CLINICAL PRACTICE GUIDELINE 18

Management of Hyperbilirubinemia in Healthy Term and Late Preterm Neonates

Association of Ontario Midwives
Delivering what matters.

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The AOM is committed, through our statement on Gender Inclusivity and Human Rights, to reflect and include trans, genderqueer and intersex communities in all aspects of our work.

In this document, there are references to sources that use gendered language to refer to populations of pregnant and birthing people. In order to accurately represent these sources, we may have maintained gendered language.

We support research and knowledge translation that engages and reflects the entire childbearing population.

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This CPG has been developed by and for midwives, contextualized within the midwifery model and philosophy of care and designed to provide information for midwives and clients engaged in complex decision-making. The information in this CPG is consistent with the best evidence available as of the date of publication, which is subject to change. The information in this guideline is not intended to dictate a course of action, but inform clinical decision-making. Midwives should use their clinical judgement on how to interpret and apply the recommendations to individual circumstances. Local standards may cause clinical practice to diverge from the suggestions within this guideline. If practice groups protocols depart from a guideline, it is advisable to document the rationale for the departure.

Midwives recognize that client expectations, preferences and interests are an essential component in clinical decision-making. Informed choice discussions involve explaining community standards, which may include applicable CPGs, hospital and practice protocols (if available) used in the community to guide provision of care. For clients to make a fully informed decision, midwives need to make clients aware of recommendations from their own profession (e.g. CPGs, CMO standards), related professions (e.g. SOGC, CPS) and those used in their community (e.g. hospital, regional guidelines). Clients may choose a course of action that may differ from the recommendations in this guideline, within the context of informed choice. When clients choose a course of action that diverges from a clinical practice guideline and/or practice group protocol the details of the discussion, the evidence shared and the client's choice should be well documented in their chart.

Management of Hyperbilirubinemia
in Healthy Term and Late Preterm Neonates

INTRODUCTION

It is estimated that sixty percent (60%) of term, and 80% of preterm newborns develop visible jaundice in the first week of life, with roughly 10% of babies fed with human milk remaining jaundiced at one month of life. (1–4) Neonatal hyperbilirubinemia is often benign; however, due to the potential short- and long-term neurotoxic effects of bilirubin, prevention, detection and management of hyperbilirubinemia in newborns remains a priority. (2,3)

Definitions

Hyperbilirubinemia of the neonate is a condition in which there is an excess of bilirubin in the blood and tissues of an infant's body. (5) Typically, the buildup of bilirubin presents as the yellowing of the skin and the whites of the eyes. This is called **jaundice**. (5) The terms **hyperbilirubinemia** and **jaundice** are used interchangeably throughout this document for simplicity.

The definition of **severe hyperbilirubinemia** is a total serum bilirubin (TSB) concentration greater than 340 µmol/L at any time during the first 28 days of life. (2) **Critical hyperbilirubinemia** is defined as a TSB concentration greater than 425 µmol/L. (2)

High levels of bilirubin may lead to **acute bilirubin encephalopathy** defined as the clinical manifestation of bilirubin toxicity. (2) Clinical presentation can progress from lethargy, hypotonia and poor suck to hypertonia of extensor muscles (with opisthotonus, rigidity, retrocollis), high-pitched cry, fever and irritability and eventually to seizures and coma. (2,6)

An infant with severe or critical hyperbilirubinemia is at greater risk of developing **kernicterus**, a diagnosis of yellow staining of the brain by bilirubin and evidence of neuronal injury. (7) However, bilirubin toxicity varies in different clinical scenarios, which makes defining normal and abnormal bilirubin concentrations challenging. (6)

Classification

Physiologic jaundice is the most common form of hyperbilirubinemia and typically becomes apparent between 24 to 72 hours of life. (1) There are no underlying pathological causes of physiologic jaundice, although some infants will receive phototherapy to manage increased bilirubin levels. (1)

Conversely, **pathologic jaundice** typically manifests as a symptom of an existing underlying condition including hemolysis, blood extravasation, sepsis and metabolic disorders. (8) It is characterized by rapidly rising bilirubin concentrations that exceed 85.5 µmol/L on the first day, 171 µmol/L on the second day, or 205.2 to 222.3 µmol/L on the third day. (8) The appearance of jaundice within the first 24 hours may be an indication of pathological jaundice, though not all pathological jaundice will present early. (6) Physiologic and pathologic jaundice may also occur simultaneously. (5,8)

Pathologic jaundice requires serious intervention, consistent follow-up and treatment at lower thresholds. Once identified, the underlying condition must be addressed in a timely manner with the appropriate intervention or an infant may be at an increased risk of serious debilitating and/or life-threatening complications. (1,6)

Prolonged jaundice is any jaundice lasting more than 14 days in term infants and more than 21 days in preterm infants. (3) More information on prolonged jaundice can be found below in the *What are the Factors Associated with Prolonged Jaundice?* section of this guideline.

