

Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Neonatal jaundice

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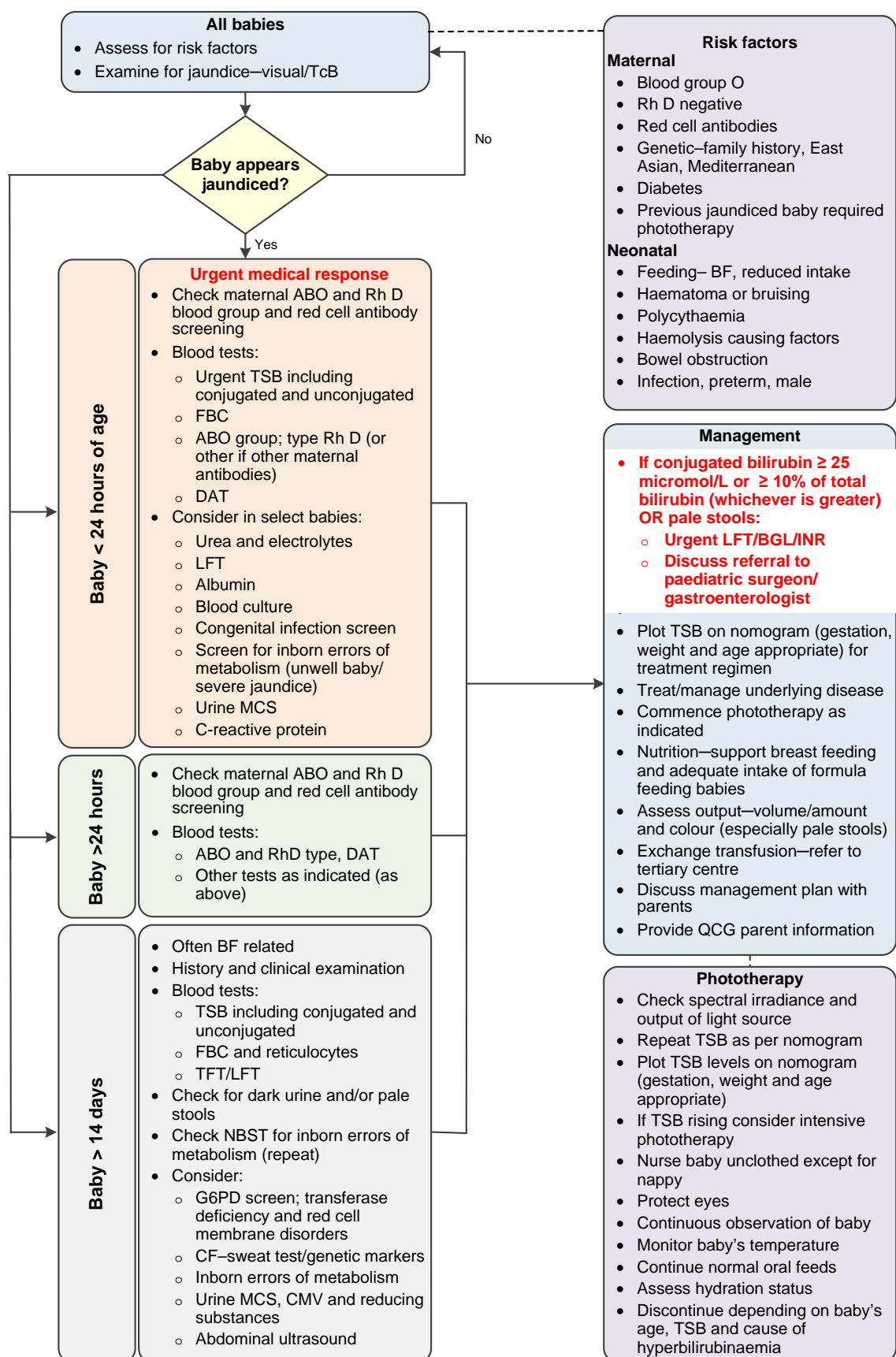
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Flowchart: Management of neonatal jaundice



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; NBST newborn bloodspot screening test; Rh rhesus; TcB transcutaneous bilirubin; TFT thyroid function tests; TSB total serum bilirubin; USS ultrasound scan; < less than; \geq equal to or 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
HDN	Haemolytic disease of the newborn
INR	International normalised units
IVIg	Intravenous immunoglobulin
LED	Light emitting diode
LFT	Liver function tests
NBST	Newborn bloodspot screening test
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 alloimmune disorders. ¹ Levels greater than 25 micromol/L (or equal to, or greater than 10%) direct bilirubin of total bilirubin level may indicate the need for further investigations ^{4,6}
Coombs test	Also known as a direct antiglobulin test. See Direct Antiglobulin Test (DAT).
Direct Antiglobulin Test	An agglutination test that detects the presence of antibodies that are bound to red blood cells cause haemolysis. Historically known as a Coombs test. ⁷
Extreme hyperbilirubinaemia	Total serum bilirubin (TSB) approaching exchange transfusion range. ⁸
Haemolysis	Destruction of red blood cells in the blood stream. ^{8,9}
Haemolytic disease of the newborn (HDN)	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. ¹⁰
Hyperbilirubinaemia	Increased level of bilirubin in the blood. ¹¹
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 with maximum body surface exposure ¹²
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. ¹³
Opisthotonus	Severe hyperextension causing backward arching of the head, neck, and spine. ¹⁴
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. ¹⁴
Sensorineural hearing loss	Acquired permanent hearing loss caused by damage to the cochlear nuclei and central auditory pathways. ¹⁵
Severe/significant hyperbilirubinaemia	Hyperbilirubinaemia requiring phototherapy and/or further treatment. ^{6,16}
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. ¹²
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 . ^{4,12}
Total serum bilirubin	The sum value of conjugated and unconjugated bilirubin. ¹⁷ May also be referred to as serum bilirubin (SBR).
Unconjugated hyperbilirubinaemia	Increased levels of unconjugated (lipid soluble) bilirubin usually caused by haemolysis, immature liver or sepsis. ⁴
Woman/women	In QCG documents, the terms woman and women include people who do not identify as women but who are pregnant or have given birth.

