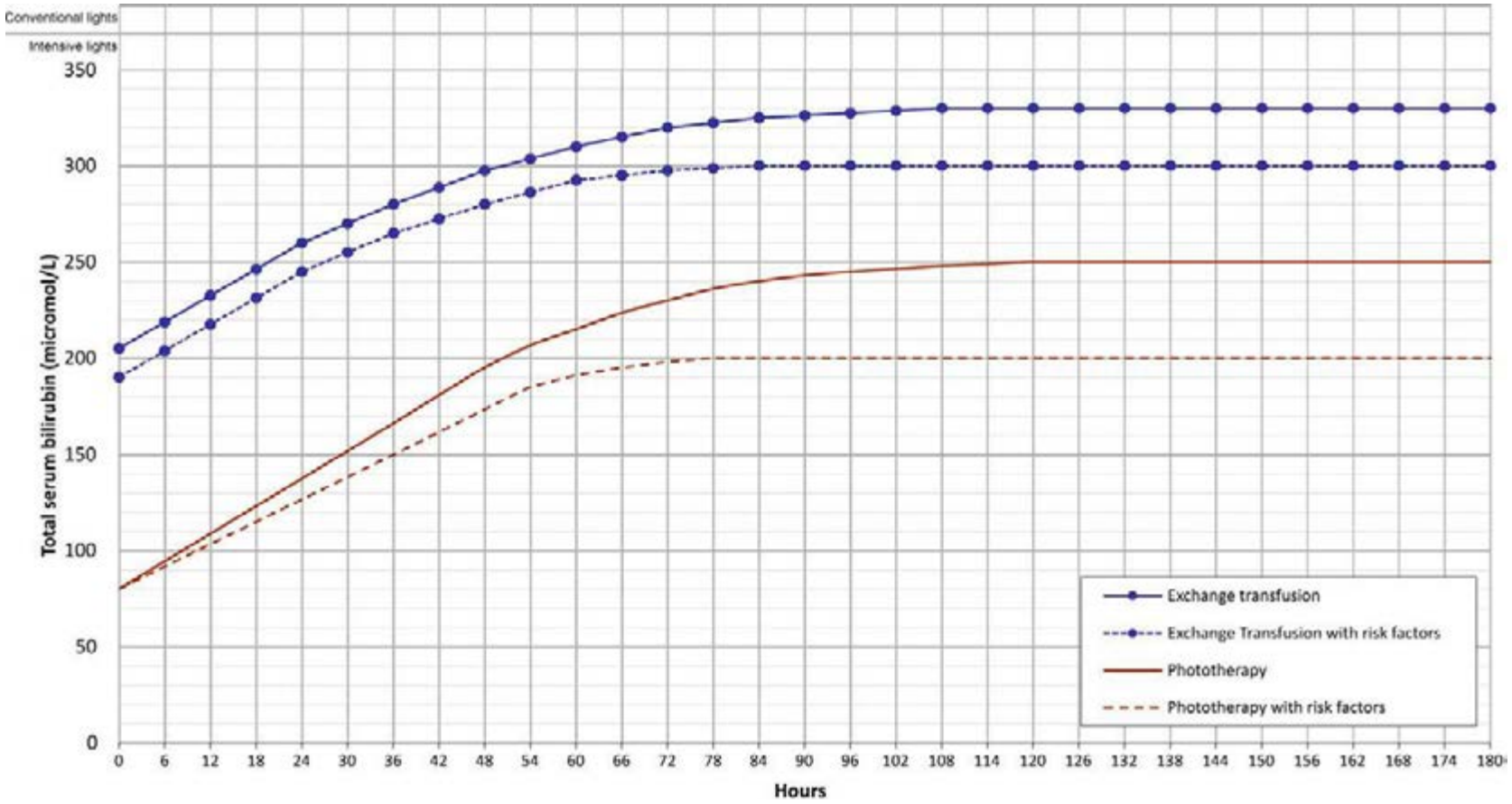
Date and time	Total Serum Bilirubin

Baby 35+0 to 37+6 weeks gestation

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

Appendix C Nomogram: Jaundice management for baby less than 35 weeks gestation, greater than 1999 g birth weight

