GUIDELINE

Jaundice

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA, Postnatal Wards

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this disclaimer

Contents

Aim

To guide staff in the recognition and optimal treatment of acute bilirubin encephalopathy and prevention of kernicterus (chronic bilirubin encephalopathy) consequently.

Risk

Failure to follow a standardised risk assessment approach to the management of jaundice may lead to delay in diagnosis and treatment resulting in hyperbilirubinaemia neurotoxicity.

Key Points

- Visual determination of bilirubin levels are inherently problematic, any infant who appears clinically jaundiced <24hrs after birth should undergo formal evaluation with either Transcutaneous Bilirubin (TcB) or Total Serum Bilirubin (TSB) measurements. These infants should be considered high risk, where a haemolytic process is the most likely cause of the jaundice.
- Use hour specific treatment graphs when making clinical decisions regarding treatment and escalation of care (Jaundice: Phototherapy and Treatment Graphs).
- Use postmenstrual age when using the treatment graphs.

Background

- More than 80% of newborn infants will have some degree of jaundice as a result of elevated serum bilirubin levels. Hyperbilirubinaemia occurs when there is an imbalance between bilirubin production, conjugation and elimination. Unconjugated hyperbilirubinaemia which occurs < 24 hours of life or is prolonged beyond 14 days should be considered pathological until proven otherwise.
- Acute bilirubin encephalopathy and kernicterus (chronic bilirubin encephalopathy) arise as a consequence of bilirubin deposition in the basal ganglia and certain brainstem nuclei. Acute cases may be observed in the first weeks of life with hypertonia, retrocollis (neck extension), opisthotonos (state arching of head, neck and spinal column) and recurrent apnoea. Kernicterus is a permanent disabling neurological condition whereby unconjugated bilirubin is deposited in the basal ganglia and brainstem nuclei. This is characterized by some or all of the following:

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

- Care should be escalated when an infant's TSB reaches or exceeds the **escalation-of-care threshold**, defined as **34 µmol/L below the exchange**

transfusion threshold, as detailed in the hour-to-hour-specific TSB, and the presence of risk factors for bilirubin neurotoxicity exchange transfusion. See Appendix 2: Escalation of care) for details and refer to the Exchange Transfusion guideline when required.

- Conjugated (direct) hyperbilirubinemia (17umol/L), which is also associated with pale stools, is considered pathological and warrants diagnostic evaluation.

Prevention of Hyperbilirubinaemia associated with isoimmune Haemolytic Disease

- Prevention of hyperbilirubinaemia begins in pregnancy by recognising and treating women who are at risk of developing antibodies to red cell antigens, which can lead to haemolytic disease of the newborn.
- Pregnant women should be tested to determine their ABO blood group and Rh(D) type. The approach to identify newborns with maternal anti-erythrocyte antibodies and guide early management is outlined in Appendix 1.
- If the maternal blood type is Rh(D) negative, the Rh type of the infant should be determined to assess the need for administration of RhIG (anti D) to the mother.
- If the maternal antibody screen is positive or unknown (no prenatal antibody screen), the infant should have a DAT and the blood group determined as soon as possible from either cord or peripheral blood.

ABO incompatibility

- Mother with blood group O becomes pregnant with a fetus with a blood group of A, B, or AB. The mother's serum contains naturally occurring anti-A and anti-B, which tend to be of the IgG class and can cross the placenta and haemolyse the fetal RBCs.
- Can lead to a more aggressive jaundice than physiological jaundice with the potential for a more rapid rise in TSB and a more prolonged resolution phase which may last several weeks. Cord blood should be sent for routine DAT at birth on all neonates born to Group O mothers.

Glucose-6-Phosphate Dehydrogenase deficiency (G6PD)

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. Measuring G6PD activity during or soon after a haemolytic event or after an exchange transfusion can lead to a falsely normal result. G6PD activity should be measured at least 3 months later.

