CLINICAL GUIDELINE	
Jaundice	
Scope (Staff):	Nursing/Midwifery and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA, KEMH Postnatal Wards

Child Safe Organisation Statement of Commitment

The Child and Adolescent Health Service (CAHS) commits to being a child safe organisation by meeting the National Child Safe Principles and National Child Safe Standards. This is a commitment to a strong culture supported by robust policies and procedures to ensure the safety and wellbeing of children at CAHS.

This document should be read in conjunction with this DISCLAIMER

Contents

Abbreviations

CBR	Conjugated bilirubin	ABO	Blood Group type A, B, O
SBR	Serum bilirubin	DAT	Direct Antibody Test
TcB	Transcutaneous bilirubin	Rh	Rhesus
UBR	Unconjugated bilirubin	PTx	Phototherapy
G6PD	Glucose-6-phosphate dehydrogenase deficiency		

Key Points

- All neonates with clinically identifiable **jaundice < 24 hours of age should be considered high risk** and have a SBR performed immediately to determine a 'baseline' and need for phototherapy. Haemolysis is the commonest cause.
- Neonates born to Rh negative mothers in whom red cell antibodies have been identified during the pregnancy, or who have not had antenatal blood group screening performed, should have a blood group and DAT performed on cord blood.
- When assessing the need for phototherapy using the SBR, the total serum bilirubin level (i.e. SBR) value should be plotted on the appropriate graph and interpreted against the baby's age in hours from birth. The conjugated bilirubin fraction should not be subtracted from the total. In cases where the conjugated bilirubin is > 20 µmol/L or the fractional component is > 20% this should be considered pathological jaundice until proven otherwise.
- Hyperbilirubinaemia is usually managed using phototherapy. The rate of rise of SBR in many instances is more important than the absolute value in determining the need for escalation of therapy, including the consideration for exchange transfusion. In general, infants at high risk for haemolysis should initially have a SBR performed on at least two occasions 4-6 hours apart in order to obtain an accurate assessment of the 'rate of rise'. Bilirubin levels rising ~10µmol/L/Hr represent aggressive haemolysis and require SCN admission, maximal phototherapy and consideration for exchange transfusion.
- Neonates in whom 'physiological' jaundice is considered to be present, may be managed on the postnatal wards, with attention to adequate feeding and hydration state. Following cessation of phototherapy (if required), delay of discharge pending SBR testing to exclude 'rebound' is unnecessary, providing ongoing clinical evaluation for jaundice can occur over subsequent days (i.e. either via Visiting Midwifery Service, or outpatient SBR testing).
- Sunlight exposure is not recommended for the management of hyperbilirubinaemia since it is an uncontrolled source of multiple wavelengths of light, only a limited spectrum of which is appropriate for management of jaundice. Sunburn is a risk and parents should be discouraged from using this approach.

Background

Jaundice occurs in ~60% of term newborns and 85% of preterm infants as a result of elevated serum bilirubin levels. Hyperbilirubinaemia may be unconjugated (i.e. lipid soluble, pre-hepatic phase) or conjugated (i.e. water soluble, post hepatic conjugation) in nature. Unconjugated hyperbilirubinaemia which occurs < 24 hours of life, or is prolonged beyond 14 days should be considered pathological until proven otherwise. Conjugated hyperbilirubinaemia represented by an absolute value of 20 µmol/L or > 20% of the total serum bilirubin (SBR) is always pathological and must be investigated in consultation with senior Paediatric staff. Phototherapy is indicated in unconjugated hyperbilirubinaemia to prevent acute bilirubin encephalopathy and kernicterus (chronic bilirubin encephalopathy) arising as a consequence of bilirubin deposition in the basal ganglia and certain brainstem nuclei.

NOTE: This guideline focusses on unconjugated hyperbilirubinaemia and its management, since this is the problem most commonly encountered in the newborn period. All cases where conjugated hyperbilirubinaemia is suspected clinically (e.g. pale stools, very dark urine, 'green-yellow' jaundice) should be discussed urgently with senior Paediatric staff.

