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1.0 Introduction

Jaundice is the most common reason for re-admission to hospital in the neonatal period ^(CDC, 2011). Neonatal Jaundice occurs due to the shorter red blood cell lifespan, higher red blood cell concentration and slower metabolism and excretion of bilirubin which leads to higher levels of unconjugated bilirubin circulating ^(Adapted, SCH, page 5). Jaundice is very common and usually benign in the term newborn infant and the late preterm infant at 35 to 36 completed weeks' gestation ^(Adopted, CPS, page 1). Critical hyperbilirubinemia is uncommon but has the potential for causing long-term neurological impairment ^(Adopted, CPS, page 1). The prevention, detection and management of jaundice in otherwise healthy term and late preterm newborn infants remain a challenge, partly because jaundice is so common and kernicterus is so rare in comparison ^(Adopted, CPS, page 1). It is estimated that 60% of term newborns develop jaundice and 2% reach a TSB concentration greater than 340 µmol/L ^(Adopted, CPS, page 1). Prompt, streamlined clinical care is necessary in order to decrease potential morbidity and mortality associated with bilirubin encephalopathy and to minimize disruption to exclusive breastfeeding and parent-child bonding in the neonatal period ^(Adapted, CPS, page 2; SickKids Consensus).


This Clinical Practice Guideline (CPG) has been adapted from the [Seattle Children's Hospital CPG, Neonatal Jaundice Pathway, \(2012\)](#) and the [Canadian Paediatric Society position statement, Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants \(2011\)](#) using the [Adapte Framework](#). The development process is discussed in detail in section 5 of this document.

1.1 The purpose of this CPG is to:

1. improve recognition of infants at risk for severe hyperbilirubinemia and to decrease potential associated morbidity and mortality.
2. enhance the quality of care delivered by improving communication and streamlining the process from the time of arrival until the time of discharge.
3. promote exclusive breastfeeding.
4. decrease length of stay by reducing unnecessary admitted days, unnecessary testing and readmission rate.
5. enhance appropriate utilization of community resources and ensure appropriate follow up.

1.2 Target Patient Population

- previously healthy neonates
- age <14 days
- born at > or equal to 35 weeks gestational age ^(Adopted, SCH, page 1)

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1.3 Exclusion Criteria (Adapted, SCH, page 1): This CPG is not intended for use in infants:

- With conjugated hyperbilirubinemia
- Meeting NICU direct admission criteria for exchange transfusion or IVIG administration
- With suspected acute bilirubin encephalopathy or displaying clinical findings associated with acute bilirubin encephalopathy such as hypotonia, weak suck or high pitched cry
- Pathologic jaundice within the first 24 hours of life
- Suspected sepsis, history of fever or ill-appearing upon assessment

2.0 Definitions

Jaundice: yellowing of the skin, conjunctivae and other mucous membranes (Adopted, SCH, page 4)

- Increased circulating bilirubin
- Deposits in tissues
- Progresses caudally
- One of the most common conditions leading to medical evaluation in neonates

Hyperbilirubinemia: Total serum bilirubin (TSB) >95th percentile for age in hours

- Jaundice does not necessarily = hyperbilirubinemia (Adopted, SCH, page 4)


Severe Hyperbilirubinemia: a total serum bilirubin (TSB) concentration greater than 340 µmol/L at any time during the first 28 days of life (Adopted, CPS, page 1)

Bilirubin Encephalopathy: a clinical syndrome, in the presence of severe hyperbilirubinemia, of lethargy, hypotonia and poor suck, which may progress to hypertonia (with opisthotonos and retrocollis) with a high-pitched cry and fever, and eventually to seizures and coma. (Adopted, CPS, page 1)

Conventional Phototherapy: a single bank of fluorescent lights placed above the incubator (Adopted, CPS, page 9) *Please note that conventional phototherapy is no longer recommended.*

Intensive Phototherapy: high intensity of light (greater than 30 µW/cm²/nm) is applied to the greatest surface area of the infant possible, may be referred to as double or triple phototherapy and typically requires at least two to three banks of lights. (Adapted, CPS, page 8)

Total Serum Bilirubin: Serum conjugated bilirubin + unconjugated serum bilirubin

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3.0 Clinical Practice Recommendations

Table 1. Grades of Recommendation
A Recommendation supported by at least one randomized controlled trial, systematic review or meta-analysis.
B Recommendation supported by at least one cohort comparison, case study or other experimental study.
C Recommendation supported by expert opinion or experience of a consensus panel.