Age of onset

- **Jaundice onset <24hrs**

Should be considered abnormal/pathological and is most likely to be a haemolytic process.

- **Jaundice between 24 hours and 14 days**

Is most commonly physiological in nature. Causes include:

  - Haemolysis.
  - Physiological jaundice.
  - Suboptimal intake hyperbilirubinaemia
  - Polycythaemia.
  - Sepsis
  - Breakdown of extravasated blood.
  - Prematurity

Prolonged or Late Onset Jaundice (> 14 days)

Is a relatively common finding but should alert to the possibility of cholestasis. Screening all jaundiced newborns at 2-weeks will detect cholestasis in relatively few cases so the following recommendations are advised:

- A thorough physical examination is crucial to evaluate a jaundiced infant. Attention to hepatomegaly, splenomegaly and ill appearance warrants special considerations, as well as direct visualisation of stool pigment.
- Measurement of total and conjugated (direct) serum bilirubin at 2 weeks in formula-fed infants.
- Measurement of total and conjugated (direct) serum bilirubin at 3 weeks in breast-fed babies that appear otherwise well clinically.
- Conjugated (direct) hyperbilirubinemia (17umol/L) is considered pathological and warrants diagnostic evaluation. A direct bilirubin concentration >20% of the total is no longer regarded as necessary for the diagnosis of cholestasis.
- As well as considering biliary atresia, also consider other causes for direct hyperbilirubinaemia including urinary tract infection, isoimmune haemolytic disease, sepsis, and some inborn errors of metabolism.
- Measurements of serum bilirubin should always be fractionated into unconjugated (indirect) or conjugated (direct) hyperbilirubinemia.

Clinical Assessment of Jaundice, Bilirubin Measurements

- All infants should be visually assessed for jaundice at least every 12hrs following birth, then 24hrly until discharge. TcB or TSB should be measured as soon as possible for infants noted to be jaundiced <24hrs after birth.
- Use hour specific treatment graphs when making clinical decisions regarding treatment and escalation of care (Jaundice: Phototherapy and Treatment Graphs).
- Throughout WA hospitals (except Fiona Stanley hospital) the TSB is measured using the Vitros ® system using reference material SRM 916a, which means there should be little if any interlaboratory variation. Where different systems are used up to 20% interlaboratory variation can be observed.
- There is good correlation between TcB measurements and TSB concentrations with TSB generally within 51µmol/L of the TcB among newborn infants with TSB concentrations <255 µmol/L. TSB should be measured if the TcB exceeds or is within 51 µmol/L of the phototherapy threshold or if the TcB is ≥255 µmol/L.
- ABL-90 Flex Radiometer has been validated as a Point of Care (POC) test in WA for use in term infants. This can be used for initial screening, with formal lab measurements recommended for decisions regarding commencement of treatment. If there is good correlation, the gas machine results may also be used for ongoing surveillance.
- It is recommended that any infant admitted to a general ward (including postnatal wards and family birth centre), have either a TcB or TSB measured between 24 and 48hrs after birth or before discharge if that occurs earlier.

Management of Low-Risk Infants (not haemolytic or early onset <24hrs)

- Decisions to initiate phototherapy or deescalate care are guided by the treatment threshold jaundice graphs, which consider gestational age, the hour-specific TSB, rate of rise of TSB and the presence of risk factors for bilirubin neurotoxicity. If more than 1 TcB or TSB measure is available, the rate of increase may be used to identify infants at higher risk of subsequent hyperbilirubinemia. A rapid rate of increase 5.1 µmol/L per hour in the first 24 hours or 3.4 µmol/L per hour thereafter is exceptional and suggests haemolysis. In this case, perform a DAT if not previously done.
- If the maternal blood is group O RhD positive and the maternal antibody screen is negative, it is recommended to test the cord blood for the infants blood type and DAT
- Neonates with ‘physiological’ jaundice may be managed on the postnatal wards, with attention to adequate feeding and hydration state.
- Refer to Appendix 3 for follow up of infants discharged who didn’t receive phototherapy. Use clinical judgement and shared decision making to determine when to repeat bilirubin within this 4 to 24hr time window. Clinical judgement

includes physical examination, presence of risk factors for the development of hyperbilirubnaemia or hyperbilirubinaemia neurotoxicity risk factors, feeding adequacy, weight trajectory, and family support.