Acute and Chronic Bilirubin Encephalopathy (Kernicterus)

Acute Bilirubin Encephalopathy

The acute manifestations of bilirubin toxicity may be observed in the first weeks after birth and include:

- Hypotonia.
- High pitched cry.
- Poor feeding.
- Lethargy.

Progression of symptoms may occur:

- Hypertonicity with opisthotonus or retrocollis.
- Seizures.
- Impaired conscious state, coma.

Bilirubin Induced Neurological Dysfunction (BIND)

Bilirubin Induced Neurological Dysfunction (BIND) is a more subtle form of encephalopathy, which can occur at levels lower than those that cause classical Kernicterus[1]. Whilst classical Kernicterus is very uncommon in preterm infants, there are concerns that BIND may be more prevalent, with under-diagnosis likely occurring due to subtle clinical manifestations. Preterm infants are at higher risk due to having increased production of bilirubin, lower albumin levels, immature blood brain barrier and immature neurons, which are more prone to injury[2]. In ventilated extremely preterm infants (501-750g) having a lower threshold to treat with phototherapy is complicated by evidence suggesting aggressive treatment can not only decrease neurodevelopmental impairment, but has a significantly increased relative risk of death[3]. Whilst there is currently no clear safe threshold treatment of hyperbilirubinaemia in preterm infants, there is at least some evidence showing treatment thresholds at which we can see improved neurodevelopment outcomes[4]. Taking a more gentle approach with the application of phototherapy to extremely preterm infants may be a method to potentially mitigate the adverse effects of phototherapy

Kernicterus - Chronic Bilirubin Encephalopathy

Kernicterus is a pathological diagnosis whereby unconjugated bilirubin is deposited in the basal ganglia and brainstem nuclei. The clinical picture is unremitting and the pathological changes are permanent in nature, resulting in chronic neurological impairment, neuro-cognitive delay and dysfunction of motor control and tone. Neurological features include:

- Athetoid cerebral palsy.
- Seizures.
- Oculomotor dysfunction.
- Sensori-neural deafness.
- Developmental delay.
- Neuro-cognitive impairment.

Diagnostic Evaluation

Early onset (< 24 hours) and Aggressive Jaundice:

Jaundice occurring within the first 24 hours of life should always be considered pathological. Haemolysis resulting from major or minor blood group antigen incompatibility is the most common cause of early and aggressive haemolysis. Early aggressive phototherapy, admission to SCN and consideration for exchange transfusion may be necessary. In circumstances where the risk of haemolysis is significant (e.g. known Rh-isoimmunisation in utero or elevated titres to red cell minor antigens), a SBR, FBP and direct antibody test (DAT) should be collected from cord blood. SBR should be monitored initially every 4-6 hours using the appropriate chart to determine the 'rate of rise', to determine the appropriate amount of phototherapy, and if necessary, to prepare for the possibility of IVIG administration or exchange transfusion. An increase in SBR of 10µmol/L per hour is considered significant and is likely to necessitate multiple-lamp phototherapy, IVIG and potentially exchange transfusion. All infants in this category should be discussed with the Paediatric consultant on call as a matter of urgency.

Causes of early jaundice include:

- Haemolysis:
  - Rhesus Iso-immunisation.
  - Minor red cell antigen incompatibility.
  - ABO incompatibility.
- Sepsis.
- Rarer causes:
  - Red cell enzyme defects (e.g. G6PD).
  - Red cell membrane defects (e.g. hereditary spherocytosis).
  - Crigler-Najjar Syndrome.

Jaundice between 24 hours and 14 days:

Jaundice occurring after the first 24 hours and lasting less than 14 days is most commonly physiological in nature. Causes of hyperbilirubinaemia with onset during this period include:

- Physiological jaundice.
- Breakdown of extravasated blood.
- Polycythaemia.
- Haemolysis.
- Sepsis

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Prolonged or Late Onset Jaundice (> 10-14 days):

Jaundice in which the onset is relatively late (i.e. > 10 days), or is prolonged should be considered pathological until possible aetiological factors have been excluded. Unconjugated hyperbilirubinaemia may occur in isolation, or in association with elevated conjugated bilirubin (e.g. idiopathic neonatal hepatitis, TORCH infections). Causes of prolonged or late-onset jaundice include:

- Ongoing haemolysis (e.g. ABO incompatibility).
- Hypothyroidism (most detected on day 3 via the newborn screening card).
- Sepsis/urinary tract infection.
- Breast milk jaundice (peak around day 7-14, duration up to 6 weeks after birth).

