

RPA Newborn Care Guidelines

Royal Prince Alfred Hospital

Jaundice

Introduction

Approximately 60% of term babies and 85% of preterm babies will develop clinically apparent jaundice.^{1,2} Most of these babies have so-called 'physiological jaundice', which typically becomes clinically apparent on day 3, peaks on day 5 to 7 and resolves by day 14.

Physiological jaundice is usually benign, however if unconjugated serum bilirubin levels get too high, bilirubin can cross the blood brain barrier where it is neurotoxic, particularly to the auditory nerve and basal ganglia. Brain injury and life long disability can result. Because of this, it is important to identify those babies at risk of the rare complication of acute bilirubin encephalopathy and kernicterus.^{1,2}

The clinical challenge is identifying the tiny minority with pathological neonatal jaundice from the large majority with benign physiological jaundice. There are important cues that jaundice may be pathological.

Incidence and risk factors:

It is clinically useful to classify jaundice according to the age of the baby when he/she becomes visibly jaundiced.

1. Early (days 1-2) - uncommon
 - Haemolytic jaundice (Rhesus, ABO, others)
2. Normal (days 3-10) - very common
 - Uncomplicated
 - G6PD deficiency - especially post discharge home
 - Complicated - see below
3. Late (days 14+)
 - Breast milk - common
 - Conjugated jaundice - uncommon
 - Inherited deficiency of glucuronyl transferase enzymes - very rare

Factors likely to make physiological jaundice worse in a given baby include:

- prematurity
- bruising
- cephalohematoma
- polycythaemia

- delayed passage of meconium
 - breast feeding
 - certain ethnic groups, esp Chinese
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Consequences:

Severe jaundice

- Definition of severe jaundice depends on the clinical setting:
 1. Uncomplicated term babies >450
 2. Babies with haemolytic jaundice - see [jaundice - haemolytic](#)
 3. Preterm babies - depends on gestational age - see below
- **Kernicterus** (bilirubin encephalopathy). This clinical syndrome includes hypertonia progressing to opisthotonia, seizures, and may lead to death. At autopsy, such babies display evidence of bilirubin staining of the basal ganglia.
- **Late sequelae to kernicterus**. These include sensorineural hearing impairment and cerebral palsy, often with ataxia and chorioathetosis.

Once a baby develops severe jaundice, the risk of progressing to kernicterus is increased by the following:

- acidosis
- drugs which displace bilirubin from albumin (esp. sulphonamides and related compounds)
- hypoalbuminaemia

The late effects of moderate levels of jaundice on extremely preterm infants is unknown, although it is generally accepted they are more at risk than term infants for the same SBR level.

Investigations:

1. Clinical evaluation

General comments

Surveillance for neonatal jaundice involves the use of regular visual assessment of skin colour and (where available and in babies born after 35 weeks) transcutaneous bilirubin measurement (TcB) to identify babies who need total serum bilirubin measurement (TSB). TSB can then be used to determine need for treatment.

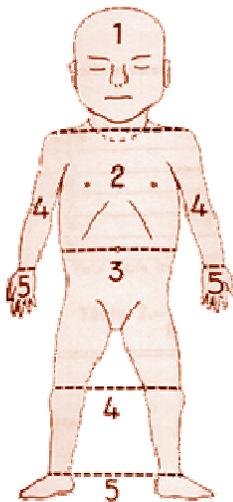
Clinical Visual Assessment of Severity of Jaundice

Visual assessment remains the mainstay of jaundice surveillance in the newborn. All babies should have ongoing assessments in the first 4 days of life, specifically those at risk of developing hyperbilirubinaemia during the neonatal period. Assessments should be at least 8 to 12 hourly in the first 48 hours of life.^{1,2}

Always assess jaundice in good light by blanching the baby's skin with a finger and observing the underlying skin colour.^{1,2} Two clinical features of increasing severity of neonatal jaundice dominate the visual assessment:

- The underlying skin colour changes from a lemon yellow to a deeper orange yellow.
- The jaundice also progresses caudally from the face with a progression to the trunk and extremities, following Kramer's rule.³ If the feet or hands are visibly yellow, the TSB is likely to be above 250 micromol/L.