- Sunlight exposure is not recommended for the management of hyperbilirubinaemia, and sunburn is a risk. Parents should be discouraged from using this approach.

Management of HIGH RISK infants (Positive antibody screen or early onset Jaundice <24hrs)

Infants at high risk for early and / or aggressive jaundice include the following:

- Preterm (risk increases with each additional week less than 40 week)
- Jaundice in the first 24 hr after birth
- Haemolysis from any cause, if known or suspected based on a rapid rate of increase in the TSB or TcB of >5µmol/l per hour in the first 24 hours or 3.4 µmol/l per hour thereafter.
- Pre-discharge transcutaneous bilirubin (TcB) or total serum bilirubin (TSB) concentration close to the phototherapy threshold
- Phototherapy before discharge
- Parent or sibling requiring phototherapy or exchange transfusion
- Family history or genetic ancestry suggestive of inherited red blood cell disorders, including glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Exclusive breastfeeding with suboptimal intake
- Scalp hematoma or significant bruising
- Down syndrome
- Macrosomic infant of a diabetic mother
- Women who are RhD negative 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 RhD isoimmunisation, intra-uterine blood transfusion may have been administered. These infants are at increased risk for unconjugated hyperbilirubinaemia.

History and Investigations

Review maternal notes:

- Blood group and RhD status.
- Antenatal prophylaxis administration of RhD immunoglobulin (RhD Ig) (Anti-D)
- Presence of any red cell antibodies and changes in titre concentrations.
- Presence of foetal hydrops, pleural/peritoneal effusion, anaemia, cardiac failure.
- Any intra-uterine blood transfusion performed.

- Mothers who received RhIG can have a positive antibody screen for anti-Rh(D), and RhIG can cause a positive DAT (anti- RhD) in the infant but generally no haemolysis.
- If an infant's DAT is known to be positive only to anti-Rh(D) because the mother received RhIG during pregnancy and the mother was known not to have Rh(D) antibodies before receiving RhIG, the infant can be treated as if the infant is DAT negative. However, any infant with a positive DAT attributable to an antibody other than anti-Rh(D) following maternal receipt of RhIG should be considered to be DAT positive.

At the time of birth perform on cord blood:

- FBC
- Blood Group and DAT
- TSB

Subsequent TcB or TSB measurements:

- Measure every 4 hours 2 times, then every 12 hours 3 times. Use (Jaundice: Phototherapy and Treatment Graphs) to determine treatment with phototherapy or escalation of care (See Appendix 2: Escalation of care).
- If more than 1 TcB or TSB measurement is available, the rate of increase may be used to identify infants at higher risk of subsequent hyperbilirubinemia.
- A rapid rate of increase 5.1 µmol/L per hour in the first 24 hours or 3.4 µmol/L per hour thereafter is exceptional and suggests haemolysis. In this case, perform a DAT if not previously done.
- Refer to section below on phototherapy units and phototherapy management

Escalation of care (near or above Exchange Transfusion Threshold)

- Care should be escalated when an infant's TSB reaches or exceeds the **escalation-of-care threshold**, defined as **34 µmol/L below the exchange** transfusion threshold, as detailed in the hour-specific TSB, and the presence of risk factors for bilirubin neurotoxicity:
  - Prematurity (Gestational age <38 weeks)
  - Albumin <3.0g/dL
  - Isoimmune Haemolytic disease
  - G6PD or other haemolytic diseases
  - Sepsis
  - Any significant clinical instability in the last 24hrs
- Conjugated (direct) hyperbilirubinemia (17umol/L), which is also associated with pale stools, is considered pathological and warrants diagnostic evaluation.