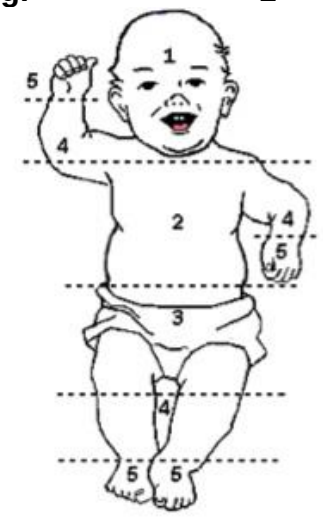
Causes of jaundice characterised by either conjugated hyperbilirubinaemia or mixed conjugated and unconjugated hyperbilirubinaemia include:

- TORCH infections (e.g. Toxoplasmosis, Rubella, Cytomegalovirus, Syphilis).
- Sepsis.
- Congenital biliary tract obstruction (e.g. Biliary atresia, choledochal cyst).
- Metabolic disorders (e.g. Hypothyroidism, Galactosaemia, α1-antitrypsin deficiency).
- Haemochromatosis.
- Idiopathic neonatal hepatitis.

Clinical Assessment

All newborns should be assessed at least every 12 hours for jaundice. Appearance and progression tends to occur in a cephalo-caudal manner. Kramer's Rule provides a mechanism for the clinical assessment of jaundice severity by the proportion of the skin involved. Whilst this provides a useful guide, visual estimation of jaundice severity is prone to error, and is particularly difficult in darkly pigmented infants. All infants in whom the severity of jaundice is in question, especially those with risk factors, should have a transcutaneous bilirubin or serum bilirubin measurement performed.

Fig. 1 - Kramer's Rule



Zone	1	2	3	4	5
Definition	Head and neck	Upper trunk	Lower trunk and thighs	Arms and lower legs	Palms and soles
TSB (micromol/L)	100	150	200	250	>250

Investigations

Categorisation of risk in Neonatal Jaundice

Infants at HIGH RISK for early/aggressive jaundice:

Infants at high risk for early and / or aggressive jaundice include those with raised antibody titres to red cell antigens, especially Rhesus and some minor group antigens. Women who are Rh(-) or in whom red cell antibodies have been detected have generally been monitored during pregnancy. Repeated titre results may be available. In severe cases of Rhesus isoimmunisation, intra-uterine blood transfusion may have been administered. These infants are at increased risk for unconjugated hyperbilirubinaemia. The following investigations should be performed:

- Review maternal notes:
    - Blood group and Rhesus status.
    - Anti-D administration status.
    - Presence of any red cell antibodies and changes in titre concentrations.
    - Presence of foetal hydrops, pleural/peritoneal effusion, anaemia, cardiac failure.
    - Need for intra-uterine blood transfusion.
- On cord blood, perform:
    - FBP, SBR.
    - Direct Antibody Test.

FBP, SBR and DAT should be performed on cord blood at the time of delivery. A repeat SBR should be performed 4-6 hours later in order to monitor the rate of rise and enable commencement of early phototherapy and preparation for intravenous immunoglobulin or exchange transfusion as necessary.