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



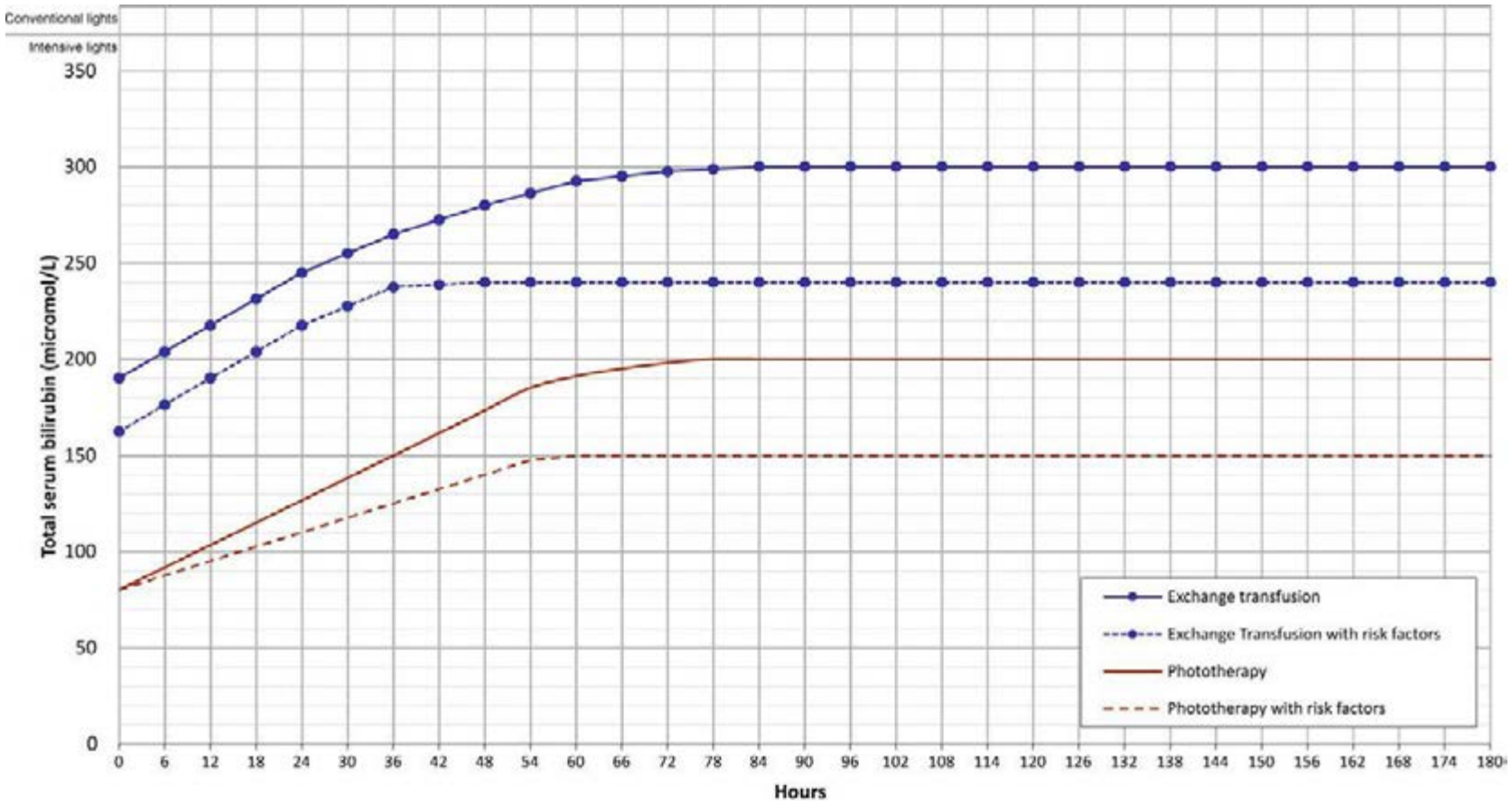
Date and time	Total Serum Bilirubin

Baby less than 35 weeks gestation, greater than 1999 g birth weight

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

Appendix D Nomogram: Jaundice management for baby less than 35 weeks gestation, 1500 g to 1999 g birth weight