- See Appendix 2: Escalation of care) for details and refer to the Exchange Transfusion guideline when required.

Phototherapy Units and Dosage

- The aim of phototherapy treatment is to lower the bilirubin level and to avoid exchange transfusion. Consider the age of the infant in hours, risk factors, and the rate of rise of serum bilirubin. See Phototherapy and Exchange Transfusion Treatment Graphs.
- Blue is the light range (420-470 nm) in which bilirubin most effectively absorbs light; when phototherapy is applied to bilirubin in the skin, the light absorbed causes photochemical reactions. The other major product from phototherapy is lumirubin, which is an irreversible structural isomer converted from native bilirubin that can be excreted by the kidneys in the unconjugated state.
- Phototherapy units have differing energy outputs. The higher the microwatts per cm^2 ($\mu W/cm^2$) the more efficient the unit is.
- Direct contact with a Bili blanket provides the most efficient form of phototherapy treatment therefore choose the appropriate size pad.
- Light dosage is dependent on distance from patient. The closer the light source is to the patient the more intense the irradiance becomes.
- Lullaby phototherapy is to commence on bright light function i.e.. select (II) switch to deliver high dose irradiance at 35 cm lamp distance from infant.
- 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 TSB, feeding and hydration status.

TYPE	STRENGTH	Low Dose Irradiance	High Dose Irradiance
		(lamp distance from infant if applicable)	
Giraffe PT Spot LED	18-45 $\mu W/cm^2/nm^{-1}$	50-60cm (23cm from roof of omnibed)	40-50cm (almost touching roof of omnibed)
Phototherapy blanket (fibre optic/LED)	Large and small pads sizes are available 35-50 $\mu W/cm^2/nm^{-1}$	Small 35$\mu w/cm^{-2}/nm^{-1}$	Large 50 $\mu w/cm^{-2}/nm^{-1}$
Lullaby	22-45 $\mu W/cm^2/nm^{-1}$	40-50cm = low light or (I) on switch	35cm =bright light or (II) on switch

Phototherapy Commencement and Complications

- Maintain stable temperature regulation - take baseline temperature then monitor as per level of care and maintain a Neutral Thermal Environment that is appropriate for the infants age and gestation. Consider both risks of overheating and hypothermia from exposure.
- Once phototherapy commences then monitoring of the TSB are essential as the skin colour will no longer be a guide to the level.
- Total fluid volume meets infant's requirements as infants under phototherapy are at risk of increased insensible water loss which can lead to dehydration
    - Adjust total fluid volume – usually >10-15%
    - Monitor urine output, stools, daily weight
    - Monitor PGL's, U&E's, Urine: Specific gravity as ordered by medical team
- Early feeding assists with elimination of meconium, reducing the available bilirubin for reabsorption and thus interfering with the enterohepatic circulation depending on the Gestational Age of patient.
- Maximise infants skin exposure to light – remove all clothes apart from nappy, check the distance of the unit being used from the infant.
- Monitor skin integrity as infants undergoing phototherapy can develop erythematous macular rash or purpuric rash associated with transient porphyrinaemia and can develop loose stools – maintain with good hygiene and appropriate nappy care regime. Review by CNC/Medical as needed.
- Protect infant's eyes from light by covering infant's eyes with appropriate size eye cover without applying excessive pressure or occlude nares, remove eye cover with each set of cares to evaluate eyes. Leave pads off for short periods when the infant is out for a cuddle or feed with parent/carer
- A benign rare condition called bronze baby syndrome can develop is a result of direct hyperbilirubinaemia.
- Document start time and type unit in use on MR489/491 and in nursing progress notes (MR420.00) and medical team to update problem list (MR485.03) and document any TSB results in the summary flow chart (485.02)