Infants with risk factors for non-physiological or jaundice potentially resistant to phototherapy:

Physiological jaundice usually presents between 24 hours and 7 days of life. Risk factors for more severe jaundice include prematurity, infection, or antibodies to red cell antigens (e.g. ABO incompatibility, minor antigens - Kell, Duffy, c, e, E and others). ABO incompatibility, particularly in the presence of a positive DAT, may produce a more aggressive picture than physiological jaundice, with potential for a more rapid rise in SBR and also a more prolonged resolution phase which may last several weeks. Jaundice resulting from haemolysis of any cause may show a resistance to phototherapy necessitating an increase in the number of phototherapy lights, use of a ‘Bili-Blanket’ and more frequent monitoring of SBR, feeding and hydration status. Haemolytic causes of jaundice are also more likely to rebound following cessation of phototherapy and a low threshold for testing the SBR in the days following withdrawal of treatment should be maintained.

Glucose-6-Phosphate Dehydrogenase deficiency (G6PD) should be considered in infants in whom the response to phototherapy is poor, or there is a relevant family, ethnic or geographic history. The condition is widespread, being present in approximately 12% of African Americans, and prevalence is higher in the Mediterranean, Middle East, Southeast Asia and Africa.[1]

Transcutaneous Bilirubin (TcB) Measurement

Transcutaneous measurement of bilirubin in this hospital uses a JM-103 bilirubinometer. TcB measurements may be performed as an initial screen for jaundice in the well, term or late preterm (>35 weeks) infant **who is greater than 24 hours of age**. Infants in whom jaundice presents less than 24 hours of age, or where other risk factors are present (e.g. preterm, maternal antibodies, possible sepsis, G6PD risk, etc.) should have an SBR performed in the first instance.

Jaundice onset	TcB	Action
< 24 hours	_____	Perform SBR
24-48 hours	> 140 µmol/L	Perform SBR
48-72 hours	>200 µmol/L	Perform SBR
> 72 hours	>260 µmol/L	Perform SBR

The trans-cutaneous bilirubin is unreliable following the commencement of phototherapy. An SBR should be performed to track progress once lights are instigated. The frequency with which monitoring should occur varies with the absolute SBR, the expected or actual rate of change of serum bilirubin level, and risk factors present. In general, high risk infants should be monitored 4-6 hourly initially. Low risk infants can be monitored daily.

Management

See, Jaundice: Phototherapy and Treatment Graphs

Infants with Aggressive/Haemolytic Jaundice

Infants in whom aggressive jaundice is present are at risk of rebound hyperbilirubinaemia following withdrawal of phototherapy. Rhesus isoimmunisation and certain minor red cell antigen incompatibilities are risk factors and infants requiring phototherapy for these problems should have lights removed sequentially once stabilisation of the SBR has occurred. An SBR should be performed the day after cessation of phototherapy, and electively post-discharge if there is suspicion that jaundice is again worsening, if there is poor feeding or lethargy. Excessive haemolysis in these circumstances may exaggerate and prolong the normal nadir in Haemoglobin level seen during the first 4-8 weeks of life, on occasion necessitating blood transfusion. Consequently, infants identified as having a haemolytic cause for jaundice should be considered for follow-up in 4-6 weeks with a FBP and reticulocyte count performed at that time. Consider prescribing folic acid on discharge of such infants.

Infants with Physiological Jaundice

Infants considered to have physiological jaundice, who are feeding appropriately and have weight loss within acceptable limits (i.e. less than 10% below birthweight) may be discharged without ongoing monitoring of SBR. Monitoring of skin colour, feeding, weight gain and lethargy should be performed by a Visiting Midwife (VMS) or Child Health Nurse.