The summary patient algorithm for Hyperbilirubinemia Management is available by [clicking here](#).

3.1 Emergency Department Management

Assessment and Diagnosis


3.1a Clinical History and Physical Examination:

- i) A comprehensive history and physical examination should be performed including but not limited to:
 - clinically pertinent history of the mother and infant including;
 - prenatal, antenatal and postnatal/neonatal course;
 - family history; and
 - assessment of risk factors for severe hyperbilirubinemia (Adapted, CPS, page 11) [Grade C].

- ii) Head to toe physical examination should include:
 - current naked weight;
 - percentage of weight loss from birth weight;
 - assessment of overall hydration status and feeding adequacy;
 - observing for bruising, cephalohematoma or other risk factors; and
 - careful assessment for any signs of bilirubin encephalopathy (SickKids Consensus) [Grade C].

3.1b Laboratory and Diagnostic Testing:


- i) Visual inspection alone is not a reliable indicator of bilirubin level in any neonate (Adapted, CPS, page 6) [Grade A]. Physical exam should be always be supplemented by laboratory investigations (Adapted, CPS, page 11) [Grade C]. All infants with suspected hyperbilirubinemia should have:

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- unconjugated and conjugated serum bilirubin levels,
- direct Coombs test,
- baseline complete blood count including hemoglobin and hematocrit levels and
- type and screen for infant's blood type if unknown (Adapted, CPS, page 7; SickKids Consensus)[Grade C],
- G6PD Assay should be considered in all cases of severe or prolonged hyperbilirubinemia [Grade C] and high risk populations (e.g. Mediterranean, Middle Eastern, African or Southeast Asian origin) or patients with a positive family history (Adopted, CPS, page 5) [Grade A], [Grade A](Adapted, CPS, page 10).
- Investigations for sepsis are not routinely recommended but should be performed if warranted by the clinical presentation and clinician assessment (Adapted, CPS, page 11) [Grade C].

3.1c Risk Factors for Hyperbilirubinemia

- i) Major Risk Factors for Severe Hyperbilirubinemia** (Adopted, SCH, page 10)
- Jaundice in the first 24 hours of life (always pathologic)
 - Blood group incompatibility with positive direct antiglobulin test (DAT) or other known hemolytic disease (such as G6PD Deficiency)
 - Gestational age 35-36 weeks
 - Previous sibling received phototherapy
 - Cephalohematoma or significant bruising
 - East Asian Race
 - Exclusive breastfeeding
- ii) Factors that Lower Risk for Severe Hyperbilirubinemia** (Adopted, SCH, page 10)
- Gestational age \geq 41 weeks
 - Exclusive bottlefeeding
 - Black race
 - Nursery discharge after 72 hours of life
- iii) Factors contributing to Pathologic Hyperbilirubinemia** (Adopted, SCH, page 7):
- **Increased hemolysis of red blood cells** (blood group incompatibility, G6PD deficiency, hereditary spherocytosis)
 - **Breastfeeding jaundice** (inadequate fluid/nutrient intake \rightarrow dehydration \rightarrow increased enterohepatic circulation)
 - **Breastmilk jaundice** (increased enterohepatic circulation due to enzyme in breastmilk)
 - **Polycythemia** (delayed cord clamping, high altitude gestation, maternal smoking)

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- **Extravasated blood** (bruising, cephalohematoma, subgaleal hemorrhage, intraventricular hemorrhage)
- **Stress related heme-oxygenase induction** (hypoxia, infection, hypothermia)

3.1d Admission Criteria (Adapted, SCH, page 1):

- All infants requiring phototherapy or within 50 µmol/L of phototherapy range
- Signs of dehydration or inadequate feeding
- Concern for significant hemolysis (i.e. DAT positive)
- In rare cases, inability to ensure necessary follow up

3.2 Inpatient Management

3.2a Overall Management: The management of patients with hyperbilirubinemia is dependent on early detection of hyperbilirubinemia, adequate hydration, phototherapy as recommended by the CPS Guidelines for Intensive Phototherapy and close monitoring of serum bilirubin and overall clinical status to ensure there is no worsening of hyperbilirubinemia once treatment has commenced (Adapted, SCH, page 19; SickKids Consensus)[Grade C].


3.2b Phototherapy: Intensive phototherapy should be given according to the CPS Guidelines for Intensive Phototherapy (Adapted, CPS, page 10) [Grade C].