1 Introduction

Neonatal hyperbilirubinaemia (jaundice) is a common condition requiring medical attention in newborn babies.¹⁸ Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life.¹¹

In 2020 3.6% of all babies born in Queensland had jaundice requiring phototherapy. Early recognition and appropriate treatment is required¹⁹ to prevent bilirubin encephalopathy and severe neurodisability.¹¹

1.1 Aetiology

Table 1. Aetiology

Aspect	Consideration
Physiology	<ul style="list-style-type: none"> Hyperbilirubinaemia (jaundice) occurs when there is an imbalance between bilirubin production, conjugation and elimination The breakdown of red blood cells (RBC) and haemoglobin^{4,20} cause unconjugated bilirubin to accumulate in the blood¹¹ Unconjugated bilirubin binds to albumin and is transported to the liver where it is converted to conjugated bilirubin Conjugated bilirubin is water soluble and eliminated via urine and faeces²¹ Unbound unconjugated bilirubin is lipid soluble and can cross the blood-brain barrier⁴
Appearance	<ul style="list-style-type: none"> The baby presents with a yellowish appearance resulting from the accumulation of bilirubin in the skin, mucous membranes and conjunctiva or sclera¹¹ <ul style="list-style-type: none"> Is a sign of elevated levels of bilirubin in the blood⁴
Onset by type	<ul style="list-style-type: none"> Pathological: <ul style="list-style-type: none"> Early onset mostly occurring within 24 hours of age Requires urgent and immediate investigation and treatment Refer to Section 3.1 Causes of pathological jaundice Physiological: <ul style="list-style-type: none"> Mild unconjugated hyperbilirubinaemia²² Occurs after 24 hours of age Is transient¹⁹ Mostly benign⁴ Refer to Section 3.2 Causes of physiological jaundice Prolonged: <ul style="list-style-type: none"> Begins or persists after day 14 in term babies and day 21 in preterm babies²⁵ Is more common in breastfed babies Refer to Section 3.3 Causes of prolonged jaundice
Clinical significance	<ul style="list-style-type: none"> Jaundice at high peak level can cause brain damage Underlying aetiology can be associated with a variety of diseases <ul style="list-style-type: none"> May be serious or life threatening Investigate (and if indicated initiate treatment) if: <ul style="list-style-type: none"> Early onset with a high peak level²¹ Elevated conjugated bilirubin component²⁰ Persists after the normal time for jaundice to resolve⁴ Present in a baby with other clinical illness or abnormalities

2 Risk factors

2.1 Maternal risk factors

Table 2. Maternal risk factors

Aspect	Consideration
Blood group	<ul style="list-style-type: none"> Blood group O Rh D negative Red cell antibodies—D,C,c,E,e and K and certain others²³
Previous baby with jaundice²⁰	<ul style="list-style-type: none"> Required phototherapy or other treatment
Diabetes²⁰	<ul style="list-style-type: none"> High red cell mass in baby where there is poorly controlled maternal diabetes (any type)
Genetic²⁴	<ul style="list-style-type: none"> East Asian²⁰ Mediterranean^{25,26} Family history of inherited haemolytic disorders (e.g. G6PD deficiency, hereditary spherocytosis)²⁰
Lifestyle	<ul style="list-style-type: none"> Smoking

2.2 Neonatal risk factors

Table 3. Neonatal risk factors

Aspect	Consideration
Feeding	<ul style="list-style-type: none"> Breast milk: <ul style="list-style-type: none"> β glucuronidase in breast milk increases the breakdown of conjugated bilirubin to unconjugated bilirubin in the gut⁴ Lipoprotein lipase and nonesterified fatty acids in breast milk may inhibit normal bilirubin metabolism^{27,28} Factors that delay normal colonisation with gut bacteria resulting in high concentration of bilirubin in the gut Low breastmilk supply (may be due to delayed milk production) or formula intake leading to dehydration and increased enterohepatic circulation^{4,29} thus resulting in increased concentration of bilirubin²⁴ Prolonged parenteral nutrition
Haematological^{18,20}	<ul style="list-style-type: none"> Factors causing haemolysis (immune or non-immune)⁴ Polycythaemia Haematoma or bruising Hyperbilirubinaemia accompanied by anaemia
Gastrointestinal³⁰	<ul style="list-style-type: none"> Bowel obstruction
Other^{4,20,24}	<ul style="list-style-type: none"> Infection Prematurity—hyperbilirubinaemia more prevalent than in term babies due to the immaturity of RBC, liver, and gastrointestinal tracts³¹ Male Severe fetal growth restriction (FGR) Delayed cord clamping²⁰ <ul style="list-style-type: none"> The benefits of delayed cord clamping (e.g. reduced risk of iron deficiency at 3–6 months of age) outweigh the perceived risks, including jaundice¹⁰ Certain medications (e.g. ceftriaxone)

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.

Regardless of the underlying cause, 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 woman or baby [refer to 6.1 Medication use]

3.1 Causes of pathological jaundice

The early onset of jaundice is a risk factor for severe hyperbilirubinaemia requiring immediate treatment.²⁴ 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.^{4,17} When jaundice has a high peak level regardless of the cause, treatment is required to prevent brain damage.

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. Causes of pathological jaundice

Aspect	Common causes	Less common causes
Haemolysis	<ul style="list-style-type: none"> • Blood extravasation <ul style="list-style-type: none"> ◦ Bruising/birth trauma • Haemorrhage (e.g. cerebral, pulmonary, intra-abdominal) • Isoimmunisation^{4,18}: <ul style="list-style-type: none"> ◦ ABO (low risk) or Rh D (high risk) alloantibodies ◦ Other blood group alloantibodies—Kell and Rh C and E are the most common¹³ 	<ul style="list-style-type: none"> • RBC enzyme defects: <ul style="list-style-type: none"> ◦ G6PD deficiency ◦ Pyruvate kinase deficiency²⁰ • Hereditary RBC membrane abnormalities: <ul style="list-style-type: none"> ◦ Spherocytosis ◦ Elliptocytosis • Haemoglobinopathies <ul style="list-style-type: none"> ◦ Alpha thalassaemia • Infection
Decreased conjugation of bilirubin in the liver^{28,32,31}	<ul style="list-style-type: none"> • Gilbert Syndrome (glucuronyl transferase deficiency disorder) • Congenital hypothyroidism 	<ul style="list-style-type: none"> • Other glucuronyl transferase deficiency disorders <ul style="list-style-type: none"> ◦ Crigler-Najjar Syndrome³³ ◦ Transient familial neonatal hyperbilirubinaemia/Lucey-Driscoll syndrome (may be severe) • Congenital hypopituitarism
Decreased excretion of bilirubin^{4,20,27}	<ul style="list-style-type: none"> • Abnormal biliary ducts (e.g. intrahepatic biliary atresia or extrahepatic biliary stenosis or atresia) • Cystic fibrosis 	<ul style="list-style-type: none"> • Conditions causing abnormal biliary ducts, (e.g. Alagille Syndrome, choledochal cyst) • Increased enterohepatic bilirubin recirculation <ul style="list-style-type: none"> ◦ Bowel obstruction, pyloric stenosis • Meconium ileus or plug, cystic fibrosis
Liver cell damage (may cause combination of decreased bilirubin uptake, conjugation and/or excretion)	<ul style="list-style-type: none"> • Congenital infections: <ul style="list-style-type: none"> ◦ <i>Cytomegalovirus</i> (CMV), ◦ <i>Herpes simplex virus</i> (HSV) ◦ Toxoplasmosis, rubella, syphilis, <i>varicella zoster</i>, parvovirus B19 causing hepatitis • Inborn errors of metabolism (e.g. urea cycle defects, galactosaemia, fatty acid oxidation defects) 	

3.2 Causes of physiological jaundice

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}

Table 5. Causes of physiological jaundice

Aspect	Consideration
Context	<ul style="list-style-type: none"> Physiological jaundice is transient, mild unconjugated hyperbilirubinaemia³⁴ More common in first born babies³⁵ Mostly benign³⁶
Causes	<ul style="list-style-type: none"> 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^{20,37} Normal population variation in maturation of bile metabolism after birth More common in breastfed baby where there is inadequate milk intake³⁴ If baby unwell, has risk factors for underlying disorder or has a TSB above the treatment line, consider pathological causes
Characteristics	<ul style="list-style-type: none"> Usually first seen on day two of life²² Peaks on day three in term babies and days five to six in preterm babies³⁸ Usually resolves in the first week to 10 days of life in a term baby or within three weeks in a preterm baby
Management	<ul style="list-style-type: none"> Usually does not require treatment³⁹ Reassure the parents and monitor the baby³⁷ Investigate unwell jaundiced baby for underlying disease Treat any pathological cause if identified