Ceasing Phototherapy and Discharge

- Therapy can be ceased when the TSB is ≥20µmol/L below treatment threshold and the infant is old enough to handle the bilirubin load. Document date and time of cessation on MR489/91, and cessation order on MR420.00. Update MR485.03.
- Perform a TSB at a minimum the day after cessation of phototherapy.
- Infants with haemolytic causes of jaundice are at greater risk of rebound when phototherapy is stopped, and they need ongoing TSB monitoring with a low

threshold for testing in the days following cessation of phototherapy. Use clinical judgment considering risk factors, response to therapy and level of TSB to determine specific timings (4 - 24 hourly).

- Infants identified as having a haemolytic cause for jaundice should be considered for a 4-6 week follow up with FBP and reticulocyte count and consider prescribing folic acid on discharge for such infants. 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
- Monitoring skin colour, feeding, weight gain and lethargy should be performed by Visiting Midwife (VMS) or Child Health Nurse.

Intravenous Immunoglobulin (IVIg) in Severe Haemolytic Disease of the Newborn

Haemolytic disease of the fetus and newborn (HDFN), also known as alloimmune HDFN or erythroblastosis fetalis, is caused by the destruction of red blood cells (RBCs) of the neonate or fetus by maternal immunoglobulin G (IgG) antibodies.

IVIg is indicated to prevent the need for first or repeat exchange transfusion in select cases of severe haemolytic disease of the newborn (HDN) undergoing intensive phototherapy. Can be used when:

- Positive Direct Antiglobulin Test (DAT)
- Total serum bilirubin (TSB) continues to rise at 8-17mmol/L/hour despite intensive phototherapy
- TSB is within 35-50mmol/L of the threshold for exchange transfusion.
- Other isoimmune haemolytic disease
- Difficulties obtaining appropriate blood for exchange transfusion
- Parental refusion for exchange transfusion.

If necessary Privigen may be re-dosed 12 hours after first administration. Studies have not shown any benefit in HDN in preterm infants.

IVIg requires parental consent for blood products. Observations and monitoring as per blood products protocols.

3B PCH - Privigen (Immunoglobulin Normal 5g/50mLs) is included in the CAHS formulary- restricted to haemolytic disease of newborn in neonatal patients and is stored in the automated dispensing machine (ADM) under Immunoglobulin to enable immediate access for use in Priority 1 retrievals after authorisation from the NETS or 3B Consultant.

KEMH - Requires Haematologist approval before issuing from Transfusion Medicine.

See Privigen 10 in Immunoglobulin Products – Transfusion Medicine Protocol.

Related CAHS internal policies, procedures and guidelines

Privigen 10 in Immunoglobulin Products

Exchange transfusion.

Useful resources (including related forms)

Jaundice: Follow up Letter

Jaundice: Threshold Graphs

Phototherapy and Exchange Transfusion Treatment Graphs

References and related external legislation, policies, and guidelines

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This document can be made available in alternative formats on request.