Kramer's Rule³



Rather than estimating the level of jaundice by simply observing the baby's skin colour, one can utilise the cephalocaudal progression of jaundice. Kramer drew attention to the observation that jaundice starts on the head, and extends towards the feet as the level rises. This is useful in deciding whether or not a baby needs to have the SBR measured. Kramer divided the infant into 5 zones, the SBR range associated with progression to the zones is as follows:

Zone	1	2	3	4	5
SBR (umol/L)	100	150	200	250	>250

Limitations to visual assessment: There are limits to the accuracy of visual estimation of TSB levels, with or without the help of Kramer's rule especially in darker skinned babies,^{1,3} and, if there is any doubt clinically, TcB or TSB measurement should be performed. Visual and TcB assessment are also inaccurate on a baby once under phototherapy as this will tend to blanch the skin.⁴ A TSB level should always be used to assess response to phototherapy.

2. Transcutaneous bilirubin measurement (TcB)

Since January 2006 transcutaneous bilirubinometry has been adopted at RPA as the first-line screening tool for jaundice in well, term and near-term babies. Transcutaneous bilirubinometry provides an extra layer of non-invasive assessment of degree of jaundice prior to taking blood for TSB levels.⁵ Commercially available Transcutaneous Bilirubinometers differ in accuracy and therefore safe use requires knowledge of the accuracy of the particular device.⁵

TcB measurements have been mainly validated in term and near-term infants and, even in more mature babies, there are limitations to the accuracy. Therefore the main goal of TcB measurement is to select more accurately those babies who need further evaluation with a TSB. The following general guidelines can be used:

- If the baby appears significantly jaundiced and the JM103 displays “---“, this means the reading is > 340, and a TSB is urgently required.
- If a TcB level is within 50 micromol/L of the threshold for phototherapy then a TSB level measurement is recommended.
- Because of differences in reliability of measurement between individual babies, trend of TcB measurements are more reliable than those made on a single value as the basis for clinical decision making.^{4,5}

Conventional phototherapy bleaches the skin making TcB level measurement unreliable after the commencement of phototherapy.⁴ However, when using bilibeds or biliblankets where the face is not exposed, the TcB may be used.

3. Total Serum Bilirubin (TSB)

The TSB remains the ‘gold standard’ measurement for treatment decisions regarding jaundice. Venous and capillary TSB levels should be treated the same.^{1,2} The total serum bilirubin as opposed to the unconjugated fraction should be used for judging treatment thresholds in Figures 1 and 2.^{1,2}

Initial TSB measurement (rather than a TcB) should be requested based on clinical observation and the following factors:

- Any baby with clinically apparent jaundice before 24 hrs.
- Any term baby with clinically estimated SBR or TcB levels more than 250 micromol/L.
- Any preterm baby with clinically estimated SBR or TcB levels more than 200 micromol/L.
- Any baby, if there is clinical doubt about the degree of jaundice.
- Any unwell baby with jaundice.
- 24 hours after ceasing phototherapy to check for a rebound in TSB level.

Repeated TSB measurement: TSB should be repeated within 12 to 24 hours in any baby with a total serum bilirubin level of less than 50 micromol/L below the phototherapy treatment line. If the TSB is more than 30 micromol/L above the phototherapy treatment line, it should be checked 4-6 hourly after commencing phototherapy to ensure that it does not continue to rise.

4. Further investigations

Investigation for a cause of neonatal jaundice should be considered in the following situations:

Early onset jaundice

- Babies of Rhesus negative mothers, or babies of mothers with a positive antibody screen, should routinely have cord blood sent for blood group and Direct Antibody (Coomb’s) Test (DAT). Any neonate who is DAT positive should have a TSB or TcB tested in the first 24 hours.
- Any neonate who is clinically jaundiced within the first 24 hours requires urgent investigation to exclude haemolysis due to Rhesus or ABO incompatibility, including TSB,

FBC and film and mother and baby's blood group & DAT.(see [Haemolytic Jaundice Guideline](#))

TSB above the phototherapy thresholds or rapidly rising TSB.