3.3 Causes of prolonged jaundice

Present in 15–40% of well, breastfed babies at 2 weeks of age, and 9% of well, breastfed babies at 4 weeks of age.²⁵ Prolonged jaundice is usually harmless but can be an indication of serious disease such as biliary atresia or serious liver disease.⁶

Table 6. Prolonged jaundice

Aspect	Common causes	Less common causes
Unconjugated hyperbilirubinaemia	<ul style="list-style-type: none"> Inadequate nutrition and hydration more common in exclusively breastfeeding baby (e.g. breastmilk jaundice^{4,26,40}) <ul style="list-style-type: none"> Commonly presents between days four and seven with a peak at two to three weeks of age, and resolves by three months of age³⁴ 	<ul style="list-style-type: none"> Infection G6PD deficiency Spherocytosis Pyloric stenosis^{4,26,27} Inherited disorders (e.g. Gilbert's Syndrome³³) Congenital hypothyroidism
Conjugated hyperbilirubinaemia		<ul style="list-style-type: none"> Biliary atresia⁴ Idiopathic neonatal cholestasis^{1,4,41,42} Inherited disorders (e.g. Alagille Syndrome) Congenital hypopituitarism Congenital CMV
Unconjugated and/or conjugated hyperbilirubinaemia	<ul style="list-style-type: none"> Congenital hypothyroidism³⁷ Haemolysis⁴³ <ul style="list-style-type: none"> Rh D or other haemolytic disease Usually unconjugated initially then conjugated bilirubin levels rise G6PD deficiency⁴⁴ <ul style="list-style-type: none"> Can cause episodic or prolonged jaundice depending on oxidant exposure 	<ul style="list-style-type: none"> Infection Metabolic disorders Congenital hypopituitarism²⁷ Parenteral nutrition Inborn errors of metabolism⁴

4 Clinical assessment

Early identification of risk factors and repeated visual assessment is required to prevent severe consequences and to diagnose underlying causes.^{20,27} In babies with significant risk factors (e.g. unwell babies, preterm babies, babies at risk for haemolytic conditions), screen using transcutaneous bilirubinometry (TcB) and/or TSB.

Table 7. Clinical assessment

Aspect	Consideration
Visual assessment	<ul style="list-style-type: none"> Examine all babies for jaundice:²⁰ <ul style="list-style-type: none"> Every 8–12 hours in the first 72 hours of life Prior to discharge [refer to Section 8 Discharge planning] Do not rely on visual examination alone^{18,45} as can lead to errors in babies who^{18,20,45}: <ul style="list-style-type: none"> Have darker skin tones^{18,20,45} Are receiving phototherapy Jaundice appears cephalocaudal and regresses in the reverse order¹⁸ There is poor correlation of TSB and visual assessment even¹⁸: <ul style="list-style-type: none"> In natural light or a well-lit room If blanching the skin with a finger¹⁸ Visual estimation of bilirubin levels
Potential signs of bilirubin encephalopathy^{27,37,46,47}	<ul style="list-style-type: none"> Lethargy Poor feeding Vomiting High pitched cry Hypotonia followed by hypertonia Opisthotonus Seizure
Feeding⁴	<ul style="list-style-type: none"> Refer to Table 13. Nutritional considerations Refer to Queensland Clinical Guideline <i>Establishing breastfeeding</i>⁴⁸
Weight	<ul style="list-style-type: none"> Assess weight in first week of life^{4,49,50} <ul style="list-style-type: none"> Loss of 10% of birth weight is acceptable in first week of life Usually return to birth weight by 7–10 days of life The percentage of weight loss on day three may be predictive of significant hyperbilirubinaemia⁵⁰ (low level evidence)
Urine	<ul style="list-style-type: none"> Four or more wet nappies per day by 72 hours of age indicates adequate milk intake⁵⁰ <ul style="list-style-type: none"> Refer to Queensland Clinical Guideline <i>Establishing breastfeeding</i>⁴⁸ Dark urine may be indicative of conjugated hyperbilirubinaemia⁴⁷ Urates are commonly present in the urine of newborn babies up to 96 hours of age^{40,47}
Stools^{47,50}	<ul style="list-style-type: none"> Three to four stools per day by the fourth day of life are usual⁵⁰ Stools change from meconium to mustard yellow by third day of life⁵⁰ Pale stools and jaundice are key indicators of liver disease⁴⁷
Pathology	<ul style="list-style-type: none"> Refer to Section 5 Investigations If conjugated bilirubinaemia is suspected also check liver function tests (LFT), INR and blood glucose level
Consultation and referral^{21,35}	<ul style="list-style-type: none"> If there are signs of conjugated hyperbilirubinaemia present (e.g. dark urine and pale stools) referral to a tertiary service for urgent investigation and treatment^{26,27,47,51} is required to reduce the risk of secondary complications^{17,52,53}

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 pathological causes.

5.1 Measurement of bilirubin

A baby's TSB or TcB and gestation are good predictors of hyperbilirubinaemia risk. There is insufficient evidence available to support universal bilirubin screening to prevent chronic bilirubin encephalopathy²⁰ and some evidence of harm (due to overuse of phototherapy).⁵³

Table 8. Measurement of bilirubin

TcB	
Measurement	<ul style="list-style-type: none"> Measure in visibly jaundiced baby if: <ul style="list-style-type: none"> Postnatal age greater than 24 hours⁴⁶ Gestation greater than 35 weeks⁴⁶—more reliable in term babies⁵⁴ Correlation of TcB with TSB on nomogram⁵⁵: <ul style="list-style-type: none"> 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^{56,57} Clinical decision regarding treatment is based on TcB trend and not one value⁵⁸ [refer to Table 14. Phototherapy treatment]
TcB meter ^{4,59}	<ul style="list-style-type: none"> Screens for unconjugated hyperbilirubinaemia Estimates bilirubin levels in the skin from wavelength patterns of light reflected from the skin and subcutaneous tissues⁶⁰ Estimates the TSB from mathematical algorithm accounting for haemoglobin and skin pigments Predictive in identifying babies who need phototherapy⁴
Precautions	<ul style="list-style-type: none"> Not recommended to assess bilirubin if: <ul style="list-style-type: none"> Jaundice is prolonged or there is conjugated hyperbilirubinaemia⁶¹ Baby receiving phototherapy (accuracy is unknown and may overestimate/underestimate levels⁶²⁻⁶⁴) Baby has had phototherapy^{4,61} Baby has had an exchange transfusion
TSB	
Measurement	<ul style="list-style-type: none"> Measure in visibly jaundiced baby if: <ul style="list-style-type: none"> Less than 24 hours of age Less than 35 weeks gestation Known DAT positive Continue measuring when⁶: <ul style="list-style-type: none"> Level is at or above treatment thresholds Therapeutic intervention is being considered
Considerations	<ul style="list-style-type: none"> Gold standard for diagnosing hyperbilirubinaemia Point of care (e.g. blood gas analyser) and laboratory testing measure the sum of conjugated and unconjugated bilirubin in serum²⁶ 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) Combine blood testing to reduce number of venepunctures to baby
Nomograms	
Context	<ul style="list-style-type: none"> Use to^{6,8,9,65,66}: <ul style="list-style-type: none"> Identify babies at risk of developing significant hyperbilirubinaemia⁶⁷ Monitor the trend of the TSB or TcB Plot TSB on nomogram appropriate for baby's age in hours, gestation and birth weight⁸ If TSB is in treatment zone or less than 50 micromol/L below treatment level repeat TSB according to nomogram⁸ Refer to Queensland Clinical Guidelines: <i>Nomograms for jaundice, phototherapy and exchange transfusion</i>⁶⁸