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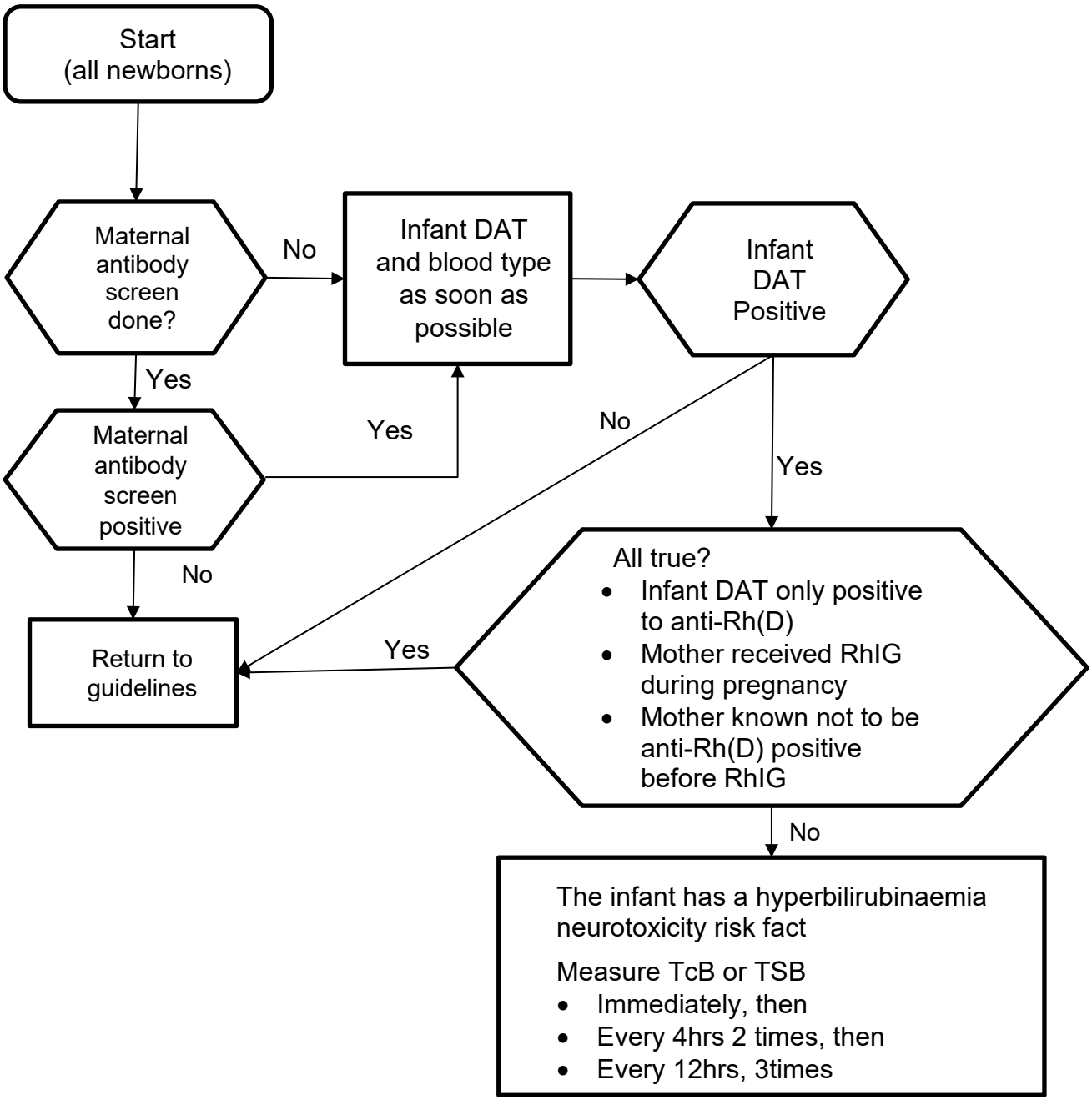
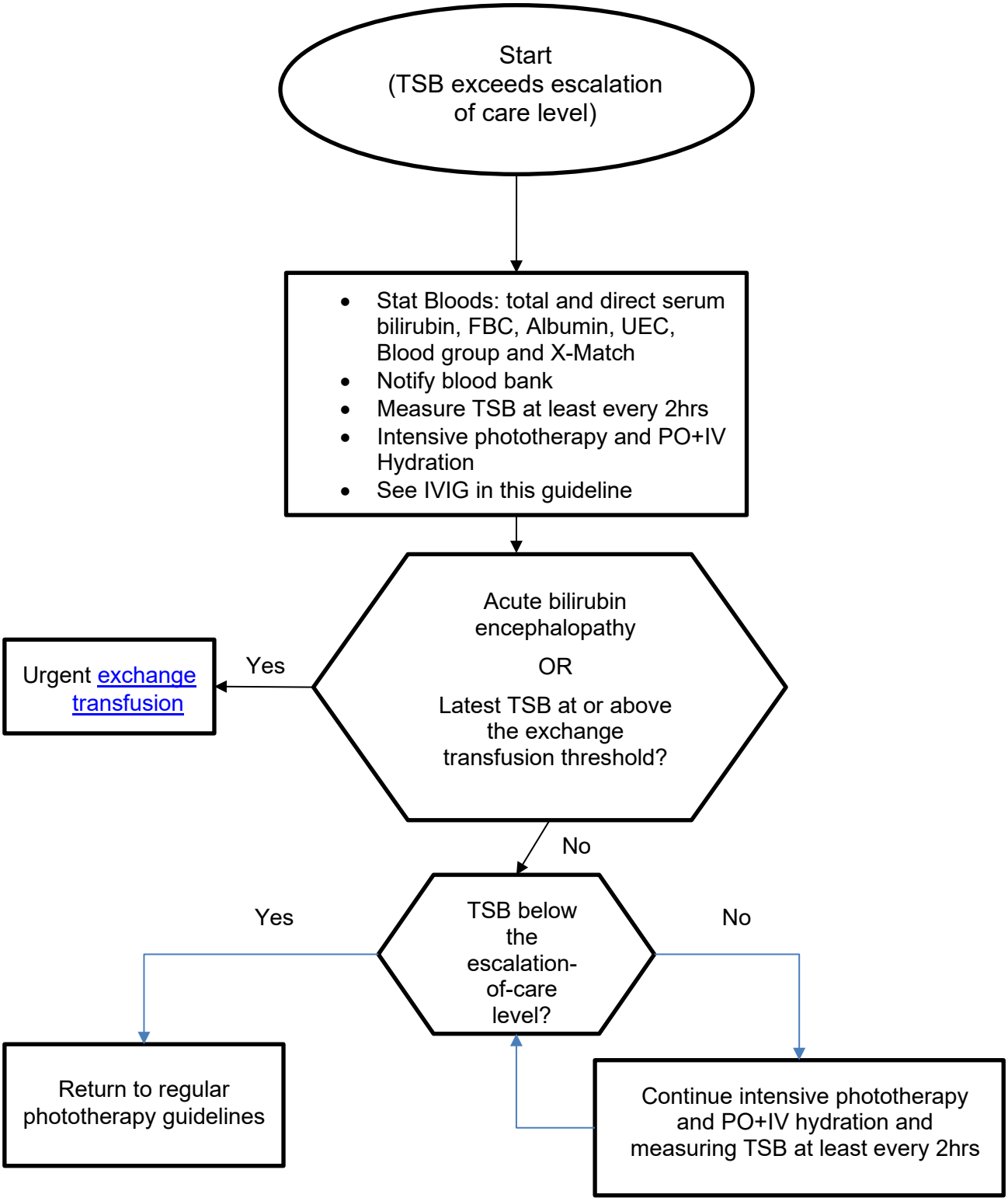
Appendix 1: Approach to identify newborns with maternal anti-erythrocyte antibodies and to guide early management