Any baby with a TSB above phototherapy threshold or other rapidly rising TSB should also be investigated. Investigations should include:

- Mother's and baby's blood group & DAT (if not already known) to assess for Rhesus or ABO incompatibility,
- Full blood count (FBC) and film with reticulocyte count to assess for haemolysis.
- G6PD screen in male babies with high risk family history or ethnic/geographic origin (Mediterranean, Middle Eastern, African, Asian). Include females if severe.
- Septic screen including blood and urine culture and sensitivity (C&S) if there is clinical concern about possible sepsis.

Jaundice approaching exchange transfusion thresholds.

Additional investigations should include:

- Conjugated bilirubin
- Serum albumin level. Low albumin levels may be a risk factor for kernicterus
- Liver function tests (LFT)

Prolonged jaundice.

Babies with prolonged jaundice (visible jaundice persisting for greater than 2 weeks in term babies and greater than 3 weeks in preterm babies) should be reviewed for history suggestive of obstructive jaundice e.g. acholic pale stools. In all babies with prolonged jaundice, blood should be taken for total and conjugated bilirubin level.

- Predominantly unconjugated prolonged jaundice (conjugated SBR less than 30 micromol/l): is usually benign breast milk jaundice but consider performing thyroid function tests to exclude thyroid agenesis/dysplasia or hypopituitarism, and a urine culture to exclude a UTI.
- Predominantly conjugated prolonged jaundice (conjugated SBR greater than 30 micromol/l): is always pathological and the baby should be investigated for intra-hepatic (e.g hepatitis) and obstructive (e.g biliary atresia) causes of prolonged jaundice. (see [Conjugated Jaundice Guideline](#))

There should be no delay in investigation because age at diagnosis of biliary atresia is an important prognostic factor for successful surgical repair. So such babies should be referred urgently to a tertiary Paediatric centre that has the facilities to investigate these babies and particularly to exclude biliary atresia.

Treatment of Neonatal Jaundice

Treatment should include general management including rehydration in babies with excess weight loss (more than 10% of birth weight) and treatment of any underlying illnesses that may be causing jaundice (e.g. infection).