- i) All infants should be placed in isolette with maximum area of skin exposed (Adapted, CPS)[Grade A].

The effectiveness of phototherapy is related to the area of skin exposed and the intensity of the light at the skin at the relevant wavelengths (Adopted, CPS, page 8)[Grade A].

The energy from light induces a conformational change in the bilirubin molecule, making it water soluble; light in the blue-green part of the spectrum is most effective (Adopted, CPS, page 8) [Grade A]. In usual clinical situations, this will require two- three phototherapy units (Adapted, CPS, page 8).

- ii) Eye patches should be used to protect the developing retina because animal studies demonstrate a potential risk (Adopted, CPS, page 8) [Grade C].
- iii) Side effects of phototherapy may include temperature instability, intestinal hypermotility, diarrhea, interference with maternal-infant interaction and, rarely, bronze discoloration of the skin (Adopted, CPS, page 8) [Grade B].
- iv) Intensive Phototherapy may be discontinued when bilirubin 50 µmol/L below applicable

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phototherapy threshold (Adapted, SCH, page 24) [Grade A].

Barak et al. (2008) compared 2 thresholds for stopping phototherapy 1 mg/dL or 3 mg/dL (17 μ mol/L and 51 μ mol/L respectively) below phototherapy threshold. There was no significant difference between duration of phototherapy or need for retreatment between the two thresholds. We are not recommending obtaining a rebound bilirubin measurement so the more conservative of the two was chosen as per the Seattle Children's Hospital guideline. This is also consistent with the NICE 2010 guidelines for the UK.

- v) Longer courses of phototherapy may be clinically indicated when there is ongoing feeding difficulty, bilirubin level is close to exchange transfusion threshold at the beginning of therapy or there is known or suspected hemolysis (Adapted, SCH, page 24).
- vi) There is no evidence to support weaning courses of phototherapy or gradual reduction in the number of phototherapy lights.

3.2c Lab Frequency: There is no high quality evidence for the timing or frequency of serum bilirubin levels (Adapted, SCH, page 19; SickKids Consensus)[Grade C]. The following policy has been adapted from Seattle Children's Hospital:


- i) Repeat serum bilirubin **every 4 hours X 2** following initiation of treatment. If bilirubin is falling, repeat serum bilirubin **every 12 hours or with next routine morning blood work** until phototherapy is discontinued (Adapted, SCH, page 19) [Grade C]. If TSB not falling, or within 50 μ mol/L of exchange transfusion threshold or patient has known or suspected hemolysis, continue checking TSB every 4 hours and re-evaluate. Remove patient from pathway as this is not the expected trajectory [Grade C].

Recommendations are aimed at detecting rapidly rising bilirubin, identifying phototherapy failure and avoiding unnecessary testing in select infants (Adopted, SCH, page 19) [Grade C].

- ii) Repeat serum bilirubin level within 2-6 hours of phototherapy initiation to confirm response (Adapted, CPS, page 10).
- iii) Total serum bilirubin may be obtained from a capillary or venous sample. Transcutaneous bilirubin measurement is not used at SickKids (SickKids Consensus) [Grade C].
- iv) Rebound bilirubin should not be routinely measured after discontinuation of phototherapy (Adopted, SCH, page 24) [Grade B].

4 studies reviewed

Maisels & Kring (2002) conducted a retrospective review of the medical records

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of 303 term and near-term newborns treated between January 1996 and December 1998, who received phototherapy during their birth hospitalization or had been discharged from the nursery and were readmitted for phototherapy. Rebound bilirubins were included if they were measured between 4 and 48 hours after discontinuing phototherapy. Only 1 infant who first received phototherapy on readmission received repeated phototherapy (p=0.02). The study concluded that it is not necessary to keep infants in the hospital to check for rebound. However, for infants who require phototherapy during their birth hospitalization and for those with significant hemolytic disease, a follow up bilirubin 24 hours after discharge is recommended.

Al-Saedi (2002) conducted a retrospective chart review of term infants with hyperbilirubinemia requiring phototherapy over a two year period. 301 infants met inclusion criteria. Discharge bilirubin and 24 hour follow up bilirubin were compared using a paired t test. Total serum bilirubin rebound after termination of phototherapy in otherwise healthy, term infants was minimal. Therefore, they concluded that rebound measurement of serum bilirubin is not required.