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



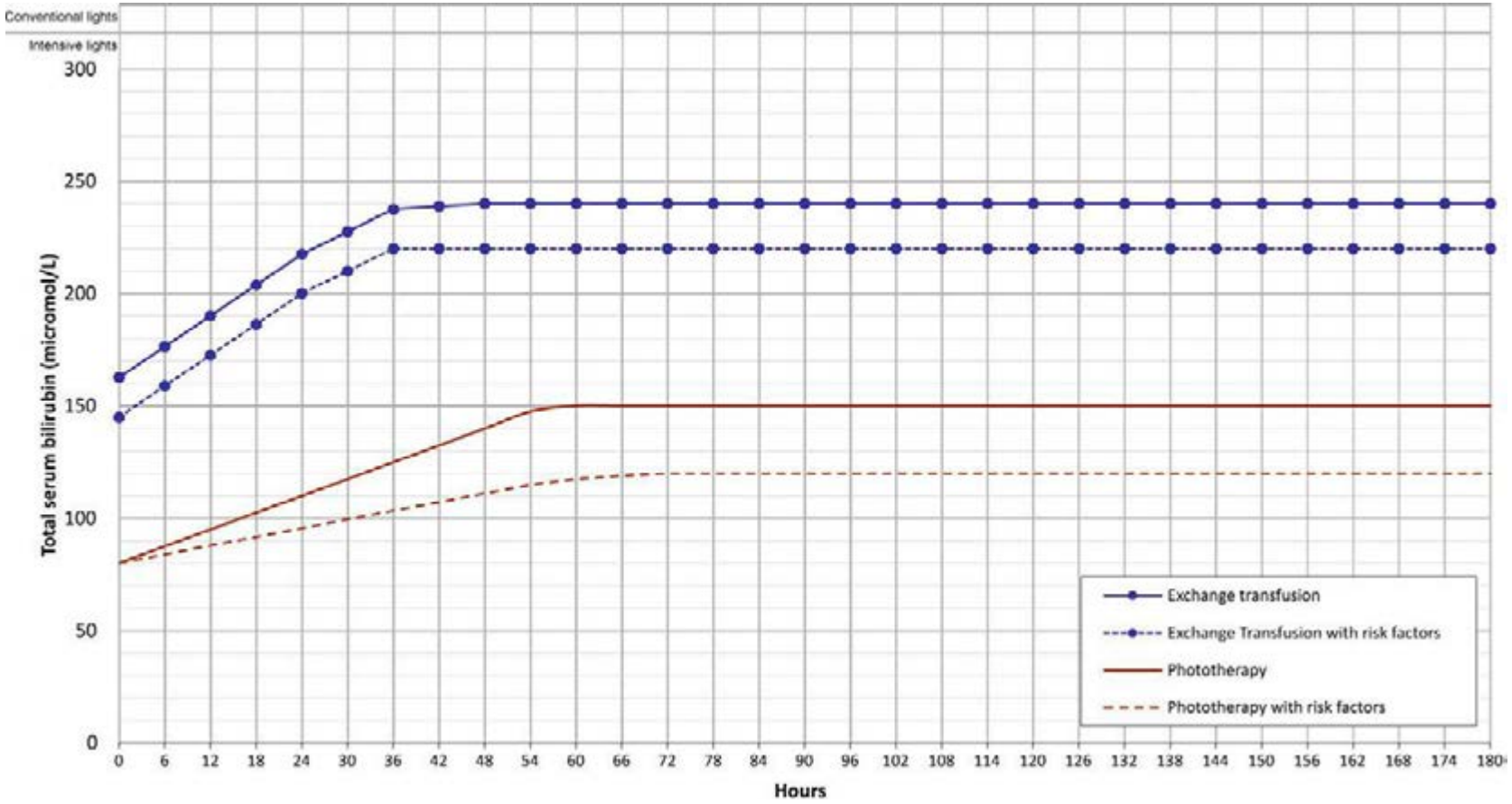
Date and time	Total Serum Bilirubin

Baby less than 35 weeks gestation, 1500 g to 1999 g birth weight

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

Appendix E Nomogram: Jaundice management for baby less than 35 weeks gestation 1000 g to 1499 g birth weight