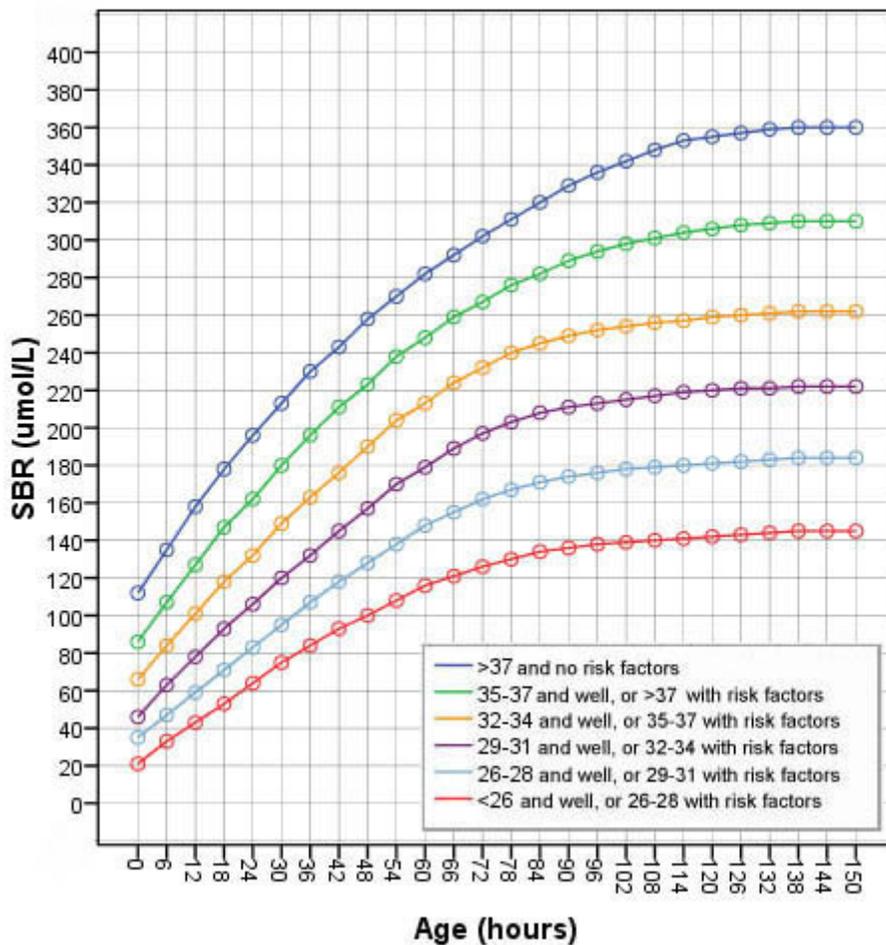
1. Phototherapy

Phototherapy is the first line treatment for neonatal jaundice and is effective in most babies in reducing TSB level. Its efficacy depends on wavelength and luminance of the light source and the skin surface area illuminated by the light.⁶ See [Phototherapy Guideline](#)

Figure 1: Phototherapy treatment thresholds

Plot TSB level according to postnatal age. If TSB is above the relevant line for gestation and risk factor criteria, then commence phototherapy.

Disclaimer: Because high medical level evidence does not exist in this area, particularly for the lower gestations, these charts result from a consensus as to safe treatment thresholds.



Source: Term and near-term data adapted from reference 1.

Risk Factors: Babies with any of the risk factors below should start phototherapy according to the line one below that indicated by their gestational age. These risk factors include:

- Haemolysis,
- G6PD deficiency,
- Asphyxia,
- Proven sepsis,
- Any baby who is unwell: e.g. lethargy, temperature instability, respiratory distress, acidosis.

- albumin less than 30gram/L (if measured)

In babies with severe (close to exchange levels) or rapidly rising SBR, the efficacy of phototherapy can be optimised by removing all clothes and nappy and having more than one light above the baby and having the baby lie on a fibre optic or LED phototherapy mat.

Stopping phototherapy

Although the line indicates the level for commencing phototherapy, once the baby is receiving phototherapy, the suggested TSB level for ceasing would be a TSB level of 280 micromol/L for term babies, and for premature babies 50 micromol/L or more below the phototherapy line.^{1,2}

A rebound in total serum bilirubin levels can occur after phototherapy is discontinued.¹ Babies born before 37 weeks gestation and those with known haemolysis disease are at increased risk of clinically significant rebound.

Unless there is identified pathology, discharge need not be delayed to observe the baby for rebound, but consider follow up TSB level measurement within 12 to 24 hours after discharge. (See Section 4 Discharge planning and transfer of care).

2. Exchange transfusion

For details of the procedure, see [medical](#) and [nursing](#) guidelines.

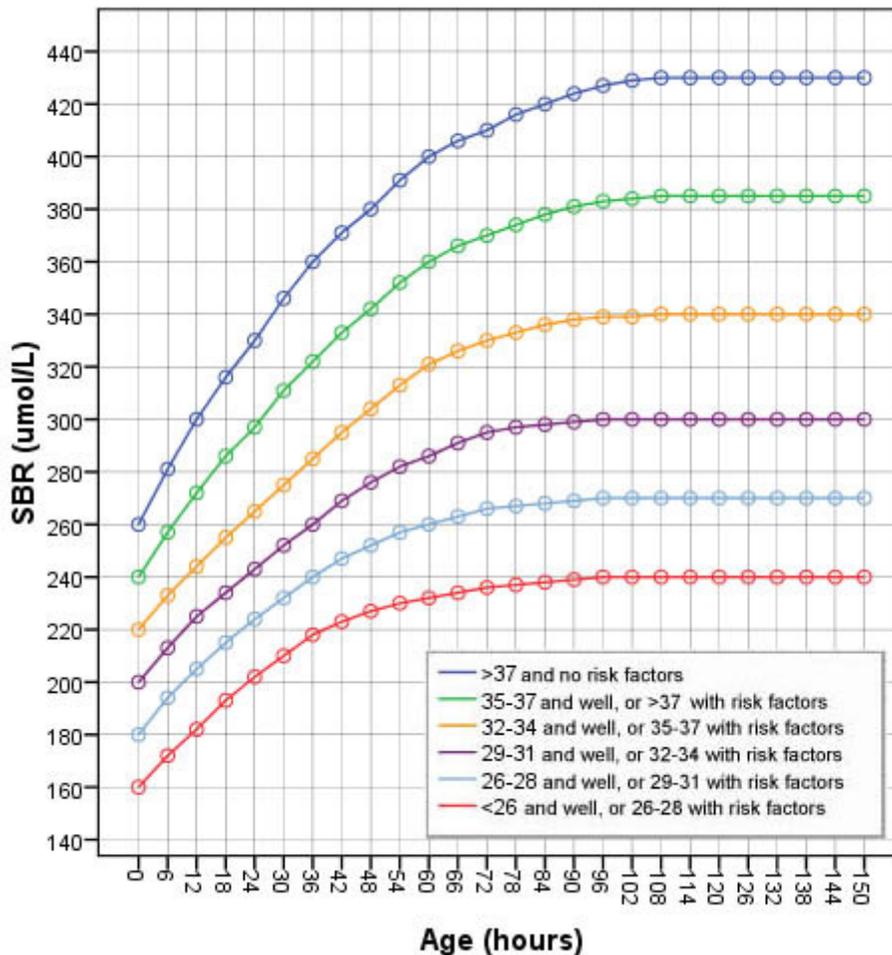
The exchange transfusion thresholds are shown in Figure 2. Such severe jaundice is a medical emergency and exchange transfusion should be performed as soon as possible. It is preferable to anticipate the need for exchange transfusion prior to TSB reaching thresholds, particularly in a baby with known haemolysis. So, consider exchange transfusion where TSB levels are rising faster than 17 micromol/L per hour despite intensive phototherapy in a baby with known haemolysis. Consider exchange in well, non-haemolytic babies only after rehydration and a period of intensive phototherapy.