5.2 Pathological jaundice investigations

Table 9. Initial investigations for pathological jaundice

Aspect	Consideration
Context	<ul style="list-style-type: none"> Jaundice appearing within 24 hours of birth always requires urgent investigation (especially to rule out haemolysis) and treatment^{11,20} 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, whose jaundice is below the exchange transfusion threshold requires²⁰: <ul style="list-style-type: none"> TSB to identify if treatment required Full blood count (FBC) to identify haemolysis and/or infection Direct antiglobulin test (DAT) to identify blood group alloimmunisation (weak positive DAT can occur in Rh D positive baby of Rh D negative mother who had antenatal immunoprophylaxis—usually of no significance if maternal antenatal antibody screen was negative)
History	<ul style="list-style-type: none"> Check maternal antenatal screening for: <ul style="list-style-type: none"> ABO Rh D group Red cell antibodies
TSB	<ul style="list-style-type: none"> Refer to Table 8. Measurement of bilirubin Measure total, conjugated and unconjugated bilirubin levels
Haematology^{4,20}	<ul style="list-style-type: none"> FBC^{4,20}—may need to be repeated if baby: <ul style="list-style-type: none"> Appears unwell and/or pale Is less than 24 hours of age Is at risk for polycythaemia: <ul style="list-style-type: none"> Appears excessively ruddy Has risk factors (e.g. maternal smoking, significant fetal growth restriction, maternal diabetes) High TSB especially if refractory to phototherapy Blood group compatibility: <ul style="list-style-type: none"> If maternal antibodies positive, test baby's cord blood or if not available test baby's blood for: <ul style="list-style-type: none"> ABO and Rh D—extended typing may be indicated if there are other maternal antibodies (e.g. Rhc/C e/E) DAT Collect routine newborn bloodspot screening test (NBST)
Infection^{4,20}	<ul style="list-style-type: none"> Blood culture—unwell baby of any age Urine—microscopy and culture <ul style="list-style-type: none"> Urinary tract infection is a potential cause of prolonged jaundice If there are other indications Investigate for congenital infections (e.g. clinical signs of suggestive history, severe jaundice, elevated conjugated bilirubin, thrombocytopenia) <ul style="list-style-type: none"> Toxoplasmosis Rubella Cytomegalovirus (CMV) Herpes simplex virus Syphilis Serial C-reactive protein may indicate of infection/inflammatory process (note: unlikely to be useful in the first 12–24 hours)
Other	<ul style="list-style-type: none"> Liver disease^{4,20}: <ul style="list-style-type: none"> Decreased albumin levels may be helpful to evaluate bilirubin binding capacity and higher risk of bilirubin toxicity. In a preterm baby, alpha-fetoprotein (fetal form of albumin) may be present in sufficient amounts to bind some bilirubin LFT as liver enzymes may be increased (e.g. in congenital infections, inborn errors of metabolism) If concerns regarding hydration consider checking the electrolytes and urea If baby looks unwell and the jaundice is severe investigate for inborn errors of metabolism (e.g. galactosaemia, tyrosinaemia)

5.3 Prolonged jaundice investigations

Use clinical judgement to determine the investigations required for a term baby who continues to be jaundiced after 10–14 days¹¹ or after three weeks for a preterm baby.⁶⁹

The most common cause of prolonged jaundice is breast milk jaundice⁷⁰ occurring in up to 30% well breastfeeding babies.⁵⁵ Do not advise to stop breastfeeding⁴ as the risk of breast milk jaundice does not outweigh the benefits.^{71,72}

- Diagnosis is based on history and clinical examination^{26,71}
- Occurs in well babies with adequate weight gain^{25,73}
- TSB peaks between days five and six⁷⁴ and generally does not exceed 200 micromol/L⁷¹
- Self-limiting²⁶
- Resolves by 12 weeks of age²⁵

Table 10. Jaundice after first week

Aspect	Consideration
Progression of early jaundice	<ul style="list-style-type: none"> • History • Weight gain • Feeding • Blood tests—TSB including conjugated bilirubin, FBC, LFT) • Thyroid function tests^{4,27}—free thyroxine (T4), thyroid stimulating hormone (TSH)
Recurrent or new presentation of jaundice	<ul style="list-style-type: none"> • Urine^{4,27}: <ul style="list-style-type: none"> ◦ Microscopy and culture—urinary tract infection is a potential cause of prolonged jaundice ◦ CMV ◦ Reducing substances—present in galactosaemia • Blood: <ul style="list-style-type: none"> ◦ FBC and reticulocyte count ◦ Repeat NBST ◦ CMV (may be requested on NBST) ◦ Targeted investigations (e.g. G6PD screen particularly if baby is a male with at risk genetic history (note: female babies may also have G6PD but less common))
Unwell baby	<ul style="list-style-type: none"> • Urine—CMV • Check stools for pale appearance (or pallor?)⁷⁵ • Abdominal ultrasound scan (USS) to assess possibility of²⁰: <ul style="list-style-type: none"> ◦ Extrahepatic biliary disease ◦ Hepatocellular disease (e.g. hepatitis) secondary to infection • Sweat test and genetic markers for cystic fibrosis • Inborn errors of metabolism²⁰ <ul style="list-style-type: none"> ◦ May be detected on NSBT—galactosaemia, primary hypothyroidism, cystic fibrosis ◦ May need testing for rare inborn errors of metabolism—amino acid organic acid, fatty acid
Genetic^{4,27}	<ul style="list-style-type: none"> • Family history • Red blood cell (RBC) metabolism disorders^{4,18} <ul style="list-style-type: none"> ◦ G6PD serum level <ul style="list-style-type: none"> ▪ 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)²⁰ • Test for glucuronyl transferase deficiency disorders • Test for red cell membrane disorders (e.g. hereditary spherocytosis or elliptocytosis) <ul style="list-style-type: none"> ◦ May have anaemia⁷⁶ or significant fall in haemoglobin and a high reticulocyte count with a negative DAT ◦ Haemolysis ◦ Increased level of lactate dehydrogenase
Percutaneous liver biopsy	<ul style="list-style-type: none"> • Rarely needed • After consultation with tertiary centre consider to exclude²⁰: <ul style="list-style-type: none"> ◦ Metabolic and storage disorders ◦ 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.^{18,20}