Yetman et al (1998) conducted a retrospective medical record review for 264 newborns receiving phototherapy to determine if a significant rebound increase occurs. The difference between total serum bilirubin at discontinuation of phototherapy and at rebound (measured between 4 and 48 hours after discontinuation) was calculated using a paired t test. There was no statistically significant difference. Study concluded that infants completing phototherapy for hyperbilirubinemia who are otherwise healthy do not require follow up solely to identify rebound bilirubin level.

Kaplan et al conducted a prospective clinical survey with 226 term and near-term neonates treated with phototherapy in a well baby nursery from January 2001 to September 2002. 30/226 neonates developed significant rebound (defined as bilirubin $\geq 256 \mu\text{mol/L}$). Of these, 22 infants were re-treated with phototherapy. Multiple logistic regression analysis showed significant risk for etiological risk factors including positive direct coombs, gestational age < 37 weeks and age ≤ 72 hours.

- vi) Rebound bilirubin **may be** considered for infants less than 37 weeks gestational age, infants being discharged at less than 72 hours of age of infants at risk for significant or ongoing hemolysis (i.e. positive direct coombs).
- vii) For healthy, term infants without etiological risk factors follow up with their primary care provider with repeat total serum bilirubin measurement at that visit should be arranged **within 24 hours**.

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3.2e Other Therapies (Reserved for NICU patient care ONLY):

- i) **IVIG:** Intravenous immunoglobulin (IVIG) reduces bilirubin concentrations in newborns with rhesus hemolytic disease and other immune hemolytic jaundice (Adopted, CPS, page 9). It acts as a competitive inhibitor for those antibodies that cause red cell destruction, release hemoglobin and cause jaundice (Adopted, CPS, page 9). Infants with a positive DAT who have predicted severe disease based on antenatal investigation or an elevated risk of progressing to exchange transfusion based on the postnatal progression of TSB concentration should receive IVIG at a dose of 1 g/kg (Adopted, CPS, page 9) [Grade A]. At SickKids, this is reserved for NICU administration ONLY.
- ii) **Exchange Transfusion:** If phototherapy fails to control the rising bilirubin concentrations, exchange transfusion is indicated to lower TSB concentrations (Adopted from CPS, page 10). For healthy term newborns without risk factors, exchange transfusion should be considered when the TSB concentration is between 375 µmol/L and 425 µmol/L (despite adequate intensive phototherapy) (Adopted, CPS, page 10) [Grade B]. At SickKids, this therapy is reserved for NICU use ONLY.

Fluids and Nutrition:

3.2f Breastfeeding

- i) Breastfeeding should continue during phototherapy (Adopted, CPS, page 10)[Grade A].
- ii) Mothers should be advised to breastfeed their infant at least 8 to 12 times per day (American Academy of Pediatrics, 2004) [Grade C].
- iii) A referral to the hospital breastfeeding program should be made for all families who express a desire to breastfeed or interest in specialized assessment and support from a lactation consultant (SickKids Consensus) [Grade C].


3.2g Feeding Difficulties

- i) Poor intake and/or dehydration associated with feeding difficulties may contribute to the development of hyperbilirubinemia (American Academy of Pediatrics, 2004).

Increasing the frequency of feedings and providing support to breastfeeding mother-infant dyads reduces the likelihood of significant hyperbilirubinemia in breastfed infants (American Academy of Pediatrics, 2004).

Interrupting breastfeeding as part of therapy for hyperbilirubinemia is associated with a major increase in the frequency of stopping breastfeeding by one month (Adopted CPS, page 9) [Grade B].
- ii) Where concerns regarding intake exist, [pre and post breastfeeding weights](#) should be

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documented (SickKids Consensus) [Grade C]

3.2h Supplemental Fluids


- i) Infants should not routinely receive supplemental intravenous or oral fluids (Adapted, SCH, page 23) [Grade C].
- ii) For breastfeeding mother-infant dyads, supplemental fluids should be avoided in order to maintain maternal milk supply and frequent breastfeeding (Academy of Breastfeeding Medicine, 2010) [Grade C].
- iii) Use maternal expressed breast milk for supplemental feeds, when available (Adopted, SCH, page 21) [Grade B].
- iv) Alternate feeding methods such as cup or finger feeding should be considered with input from hospital lactation consultants.
- v) Supplemental fluids should be administered, orally or by intravenous infusion, to infants receiving phototherapy who are at an elevated risk of progressing to exchange transfusion (Adopted, CPS, page 10) [Grade A].
- vi) This includes infants within 50 µmol/L of exchange transfusion or with rapidly rising TSB or with clinical concern for significant dehydration (i.e. weight loss >10% of birth weight) (Adapted, SCH, page 23) [Grade C].
- vii) If intravenous fluids are required, [serum electrolytes should be checked and fluid choice based on individual patient status.](#)
- viii) Supplementary fluids should be stopped once TSB has fallen to at least 50 µmol/L below exchange transfusion threshold and infant is feeding well (Adapted, SCH, page 23) [Grade C].