Babies with known rhesus sensitisation are a special case (see [Haemolytic Jaundice Guideline](#)), and cord blood should be tested for group and DAT, haemoglobin and TSB. Cord haemoglobin less than 100 gram/l and/or SBR above 120 micromol/L should lead to consideration of early exchange transfusion. If not qualifying for immediate exchange, consider giving IVIG early while intensive phototherapy is delivered.

Figure 2. Exchange transfusion thresholds

Plot TSB level according to postnatal age, if above the relevant line for gestation and risk factor criteria, then discuss indication for exchange transfusion with senior consultant.

Disclaimer: Because high medical level evidence does not exist in this area, particularly for the lower gestations, these charts result from a consensus as to safe treatment thresholds.



Source: Adapted from reference 1

Risk Factors: In babies with any of the risk factors below, exchange transfusion should be considered according to the line one below that indicated by their gestational age. These risk factors include:

- Haemolysis,
- G6PD deficiency,
- Asphyxia,
- Proven sepsis,
- Any baby who is unwell: e.g lethargy, temperature instability, respiratory distress, acidosis.
- Bilirubin / albumin ratio > 0.94(> 37 weeks), 0.84 (37-34 weeks), 0.8 (<34 weeks)
(Note: 1gram/L albumin = 15.15 micromol/L albumin)

3. Intravenous Immunoglobulin (IVIG)

There is some evidence that IVIG will reduce the need for exchange transfusions in babies with Rhesus haemolytic disease and other immune haemolytic jaundice.⁷ The evidence is limited by small numbers in the trials and the conclusion of the Cochrane review is cautious about

recommending this treatment. A recent trial showed no benefit but, reflecting the changing landscape of Rh Disease, 66% of the babies enrolled had had in-utero transfusions where the chance of needing exchange will be lower.⁸

IVIg should be considered in isoimmune haemolysis where there is a need to slow the rate of rise of bilirubin in babies who may need an exchange transfusion, particularly if there is likely to be any delay in implementing the exchange. The dose required is 1.0 gram per kg given intravenously over 2 hours; this may be repeated 12 hours later if the TSB levels are still rising.¹

4. Intravenous albumin

The rationale for albumin supplementation is empirical; there is no high quality evidence to support its effectiveness. Consider administering 20% albumin (1 to 2g over 1 hour) as a rehydration fluid for babies with acute bilirubin encephalopathy or possibly even those approaching the level for exchange transfusion where there may be co-existent dehydration and particularly when the serum albumin level is less than 30 gram/L.

5. Other interventions

While these strategies appear biologically plausible, they are not widely used. Apart from the occasional use of phenobarbitone for severe conjugated jaundice, none are currently employed in this nursery.