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



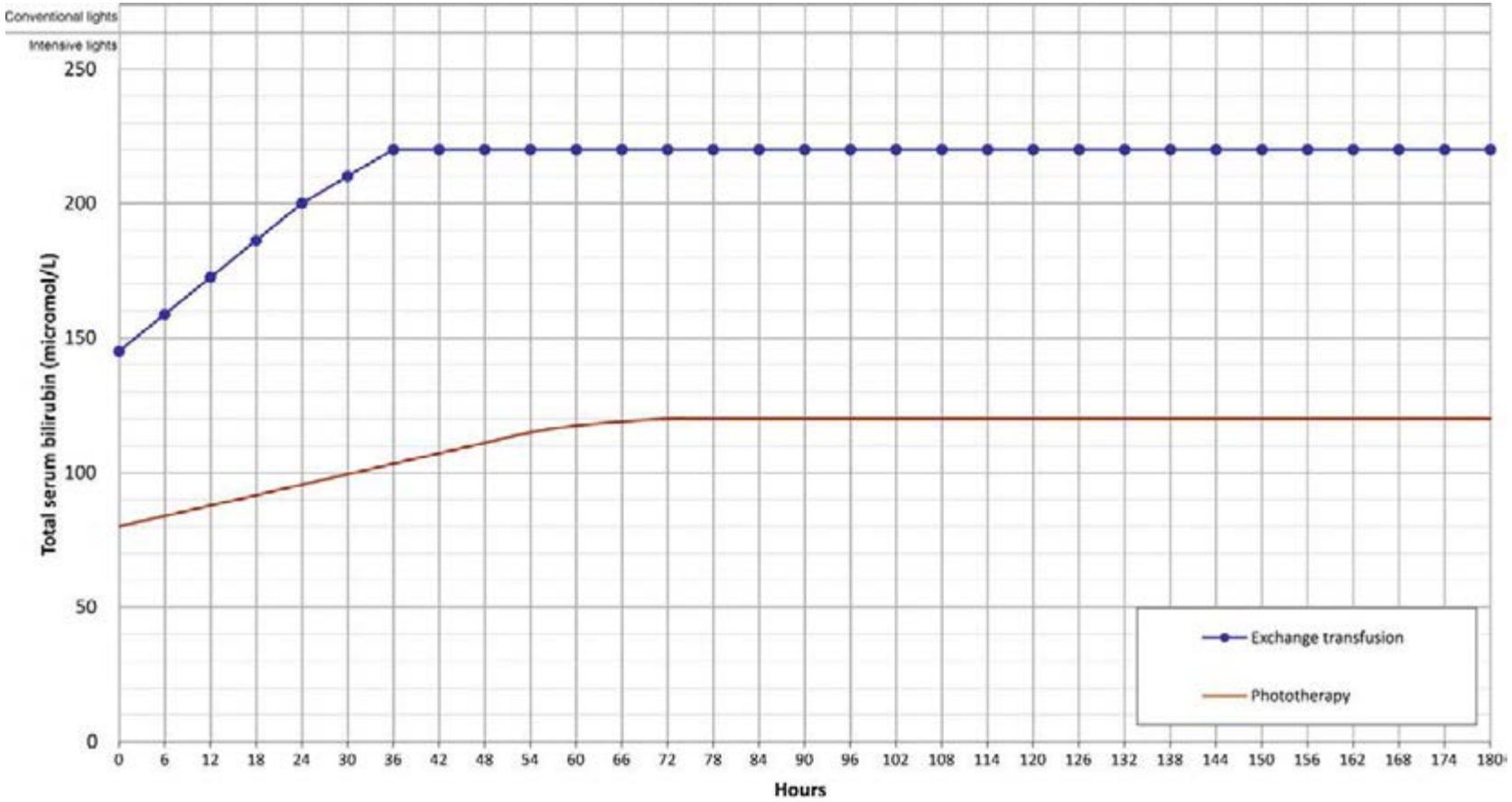
Date and time	Total Serum Bilirubin

Baby less than 35 weeks gestation, 1000 g to 1499 g birth weight

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

Appendix F Nomogram: Jaundice management for baby less than 35 weeks gestation less than 1000g birth weight

1. In the presence of risk factors (sepsis, haemolysis, acidosis or asphyxia) use the lower line.
2. If baby is greater than 12 hours old with total serum bilirubin (TSB) 1–50 micromol/L below the line, repeat the TSB within 6–24 hours.
3. Babies under phototherapy:
    a. Consider measuring the TSB 4–6 hourly until the rise of serum bilirubin is known to be controlled, then measure TSB 12–24 hourly.
    b. Stop phototherapy if the TSB is greater than 50 micromol/L below line and recheck in 12–24 hours.
4. If baby presents with TSB above threshold and the TSB is not expected to be below the threshold after 6 hours of intensive phototherapy, an exchange transfusion is indicated.
5. If there are signs of bilirubin encephalopathy an immediate exchange transfusion is recommended.



Date and time	Total Serum Bilirubin

Baby less than 35 weeks gestation, less than 1000 g birth weight

Adapted from: American Academy Pediatrics American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004; 114:297–316; Maisels M, Bhutani V, Bogen D, Newman T, Stark A, Watchko J. Hyperbilirubinemia in the newborn infant ≥35 weeks' gestation: An update with clarifications. Pediatrics. 2009; 124(4):1193–1198; Horn A, Kirsten G, Kroon S, Henning P, Moller G, Pieper C, et al. Phototherapy and exchange transfusion for neonatal hyperbilirubinaemia: neonatal academic hospitals' consensus guidelines for South African hospitals and primary care facilities. South African Medical Journal. 2006; 96(9):819–24; Morris BH, Oh W, Tyson JE, Stevenson DK, Phelps DL, O'Shea T et al. Aggressive vs conservative phototherapy for infants with extremely low birth weight.
New England Journal of Medicine. 2008;359(18):1885–96.

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