Table 11. Management

Aspect	Consideration
Context	<ul style="list-style-type: none"> Management of hyperbilirubinemia involves interpretation of TSB or TcB levels on a nomogram based on gestation, age and birth weight²¹ Utilise nomograms for guidance with developing individualised management and follow up plans⁸
Nomogram use	<ul style="list-style-type: none"> In the presence of risk factors (confirmed sepsis, haemolysis, acidosis or asphyxia) use the lower line of the nomogram, 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: <ul style="list-style-type: none"> 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 six hours of intensive phototherapy An immediate exchange transfusion is recommended if there are signs of bilirubin encephalopathy^{8,9} <ul style="list-style-type: none"> Consult urgently with a neonatologist by contacting RSQ Refer to Queensland Clinical Guidelines <i>Nomograms for jaundice, phototherapy and exchange transfusion</i>⁶⁸

6.1 Medication use

Table 12. Medication use

Aspect	Consideration
Context	<ul style="list-style-type: none"> Certain medications may cause bilirubin to be displaced from albumin binding sites in babies with hyperbilirubinaemia^{37,77}
Medications	<ul style="list-style-type: none"> Contraindicated in a jaundiced or at risk of jaundice baby⁷⁸: <ul style="list-style-type: none"> Sulfamethoxazole⁷⁹ such as in trimethoprim/sulfamethoxazole (co-trimoxazole) or other sulphur medications <ul style="list-style-type: none"> Potentially interfere with several steps of bilirubin metabolism and can markedly increase the risk of bilirubin encephalopathy Use the following medications with caution: <ul style="list-style-type: none"> Digoxin Diazepam Salicylates Diuretics (e.g. frusemide and hydrochlorothiazide) Ceftriaxone^{4,26} Ibuprofen⁸⁰

*Refer to an Australian pharmacopoeia for complete drug information

6.2 Nutrition

Inadequate feeding and/or intake leads to reduced caloric intake and dehydration resulting in elevated TSB.

Table 13. Nutritional considerations

Aspect	Consideration
Breastfeeding	<ul style="list-style-type: none"> Breastfed babies are more prone to developing prolonged jaundice than formula fed babies if there is^{29,81}: <ul style="list-style-type: none"> Inadequate milk production Insufficient intake of breast milk Encourage breastfeeding—baby may need to feed 8–12 times per day²⁰ <ul style="list-style-type: none"> Offer breastfeeding support Consider referral to lactation consultant If extra fluids required offer expressed breast milk Routine supplementary feeds not recommended²⁶ even if having phototherapy Refer to Queensland Clinical Guideline <i>Establishing breastfeeding</i>⁴⁸ Increase surveillance and monitor for insufficient intake and dehydration
Formula	<ul style="list-style-type: none"> Monitor for adequate intake of formula⁴⁰
Intravenous fluids	<ul style="list-style-type: none"> Not routinely required Consider use based on individual clinical circumstances <ul style="list-style-type: none"> Correction of dehydration, Hypovolemia and/or hypernatremia with significant volume depletion Oral intake is inadequate⁵¹ Receiving phototherapy with TSB levels near exchange transfusion level²⁰
Probiotics	<ul style="list-style-type: none"> Some small studies in term babies have identified probiotics may reduce: <ul style="list-style-type: none"> Hyperbilirubinaemia Duration of phototherapy^{82,83}

6.3 Phototherapy

Phototherapy (especially intensive phototherapy for a high risk baby) can decrease the need for an exchange transfusion.¹² Phototherapy may be intensified by adding an additional light source (e.g. light emitting diode (LED) blanket and overhead lights).⁶

Table 14. Phototherapy treatment

Aspect	Consideration
Mechanism of action	<p>Phototherapy converts bilirubin to water-soluble isomers that:</p> <ul style="list-style-type: none"> ○ Are more readily excreted via urine and liver without conjugation and ○ Cannot cross the blood brain barrier <ul style="list-style-type: none"> • Clinical response of baby depends on: <ul style="list-style-type: none"> ○ Efficacy of the phototherapy unit ○ Balance between rate of bilirubin production and elimination¹² ○ Adequacy of skin exposure and time under phototherapy • Refer to Appendix A: Phototherapy
Considerations⁸⁴	<ul style="list-style-type: none"> • TSB level plotted on nomogram • Gestation of baby • Age in hours of baby at time of testing¹² • Individual neurotoxicity risk factors^{12,18} <ul style="list-style-type: none"> ○ Refer to Section 7.2 Bilirubin induced neurologic dysfunction • If access to TSB result is delayed: <ul style="list-style-type: none"> ○ Test TSB when bilirubin level on TcB is 70% of the treatment line (based on the baby's gestational age, weight and age) ○ Commence phototherapy when the TcB plots on the treatment line for phototherapy for baby with risk factors ○ Review indication and need for phototherapy based on TSB when available
Contraindications	<ul style="list-style-type: none"> • Congenital erythropoietin porphyria, or family history⁸⁵ (very rare disorder) <ul style="list-style-type: none"> ○ Porphyrins are photosensitisers cause injury to tissue (severe blistering and photosensitivity) when exposed to light⁸⁶
Precautions	<ul style="list-style-type: none"> • Refer to an Australian pharmacopoeia for complete drug information regarding the use of medications and topical skin preparations during phototherapy <ul style="list-style-type: none"> ○ Refer to Section 6 Medication use • Concomitant use of photosensitising medications: <ul style="list-style-type: none"> ○ 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 phototherapy⁸⁵ as plastic covers or optical filters remove potentially harmful ultraviolet light¹² • Do not use white lights painted blue or covered with blue plastic sheaths¹² • TcB may not be as reliable as TSB during and after phototherapy⁴⁶ <ul style="list-style-type: none"> ○ Follow manufacturer instructions for use after phototherapy
Side effects/ complications	<ul style="list-style-type: none"> • if jaundice is not severe use fibreoptic or LED blanket, or timed interruptions for breastfeeding^{87 18} • Small increased risk for seizures (approximately 1–2 babies per 10,000 treated)⁵³ • Blue light phototherapy—potential risk factor for melanocytic nevus development⁸⁸
If cholestatic jaundice and conjugated hyperbilirubinaemia	<ul style="list-style-type: none"> • May develop dark grey-brown discoloration of the skin^{8,85} <ul style="list-style-type: none"> ○ Known as 'bronze baby syndrome' ○ Gradually disappears after discontinuation of phototherapy ○ Not a contraindication to phototherapy⁸⁵—consider need for continued phototherapy when the conjugated bilirubin reaches between one third and one half of the total bilirubin • If eyes exposed to light, may damage retina⁸⁵ • May increase cutaneous blood flow (photorelaxation) and insensible water loss through <ul style="list-style-type: none"> ○ Skin^{85,89} ○ Loose stools²⁰ ○ Develop purpura and bullous eruptions⁸ ○ Transient rashes (usually of no clinical significance)