(Adapted from Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation)[2]



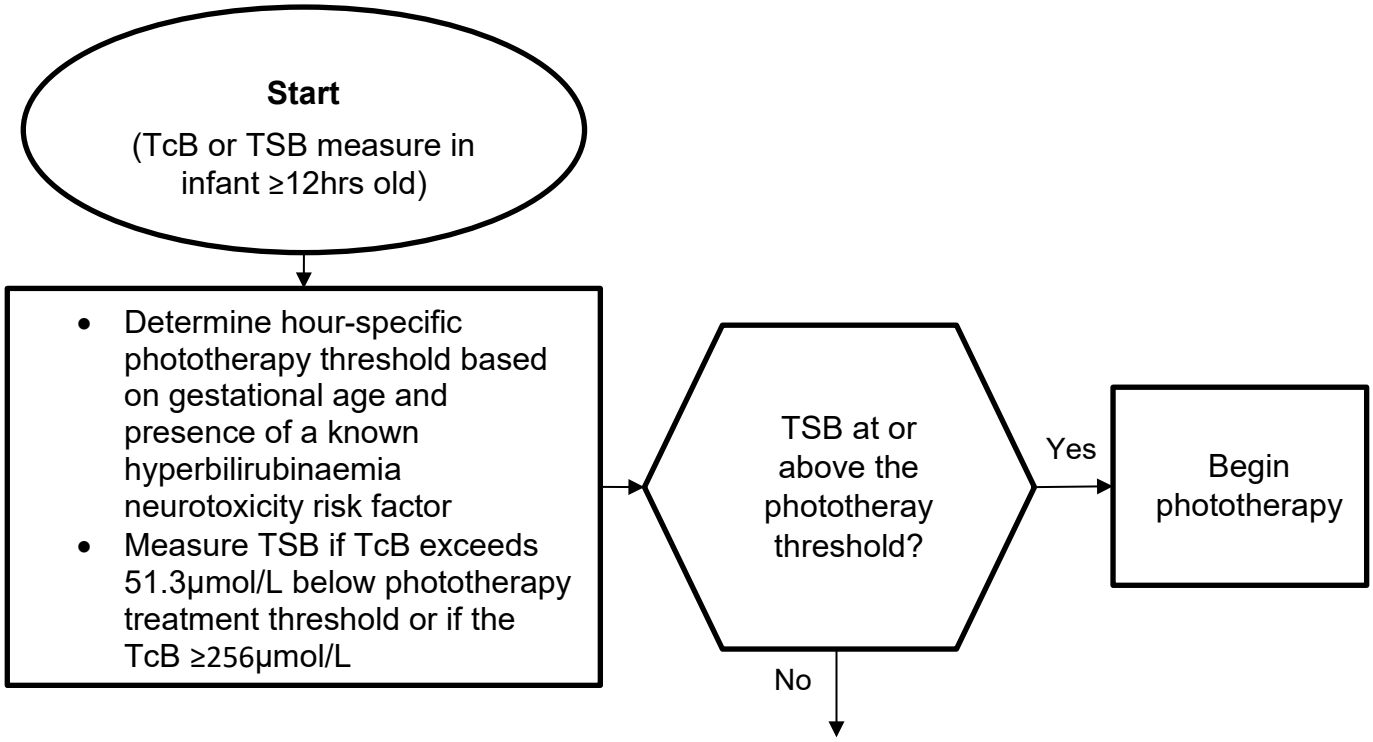
Appendix 2. Approach to escalation of care.

The escalation -of-care threshold is 34 µmol/L below the exchange transfusion threshold. Adapted from "Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation"[2]



Appendix 3: Flow diagram for infants during the birth hospitalization to determine post-discharge follow-up for infants who have not received phototherapy.

Adapted from Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation[2]



Phototherapy threshold minus TcB or TSB		Discharge Recommendations
1.7 - 33µmol/L	Age <24hrs	Delay discharge, consider phototherapy, measure TSB in 4 – 8 hrs
	Age ≥24hrs	Measure TSB in 4 – 24hrs Options: • Delay discharge and consider phototherapy • Discharge without phototherapy but with close follow-up
34 - 58µmol/L	Regardless of age or discharge time	TSB or TcB in 4 to 24hrs
60 - 92µmol/L	Regardless of age or discharge time	TSB or TcB in 1 - 2days
94 - 118µmol/L	Discharging <72hrs	Follow-up within 2 days; TcB or TSB according to clinical judgement
	Discharging ≥72hrs	Clinical judgement
≥120µmol/L	Discharging <72hrs	Follow-up within 3 days; TcB or TSB according to clinical judgement
	Discharging ≥72hrs	Clinical judgement