Quick Reference A: Causes of Neonatal Jaundice

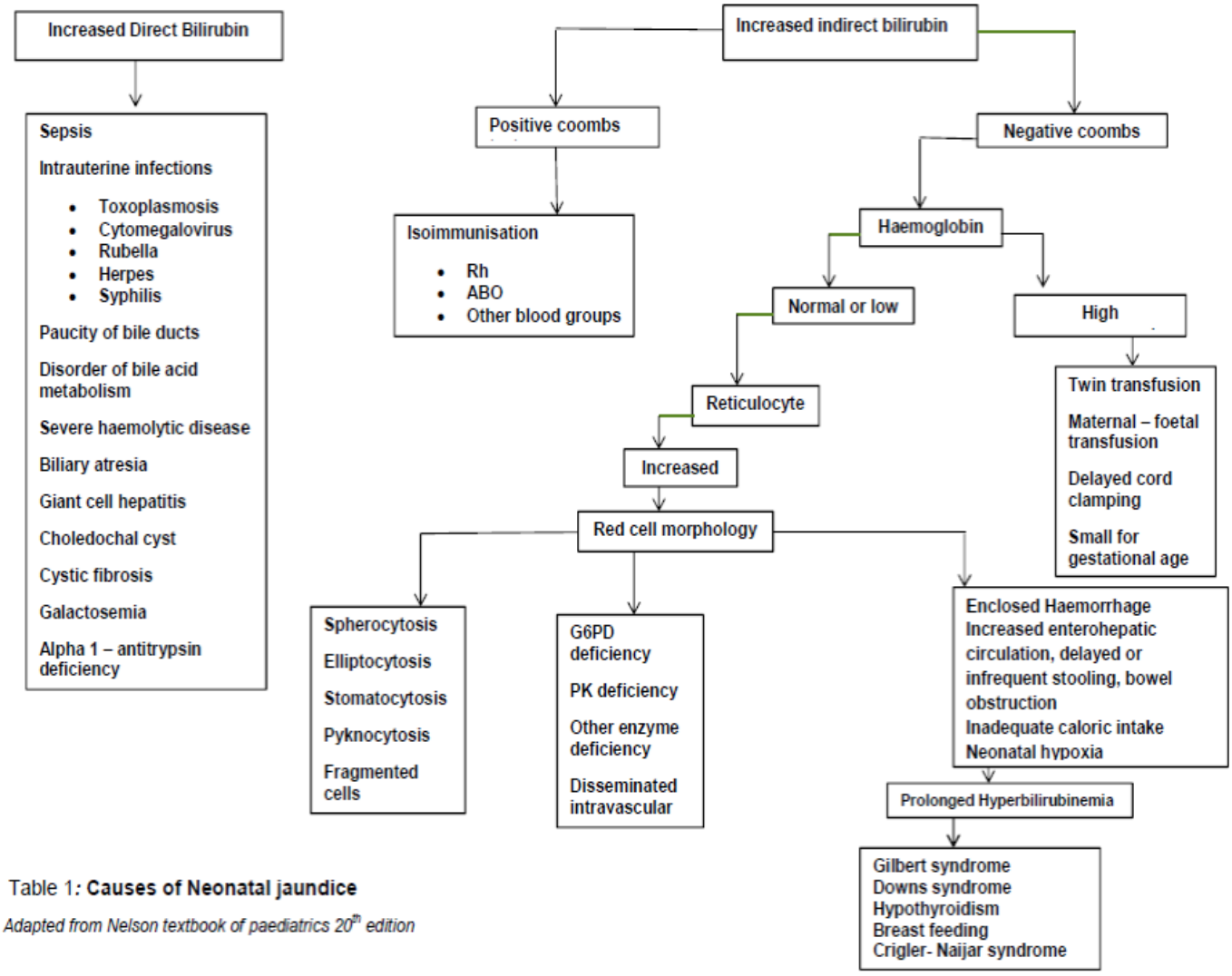


Table 1: **Causes of Neonatal jaundice**

Adapted from Nelson textbook of paediatrics 20th edition

Quick Reference B: Jaundice Assessment & Management Flow Chart

Approach to Jaundice in the Infant ≥35 Weeks Gestation
All infants should be clinically evaluated for jaundice every 8-12 hours

High Risk

Any of:
Rh Iso-immunisation

Rh(-) mother, Ab+

In-utero blood Tx, IVIG

High antenatal titres of

At Delivery:

Cord blood:

Urgent DAT, SBR, FBP

Discuss with Consultant

Moderate Risk

Any of:
Maternal Group O

Antenatal antibodies to minor antigens

Preterm <38 w

Sick Infant (e.g. sepsis)