6.3.1 Care during phototherapy

Table 15. Phototherapy care

Aspect	Consideration
Clinical Care	<ul style="list-style-type: none"> • If possible do not separate mother and baby during phototherapy <ul style="list-style-type: none"> ◦ Provide information to support the woman and family during treatment and/or phototherapy • Nurse baby with only a nappy and fold down to exposure maximum skin surface area ^{12,85} <ul style="list-style-type: none"> ◦ If baby has loose stools, consider the use protective barrier creams on buttocks • Use eye protection <ul style="list-style-type: none"> ◦ Lubricating eye drops may be indicated⁸⁵ ◦ Monitor for eye discharge, conjunctivitis and eye protection placement • Continuously observe baby • Monitor baby's temperature: <ul style="list-style-type: none"> ◦ If halogen lights are used, risk of hyperthermia ◦ If unclothed baby nursed in bassinette/cot under lights where there is cool ambient temperature ◦ Nurse preterm baby in incubator or under radiant warmer/waterbed (where available) • Usual oral feeds in term babies⁸⁵ • Clinically assess hydration status²⁰
Application of lights	<ul style="list-style-type: none"> • Check <ul style="list-style-type: none"> ◦ Spectral output of light source is within acceptable parameters ◦ Irradiance level is uniform over exposed surface of baby • Expose the maximum area 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 <ul style="list-style-type: none"> ◦ If bilirubin levels have not reduced adequately briefly disrupt phototherapy during eye care and blood collection • Re-check TSB during treatment to measure the rate of response in bilirubin load reduction • Refer to Appendix A: Phototherapy
Ceasing phototherapy	<ul style="list-style-type: none"> • Criteria for discontinuing phototherapy depends on: <ul style="list-style-type: none"> ◦ Age of baby when phototherapy initiated ◦ Cause of hyperbilirubinaemia • Discontinue phototherapy when TSB reduced below recommended amount [refer to nomograms] <ul style="list-style-type: none"> ◦ Be aware of possible rebound increase in TSB⁵¹ • Continue monitoring bilirubin levels at regular intervals for several hours after ceasing • If baby had haemolytic jaundice or other early onset jaundice and is discharged before 3–4 days, follow up TSB 24 hours after discharge^{8,9} <ul style="list-style-type: none"> ◦ Cease phototherapy using clinical judgement considering suitable duration of phototherapy for underlying cause and severity of jaundice
Rebound hyperbilirubinaemia	<ul style="list-style-type: none"> • Early cessation of phototherapy may result in rebound hyperbilirubinaemia within 72 hours^{90,91} • Risk depends on baby's: <ul style="list-style-type: none"> ◦ Gestation ◦ Age when phototherapy started ◦ TSB relative to treatment thresholds when the phototherapy ceased • Consider repeat TSB measurement 12–18 hours after ceasing phototherapy⁶

6.3.2 Phototherapy in the home

Although evidence is limited, home phototherapy may be considered as a safe alternative to inpatient phototherapy for otherwise healthy newborn babies with hyperbilirubinemia.⁹² Follow local protocols for inclusion, exclusion and escalation criteria.

Table 16. Home phototherapy

Aspect	Consideration
Criteria/inclusion	<ul style="list-style-type: none"> • Discuss with parents their motivation, abilities⁸⁷ and understanding of safer sleeping principles • Unconjugated hyperbilirubinaemia <ul style="list-style-type: none"> ◦ TSB not greater than 50 micromol/L above the treatment line ◦ Conjugated bilirubin not greater than 10% of TSB • Baby is: <ul style="list-style-type: none"> ◦ Otherwise well and fit for discharge ◦ Feeding well ◦ Greater than 24 hours of age ◦ Greater than 37 weeks gestation ◦ Birth weight greater than 2500 grams • Parents able to transport baby to pathology service for TSB or a home pathology collection service is available • Proximity to local hospital⁸⁷
Exclusion	<ul style="list-style-type: none"> • Jaundice in first 24 hours of age • Poor feeding • Temperature instability • Lethargy • Alloimmune haemolytic disease • Asphyxia/acidosis • Infection • Abnormal liver function tests
Parent information	<ul style="list-style-type: none"> • Verbal instructions and written documentation on: <ul style="list-style-type: none"> ◦ When to seek advice ◦ Importance of safer infant sleeping principles <ul style="list-style-type: none"> ▪ Refer to Queensland Clinical Guideline <i>Safer infant sleep</i>⁹³ ◦ Temperature monitoring and management ◦ Assessment of hydration <ul style="list-style-type: none"> ▪ Written feeding plan ◦ Signs of increasing hyperbilirubinaemia ◦ Manufacturer's instructions on use of phototherapy equipment • Equipment <ul style="list-style-type: none"> ◦ Phototherapy unit ◦ Phototherapy disposable covers ◦ Eye covers ◦ Digital thermometer • Observation chart <ul style="list-style-type: none"> ◦ Phototherapy ◦ Feeding/output ◦ Temperature • Provide contact information for any concerns • Refer to Queensland Clinical Guideline parent information <i>Jaundice in newborn babies</i>

6.4 Exchange transfusion

A TSB at exchange transfusion level is a medical emergency and requires urgent management.^{6,8,45}

Table 17. Exchange transfusion

Aspect	Consideration
Mechanism of action	<ul style="list-style-type: none"> • Rapidly reduces the levels of bilirubin by removing small aliquots of blood from the baby and replacing it with donor blood component^{8,9,45} • 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
Indications	<ul style="list-style-type: none"> • TSB continues to rise despite intense phototherapy^{51,94} • Refer to nomogram appropriate for baby's gestation, weight and age <ul style="list-style-type: none"> ◦ Refer to Queensland Clinical Guidelines <i>Nomograms for jaundice, phototherapy and exchange transfusion</i>⁶⁸ • Baby showing signs of acute bilirubin encephalopathy^{94,95} • Symptomatic babies with any moderate to advanced signs of bilirubin-induced neurologic dysfunction (BIND)⁵¹
Escalation	<ul style="list-style-type: none"> • Perform in a Neonatal Unit • Contact Retrieval Services Queensland (RSQ) for: <ul style="list-style-type: none"> ◦ Advice and discussion of management with neonatologist ◦ Transfer or retrieval of the baby to a CSCF level 6 service that has detailed exchange transfusion protocols
Exchange transfusion²⁰	<ul style="list-style-type: none"> • If transfusion to occur urgently outside a level 6 service, liaise with an expert multidisciplinary team with established protocols • Obtain a NBST prior to transfusion <ul style="list-style-type: none"> ◦ CMV PCR may be obtained from this blood sample, if required/requested • Use plasma that is¹⁰: <ul style="list-style-type: none"> ◦ Group O Rh D negative or for the baby with non-A, B or D antibodies, negative for the relevant antigen ◦ CMV negative (if available) ◦ Irradiated⁴ • Exchange double the baby's blood volume (160 mL/kg)⁴ • Continue intensive phototherapy during the transfusion • Consider blood gas monitoring
Risks	<ul style="list-style-type: none"> • Discuss with the family risks of exchange transfusion including: <ul style="list-style-type: none"> ◦ Fluid overload ◦ Infection ◦ Thrombocytopenia ◦ Metabolic imbalance <ul style="list-style-type: none"> ▪ Hypoglycaemia ▪ Hypocalcaemia ▪ Hypokalaemia ◦ Coagulopathy ◦ Air embolism⁴ ◦ Thrombosis²⁰ ◦ Necrotising enterocolitis^{20,21} ◦ Blood loss
Post exchange transfusion	<ul style="list-style-type: none"> • Continue intensive phototherapy • Measure TSB within two hours of exchange transfusion⁴⁵

6.5 Supplementation

For babies who develop anaemia due to haemolysis, supplemental folic acid may be beneficial. Supplemental iron is contraindicated unless iron deficiency is documented (iron overload syndromes are more common).