3.2i Discharge Criteria (Adapted from SCH, page 25):

- Patient off phototherapy and otherwise well
- Follow up appointment arranged and confirmed for next day
- No concern for significant or ongoing hemolysis
- Feeding Adequately

3.2j Discharge Summary Requirements (SickKids Consensus):

- Most recent bilirubin and risk stratification of patient

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- Naked Discharge weight
- Current feeding plan and hydration status
- Follow up plan including confirmed date and time of follow up appointment
- Contact information for local breastfeeding clinic

3.2k Other Considerations

- Parents should be provided with information on jaundice from [About Kids Health](#) in their first language if available
- Consent should be obtained and a referral to [Healthy Babies Healthy Children](#) should be made for all families

3.3 Key review criteria/indicators for monitoring and audit purposes

- Length of stay
- Number of patients undergoing unnecessary testing (i.e. blood cultures)
- Readmission rate

4.0 Related Documents

[Canadian Pediatric Society Guideline](#)

[Guidelines for Intensive Phototherapy](#) (35 weeks or more gestational age)

[Guidelines for exchange transfusion](#) (35 weeks or more gestational age)

[AAP Clinical Practice Guideline](#)


[NICE guideline](#)

[Quality Based Procedures Clinical Handbook for Hyperbilirubinemia](#)

5.0 Statement of Evidence

Not all recommendations from the **Seattle Children's Hospital (SCH) CPG**, Neonatal Jaundice Pathway (2012) and the **Canadian Paediatric Society position statement**, Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (2011) were adopted for the SickKids Management of Hyperbilirubinemia in Neonates Clinical Practice Guideline.

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Recommendations that were relevant to the care offered within SickKids were either (i) adopted (taken verbatim from SCH/CPS), or (ii) adapted (taken from SCH/CPS with slight modifications for use at SickKids). In addition, there are a select number of SickKids consensus recommendations that were included that were not taken from the SCH/CPS guideline and these are clearly identified by "SickKids Consensus" in parentheses throughout the guideline text. The research considered when developing the recommendations is discussed in the original publications. Please click the links at the beginning of this paragraph to access the original publications for more detailed information.

This CPG discusses inpatient assessment, treatment and management of neonates with hyperbilirubinemia. It is a continuation of care provided in the Emergency Department using the Department of Emergency Medicine Paediatric Hyperbilirubinemia Order Set.


A systematic search for existing Clinical Practice Guidelines was conducted in September 2012 using the Internet and the OVID database (MEDLINE, Embase) to search for CPGs. To be included as a potential CPG to adapt for use at SickKids, the CPG must have met the following criteria:

- Published or updated within the past 5 years (2005 or after)
- Included clearly articulated and directive recommendation statements (i.e. easily extracted for practice)
- Included neonatal specific recommendations
- Included at least one section relevant to:
 1. Assessment/Diagnosis
 2. Treatment
 3. General Management
 4. Referral/follow-up

5.1 CPG Selection: The identified guideline was screened to ensure that the clinical questions developed by the working group were covered. Seattle Children's Hospital CPG, Neonatal Jaundice Pathway, (2012) and the Canadian Paediatric Society position statement, Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (2011) were selected and adapted using the *Adapte Framework* and assessed using the *AGREE tool*. Group consensus was to adapt this guideline and modifications were discussed & agreed upon by consensus.

5.2 Adaptation Process: A small writing group (1 nurse practitioner, 1 resident and 1 guideline developer) produced the first iteration of this guideline. The first draft was circulated to an interdisciplinary development group of health care professionals (see section 5.3) from within the Paediatric Emergency Medicine and General Paediatrics Departments for review and input. The guideline was sent to internal and external reviewers for review.

5.3 Process for updating this CPG: Once the guideline has been in place for three years, the development team will reconvene to explore the continued validity of the guideline. This phase can be initiated at any point that evidence indicates a change is needed.

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5.4 Guideline Group and Reviewers

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Scheduled Review Date: May 1, 2017

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Attachments:

[CPG Patient Care Algorithm.docx](#)

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