If Jaundiced:
TcB/SBR

Repeat TcB/SBR 12-24hrly

Low Threshold for DAT

TcB/SBR 12-24 hrly

Consider CRP, FBP if possible sepsis

Low Risk

All of:
Term ≥ 38 w

Jaundice onset ≥48

Anti-D given to Rh(-) mother

No antibodies detected

If Jaundiced:
TcB / SBR

Repeat TcB/ SBR daily

Monitor Feeding

Consult Phototherapy Chart; See Threshold Graphs or Phototherapy Guideline

Needs PhotoTx? Or DAT+

Yes
Discuss with Consultant:
?SCN Admission,
PhotoTx strategy
Concerning rate of Rise of SBR: 4-5µmol/L/hr
Repeat SBR 4-6 hrly

No
Repeat SBR in 6-12 hours until rate of rise clear
If below Tx range at 24 hours treat as per moderate risk

Needs PhotoTx?

Yes
Start PhotoTx
SBR, DAT next day*
Wean photoTx daily
Consider SBR day after discharge to monitor 'rebound'

No
TcB/SBR in 12-24 hours

Needs PhotoTx?

Yes
Start PhotoTx
SBR, DAT following day *
Daily Weight
Attention to feeding

No
Inspect for jaundice daily
TcB/ SBR if jaundiced

* Direct Antibody Test (DAT) should be done on all infants at risk of haemolysis and any infant requiring phototherapy.

Discharge Planning

- Consider SBR day after discharge for DAT (+) jaundice needing PhotoTx (baby will need to return to EC)
- Physiological jaundice may be monitored by parents/VMHS at home. SBR may be performed prn
- Continuing admission for 24 hours after stopping PhotoTx is not mandatory if the infant is feeding well, weight is <10% below BW and monitoring (via VMS or CHN) is available post-discharge
- Haemolytic jaundice (e.g. Rh or ABO incompatibility) is more likely to 'rebound', has more prolonged course and on occasion may result in anaemia in the weeks after discharge.

Related CAHS internal policies, procedures and guidelines

Jaundice: Phototherapy

Exchange Transfusion

References and related external legislation, policies, and guidelines

1. American Academy of Pediatrics. Subcommittee on Hyperbilirubinaemia. Management of Hyperbilirubinaemia in the Newborn Infant 35 or More Weeks of Gestation. Pediatrics. 2004; 104(1):297-316.
2. Bhutani VK and the Committee on the Fetus and Newborn. American Academy of Pediatrics. Phototherapy to prevent severe neonatal hyperbilirubinaemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2011; 128(4):e1046-e1052.
3. Canadian Paediatric Society. Position Statement (FN2007-02). Guidelines for detection, management and prevention of hyperbilirubinaemia in term and late preterm newborn infants. Paediatr Child Health. 2007; Vol 12, Supp B: 1B-12B.
4. Atkinson M, Budge H. Review of the NICE guidance on neonatal jaundice. Arch Dis Child Educ Pract Ed. 2011;96:136-140.
5. Kramer LI. Advancement of dermal icterus in the jaundiced newborn. Am J Dis Child. 1969;118(3):454-458.
6. Polin RA, Fox WW, Abman SH. Fetal and Neonatal Physiology. 3rd Edition. 2004. pp 1206-09.
7. Rennie JM. Roberton's Textbook of Neonatology. 4th Edition. 2005. pp 671-6768.
8. De Luca D, Zecca E, de Turris P, Barbato G, Marras M, Romagnoli C. Using Bilicheck™ for preterm neonates in a sub-intensive unit: Diagnostic usefulness and suitability. Early Human Development. 2007 (83); 313-317.
9. Schmidt ET, Wheeler CA, Jackson GL, Engle WD. Evaluation of transcutaneous bilirubinometry in preterm neonates. J Perinat. 2009; 29: 564-569.
10. Fouzas S, Karatza AA, Skylogianni E, Mantagou L, Varvarigou A. Transcutaneous bilirubin levels in late preterm neonates. J Pediatr. 2010; 157: 762-766.

Useful resources (including related forms)

Jaundice: Follow up Letter

Jaundice: Threshold Graphs

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