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

6.5.1 Ferrous sulphate

Table 18. Ferrous sulphate

Aspect	Consideration
Context	<ul style="list-style-type: none"> Iron is critical for growth and central nervous system (CNS) development⁹⁶ Iron deficiency is associated with impaired neurological and behavioural development⁹⁷ 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
Ferrous sulphate*	<ul style="list-style-type: none"> Use with caution in any baby who has a haemolytic condition (endogenous iron stores may be high not low) <ul style="list-style-type: none"> Well term babies usually have adequate iron stores for 4–6 months⁹⁸ Undertake iron studies before commencing treatment to confirm iron deficiency and absence of iron overload Refer to Queensland Clinical Guidelines NeoMedQ Neonatal Medicines Ferrous sulphate⁹⁹ for dosing and frequency according to gestational age

*Refer to an Australian pharmacopoeia for complete drug information

6.5.2 Folic acid

Table 19. Folic acid

Aspect	Consideration
Context	<ul style="list-style-type: none"> Folic acid aids in the maturation of RBC¹⁰⁰ Babies who are low in folic acid are anaemic and fail to thrive¹⁰⁰ Folic acid is critical for numerous aspects of metabolism, including brain development
Folic acid*	<ul style="list-style-type: none"> Does not reduce incidence or severity of anaemia in babies with a positive DAT¹⁰¹ Indicated for use in babies with anaemia caused by haemolytic disease where there has been a high red cell turnover Dose: 50–100 microgram/kg/day Commence from seven days of age Adverse effects are rare but may include: <ul style="list-style-type: none"> Rash High temperature Diarrhoea

*Refer to an Australian pharmacopoeia for complete drug information

7 Complications of untreated unconjugated hyperbilirubinaemia

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.¹⁰² There is necrosis of neurons in the basal ganglia resulting in irreversible neuro-disabilities.^{4,20,45,46,94} The Australian incidence of extreme hyperbilirubinaemia is 9.4/100 000 live births.⁴⁶

7.1.1 Acute bilirubin encephalopathy

Table 20. Acute bilirubin encephalopathy

Aspect	Consideration
Context	<ul style="list-style-type: none"> Often occurs in the first days of life and causes a temporary alteration in neurologic state^{41,94,95} Early treatment of hyperbilirubinaemia reduces poor neurological outcomes⁴
Risk factors⁹⁴	<ul style="list-style-type: none"> ABO incompatibility Rh D isoimmunisation G6PD deficiency Prematurity Infection Exclusively breastfeeding
Signs	<ul style="list-style-type: none"> Initially subtle and non-specific^{94,95,103}: <ul style="list-style-type: none"> Poor feeding High pitched cry High temperature Lethargy Increase in severity as bilirubin levels increase Subsequently progressive disturbance in neurobehaviour⁹⁵: <ul style="list-style-type: none"> Hypertonia Retrocollis Opisthotonus
Disease progression	<ul style="list-style-type: none"> May lead to: <ul style="list-style-type: none"> Athetoid cerebral palsy¹⁰⁴ Deafness Blindness due to paralysis of ocular muscles⁹⁴
Preterm babies	<ul style="list-style-type: none"> Recognition of signs may be challenging^{94,95}: <ul style="list-style-type: none"> Apnoea and oxygen desaturations may be the only sign⁹⁵ Higher risk due to immature CNS and neuronal pathways

7.1.2 Chronic bilirubin encephalopathy

Table 21. Chronic bilirubin encephalopathy

Aspect	Consideration
Context	<ul style="list-style-type: none"> Permanent sequel of bilirubin toxicity Becomes evident in the first year of life⁹⁵ History of severe and prolonged hyperbilirubinaemia^{94,95}
Risk factors include²⁰	<ul style="list-style-type: none"> Prematurity Infection Asphyxia
Common signs^{94,95}	<ul style="list-style-type: none"> Choreo-athetoid cerebral palsy^{102,103} Gaze paralysis Hearing loss Enamel dysplasia of deciduous teeth
Magnetic resonance imaging investigations	<ul style="list-style-type: none"> Damage to basal ganglia, central and peripheral auditory pathways, hippocampus, subthalamic nuclei or midbrain^{94,95} and globus pallidus¹⁰⁵ Cerebral cortex mostly undamaged²⁰
Sensorineural hearing loss (SNHL)¹⁰⁶	<ul style="list-style-type: none"> History of extremely high TSB levels (greater or equal to 450 micromol/L) increase the risk Timely exchange transfusion may reduce risk

7.2 Bilirubin induced neurologic dysfunction

Bilirubin induced neurologic dysfunction (BIND) is a syndrome of subtle bilirubin neurotoxic disorders. It can occur in the absence of kernicterus.^{51,102,107,108} BIND is diagnosed on clinical manifestations in infancy and early childhood, and a history of neonatal hyperbilirubinaemia.⁵¹ The incidence of BIND is unknown.¹⁰⁹

Table 22. Bilirubin induced neurologic dysfunction

Aspect	Consideration
Context	<ul style="list-style-type: none"> Based on clinical observation as there are no specific biomarkers¹⁰² Severe and irreversible¹⁰² No defined dose-dependent phototherapy association between moderate or extreme hyperbilirubinemia and neurologic outcomes⁵¹ History of bilirubin levels lower than those associated with acute and chronic bilirubin encephalopathy¹⁰⁷ <ul style="list-style-type: none"> May result from prolonged jaundice with moderate hyperbilirubinaemia below treatment threshold¹⁰²
Risk factors	<ul style="list-style-type: none"> Prematurity⁷² Duration and level of serum unconjugated bilirubin¹⁰⁷ Capacity of albumin to bind to bilirubin⁹⁴ Individual vulnerability of CNS making bilirubin toxicity inherent in each baby¹⁰²
Clinical manifestations	<ul style="list-style-type: none"> Clinical signs not completely categorised in term and preterm babies⁹⁴ Neuromotor signs: <ul style="list-style-type: none"> Muscle tone abnormalities Hyperexcitable neonatal reflexes Speech and language difficulties Central processing abnormalities (e.g. visuomotor dysfunction, sensorineural hearing loss (SNHL))

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.¹¹⁰

Table 23. Auditory toxicity

Aspect	Consideration
Context	<ul style="list-style-type: none"> Relationship between TSB and SNHL¹⁵ Non-linear—there is a probable threshold effect¹⁵ 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^{110,111}	<ul style="list-style-type: none"> 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 SNHL¹¹⁰ due to hyperbilirubinaemia or other cause