- *Improve liver function:* **Phenobarbitone** (induces enzymes)
 - *Reduce enterohepatic circulation:* **Agar, activated charcoal, etc.** (sequesters bilirubin in gut)
 - *Reduce production of bilirubin* **Tin mesoporphorin** inhibits enzyme haemoglobin oxidase. Experimental only.
 - *Interruption of breast feeding:* Although there is some observational data associating breast feeding with higher early bilirubin levels there is no evidence that interrupting breast feeding is effective in lowering bilirubin level. Such practice would have important potential harms in terms of interfering with the establishment of lactation or undermining maternal confidence in her ability to successfully breast feed.⁹
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6. Breast Milk Jaundice

This occurs infrequently, peaks in the 2nd or 3rd week, and may persist at moderately high levels for 3-4 weeks before declining slowly. It is a diagnosis of exclusion. The main conditions to be excluded are hypothyroidism and hypopituitarism. In an otherwise well infant, breast milk jaundice is considered a benign condition. If feeding with breast milk is stopped, the serum bilirubin usually falls, however this would very rarely be indicated. The potential harms of stopping breast feeding would outweigh any risks of a mild or moderate hyperbilirubinaemia. The aetiology is unknown, but there is some support for both a hormonal factor in the milk acting on the infant's hepatic metabolism, and an enzyme (lipase) facilitating intestinal absorption of bilirubin.

Discharge and transfer of care planning

Discharge and transfer of care:

Early discharge (before 72 hours) is a risk factor for the development of severe hyperbilirubinaemia, mainly because outpatient surveillance cannot be as close as that provided in the postnatal ward. Infants are at risk of developing significant jaundice after they have gone home.

At RPA, parents are provided with information about jaundice, including what to look for and who they should contact if there are concerns. Further written Parent information can be accessed at:

- The American Academy of Pediatric information sheet can be found at <http://www.healthychildren.org/English/news/pages/Jaundice-in-Newborns.aspx> in English, Spanish, Chinese and Italian.
- NSW Health multilingual Fact Sheet Jaundice in Newborn Babies for information in Arabic, Chinese Traditional, English, Indonesian, Khmer, Korean, Serbian, Tamil, Thai, Turkish and Vietnamese: http://www.mhcs.health.nsw.gov.au/publication_details/7295.asp

Risks of naphthalene-based moth repellents: All parents should be advised to thoroughly wash any baby clothes that have been stored with moth repellents containing naphthalene prior to use. See NSW Health multilingual factsheet No 8780 Health Risks from Exposure to Naphthalene in Moth Balls and Toilet Deodorant Cakes for information in many languages at http://www.mhcs.health.nsw.gov.au/topics/Early_Childhood.html#8780

Contacting Health Care Professionals: Parents should be advised to contact a healthcare professional if:

- their baby becomes jaundiced
- baby's jaundice is worsening
- jaundice is persisting beyond 14 days
- their baby is passing pale stools

Post Discharge Surveillance.

Hospital Based Domiciliary Midwives: RPA has a team of domiciliary midwives whose role it is to visit and provide surveillance of early discharged mothers and babies for the first 4-5 postnatal days. These midwives are equipped with transcutaneous bilirubinometers and have the skill to take capillary or venous blood for TSB if needed. Mobile phototherapy devices are available to treat babies at home in cases where the jaundice has already been investigated and the level is not too far above treatment thresholds.

Severe jaundice after discharge: For babies who develop jaundice after discharge, any TSB above treatment thresholds should be admitted directly to the newborn nursery or to the maternity unit with the mother for immediate investigation and phototherapy. They should not be admitted through the hospital emergency department where unnecessary delays may occur. This is particularly true in babies with TSB above the recommended exchange thresholds (see Figure 2) or a TSB of 428 micromol/L or more. This is a medical emergency.

Prolonged Jaundice: Any term baby with clinically apparent jaundice beyond 2 weeks of age should be referred for investigation. The critical investigation to exclude pathology is a conjugated bilirubin level (should be less than 30 micromols/l).

Key Points

Key Point	Level of evidence
Phototherapy is a safe, effective method for lowering serum bilirubin, and reduces the need for exchange transfusion	★★★★★ ⁸
The level for starting phototherapy is based on observational data only	★★

References

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