8 Discharge planning

Table 24. Discharge planning

Aspect	Consideration
Pre-discharge	<ul style="list-style-type: none"> Identify baby at risk of jaundice <ul style="list-style-type: none"> Refer to Section 2 Risk factors Assess for jaundice prior to discharge especially if less than 72 hours of age¹⁸ Review babies who are discharged before 72 hours of age within two days following discharge¹⁸ Consider pre-discharge measurement of TcB <ul style="list-style-type: none"> If concerns for follow up (e.g. distance to health services) recommend pre-discharge TcB
Parent information^{18,45,81}	<ul style="list-style-type: none"> Provide parents with both written and verbal information <ul style="list-style-type: none"> Refer to Queensland Clinical Guideline parent information <i>Jaundice in newborn babies</i>
Advise review needed if	<ul style="list-style-type: none"> Jaundice: <ul style="list-style-type: none"> Appears at less than 24 hours of age (urgently) Any time in the first week of life Visible after 12 days of age (requires investigation) Increasing since last healthcare professional review Feeding: <ul style="list-style-type: none"> Inadequate Vomiting Baby losing weight⁴⁸ Output: <ul style="list-style-type: none"> Fewer than six wet nappies per day Pale stools Dark urine
Follow up	<ul style="list-style-type: none"> Home visiting midwife General practitioner Child health services Paediatrician/neonatologist if baby treated for extreme hyperbilirubinaemia or exchange transfusion <ul style="list-style-type: none"> Discuss follow up FBC, where appropriate If baby re-presents with jaundice after discharge refer to: <ul style="list-style-type: none"> Section 4 Clinical assessment and investigation Section 6 Management Queensland Clinical Guideline <i>Newborn baby assessment (routine)</i>¹¹² Queensland Clinical Guideline <i>Establishing breastfeeding</i>⁴⁸

9 Other treatments

9.1 Treatments of no benefit

The following treatments have not been proven to reduce neonatal hyperbilirubinaemia. Additionally, there is no evidence of benefit and evidence of possible harm to the baby

Table 25. Treatments of no benefit

Aspect	Consideration
Intravenous immunoglobulin (IVIg) ^{10,113,114}	<ul style="list-style-type: none"> Fractionated blood product¹¹⁵ A Cochrane review of nine studies with 658 participants provided limited evidence that IVIg treatment in newborns reduced the need for exchange transfusion however the studies were at a high risk of bias and no recommendations made¹¹⁶ Possible risks of harm include transfusion-related lung injury and necrotising enterocolitis¹¹⁶
Medications	<ul style="list-style-type: none"> Laxatives to assist passing of meconium includes: <ul style="list-style-type: none"> Agar^{8,45} Manna¹¹⁷ Glycerine^{8,45} Oral zinc to reduce hyperbilirubinaemia or need for phototherapy¹¹⁸ Antenatal phenobarbital in red cell isoimmunised pregnant women¹¹⁹ Activated charcoal⁴⁵ Metalloporphyrin²⁰: <ul style="list-style-type: none"> Inhibits haem oxygenase and production of bilirubin Treatment of unconjugated hyperbilirubinaemia with a metalloporphyrin is experimental⁴⁵ Not approved in many countries⁴⁵
Other therapies	<ul style="list-style-type: none"> Acupuncture Homeopathy Traditional Chinese medicine⁴⁵

9.2 Unproven benefit

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 26. Unproven benefit

Aspect	Consideration
Prophylactic phototherapy ¹²⁰	<ul style="list-style-type: none"> • Lowers serum bilirubin • May have an effect on the rate of exchange transfusion <ul style="list-style-type: none"> ◦ Note: Commence phototherapy early in babies with significant alloimmune haemolytic disease (e.g. Rh D), without waiting for postnatal TSB especially if an intrauterine transfusion was not given
Medications	<ul style="list-style-type: none"> • Albumin infusion <ul style="list-style-type: none"> ◦ Benefits unknown^{51,121} • Vitamin D supplementation¹²² <ul style="list-style-type: none"> ◦ Low levels of vitamin D may be associated with neonatal jaundice • Ursodiol²⁰: <ul style="list-style-type: none"> ◦ Hydrophobic bile salt ◦ Decreases cholesterol production and then dissolves it in bile ◦ Unknown risks and benefits • Clofibrate^{20,123} <ul style="list-style-type: none"> ◦ A fibric acid derivative ◦ Improves activity of glucuronyl transferase ◦ Increases the conjugation of unconjugated bilirubin in the liver ◦ Insufficient data to make recommendations for use in combination with phototherapy ◦ More studies are required to verify safety and long-term neurodevelopmental outcomes
Filtered sunlight ^{40,124}	<ul style="list-style-type: none"> • Not recommended for treatment or prevention of neonatal jaundice in Queensland • Sunlight alone has not been demonstrated as an effective treatment for hyperbilirubinaemia • Sunlight contains harmful ultraviolet light and infrared radiation <ul style="list-style-type: none"> ◦ Prolonged exposure has the potential to cause skin damage and difficulties in maintaining temperature (hypothermia or hyperthermia)

Appendix A: Phototherapy

Aspect	Consideration
Equipment	<ul style="list-style-type: none"> Phototherapy light sources include:¹² <ul style="list-style-type: none"> LED lights tungsten Fluorescent tubes Metal halide bulbs LEDs, fluorescent tubes and halogen light sources reduce TSB levels at similar rates in both term and preterm babies¹²⁵, however LEDs are more power efficient, portable and have lower heat production^{126,127} Generally fluorescent tubes are suitable for term babies and halogen for preterm 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 phototherapy lights Periodically check spectral irradiance of phototherapy⁸ Undertake electrical and fire hazard safety checks on phototherapy units to reduce risks in an environment with high humidity and oxygen¹²
Dose	<ul style="list-style-type: none"> Measure dose during phototherapy using radiometer^{12,85} <ul style="list-style-type: none"> Make several measures in different locations on baby and average Achieve average irradiance reading over 80% of baby's body surface area Clinical effect of phototherapy evident within four to six hours of initiation¹² Depends on: <ul style="list-style-type: none"> Rates of bilirubin production Enterohepatic circulation Bilirubin elimination Degree of bilirubin deposition in the tissues Rates of photochemical reactions of bilirubin
Irradiance of light	<ul style="list-style-type: none"> Higher spectral irradiance results in more rapid decline in bilirubin There is no evidence of a saturation point for phototherapy (i.e. an irradiation level above which there is no further decrease in TSB⁸⁹) Different devices deliver significantly different levels of irradiance <ul style="list-style-type: none"> Standard treatment: 25–30 microwatts per square centimetre per nanometre (microW/cm²/nm) (430–490 nm) Intensive treatment: 30 microW/cm²/nm or more (430–490 nm)
Light source	<ul style="list-style-type: none"> Use additional light source under baby for intensive phototherapy <ul style="list-style-type: none"> May be fibre-optic pad, light emitting diode (LED) mattress or bank of special blue lights
Distance	<ul style="list-style-type: none"> Maximise irradiance by minimising the distance between the baby and the light source <ul style="list-style-type: none"> Usually 10–15 cm for term and near term babies For halogen or tungsten lights follow manufacturer's recommendations to avoid overheating or burning baby¹² Reduce the distance of the phototherapy lights from the baby as much as possible⁸⁹ following manufacturer's instructions <ul style="list-style-type: none"> Visual estimations of brightness or use of photometric or colourmetric light meters are not appropriate⁸⁹ Treat preterm babies in incubator ensuring light rays are perpendicular to incubator surface to minimise light reflectance⁸⁵

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