Incidence of severe hyperbilirubinemia

Ontario's 2013 version of the Quality Based Procedures Clinical Handbook for Hyperbilirubinemia in Term and Late Pre-Term Infants (≥ 35 weeks) reported a total of 9884 cases of hyperbilirubinemia[1] in 2011/12. (4) This represents approximately 7.6% of the roughly 130 000 infants born at or beyond 35 weeks' gestation. (4) A 2006 Canadian study found an estimated incidence of infants with critical hyperbilirubinemia (TSB > 425 µmol/L) or infants who underwent exchange transfusion in the first 60 days of life to be 0.04% (1 in 2480 live births). (7) An updated investigation after the implementation of Canadian universal screening guidelines from 2011-2013 found that the incidence of critical hyperbilirubinemia had declined to 1 in 8600 live births. (9)

The incidence of acute and chronic encephalopathy remains uncertain. The Canadian Pediatric Surveillance Program (CPSP) reported that from 2002-2004, 258 term infants required exchange transfusion or had critical hyperbilirubinemia (excluding neonates with Rh isoimmunization). (7) Twenty percent of these infants had at least one abnormal neurological sign at presentation, and 5% had documented hearing loss or significant neurological sequelae at discharge. The mean peak TSB was 471 µmol/L. During this time, the live birth rate was 330,000/year, which leads to a minimal incidence of approximately 4 in 10 000 live births. (7) An updated report from 2007-2008 reported an incidence of chronic bilirubin encephalopathy of 1 in 44 000 live births. (10)

Complications of severe hyperbilirubinemia

In Canada, severe hyperbilirubinemia is the most common reason for re-admission to hospital during the neonatal period. (7) When acute bilirubin encephalopathy is untreated, infants may develop kernicterus, sometimes referred to as chronic bilirubin encephalopathy: the clinical sequelae of acute bilirubin encephalopathy including athetoid cerebral palsy, hearing deficits, developmental delay and oculomotor disturbances. (6)

AIM OF THE GUIDELINE

Statement of purpose

The goal of this document is to provide an evidence-based clinical practice guideline (CPG) on the prevention and management of severe hyperbilirubinemia that is consistent with the midwifery philosophy and model of care. Midwives in Ontario are encouraged to use this CPG as a tool in clinical decision-making.

Objectives

The objective of this CPG is to provide a critical review of the research literature on the management of severe hyperbilirubinemia in the otherwise healthy term or late preterm neonate (gestational age ≥ 35 weeks) within the context of provision of midwifery care in Ontario. Evidence relating to the following will be discussed:

- Definition and incidence
- Risk factors
- Prevention
- Screening
- Treatment
- Client experiences

Outcomes of interest

The following outcomes were rated as either 'critical' or 'important' following the GRADE process for each research question addressed in the guideline.

Critical:

- Neonatal mortality
- Chronic bilirubin encephalopathy
- Acute bilirubin encephalopathy
- Need for exchange transfusion
- Severe hyperbilirubinemia

Important:

- Need for phototherapy
- Duration of phototherapy
- Bilirubin levels
- Hospital readmission
- Readmission length of stay
- Diagnostic accuracy of screening tests
- Adverse treatment effects
- Human milk feeding

[1] 'Hyperbilirubinemia' is defined as "all normal newborns (all newborn babies, born at 35 weeks 0 days gestation or greater either in hospital or at home) + 'infants with jaundice' (jaundice defined as: 1.kernicterus due to isoimmunization, other specified kernicterus, kernicterus, unspecified; 2. neonatal jaundice due to other excessive hemolysis: due to bruising, bleeding, infection, polycythemia, drugs or toxins transmitted from mother or given to newborn, swallowed maternal blood, other specified excessive hemolysis, excessive hemolysis, unspecified; 3. neonatal jaundice from other and unspecified causes: associated with preterm delivery, inspissated bile syndrome, other and unspecified hepatocellular damage, breast milk inhibitor, other specified causes, unspecified)"

Methods

This CPG uses the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology for guideline development. The GRADE process determines the certainty of the evidence (how certain we should be in the results) as well as the strength of the recommendation. Certainty of evidence in this CPG is rated from very low to high, according to five GRADE domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. Methodological concerns about the included studies, variability across results, applicability of the evidence to our context, precision of the results and completeness of the evidence base are considered as part of these domains.

The work group's judgements about the certainty of evidence reflect the work group's confidence that available evidence correctly reflects the true effect of the intervention and is sufficient to support decision-making.

CERTAINTY OF EVIDENCE	How certain we ought to be about an estimate of effect or association
High	Further research is very unlikely to change confidence in the estimate of effect. • This evidence provides a very good basis for decision-making.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate. • This evidence provides a good basis for decision-making.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. • This evidence provides some basis for decision-making.
Very low	Any estimate of effect is very uncertain. • This evidence does not provide much of a basis for decision-making.

Based on: (11–13)

Recommendations in this CPG are based on formal ratings of the certainty of evidence and are described as either strong or weak according to the GRADE approach. The strength of recommendation reflects the extent to which the Hyperbilirubinemia CPG Work Group (WG) is confident that the benefits of a recommended intervention outweigh its harms, or vice versa. The strength of recommendation is influenced by the certainty of supporting evidence, the balance between desirable and undesirable effects and the perceived variability or uncertainty in clients' values and preferences with respect to the intervention. (11-15) It is for these reasons that weak recommendations use the terminology "may" and strong recommendations use the terminology "should" within this CPG.

Good practice statements in this CPG represent guidance that the WG deemed important but that were not appropriate for formal ratings of certainty of evidence. Good practice statements are made when the WG is confident that the action has net benefit to the client and that sensible alternatives do not exist. (16)

Complete **GRADE evidence tables** used to summarize research and inform the recommendations in this guideline are available on the AOM website. A full description of the AOM's approach to clinical practice guideline development using GRADE is also available on the AOM website.

TYPES OF STATEMENTS IN THIS CPG

- **Work group remarks, clinical considerations, values and preferences:** Summarizes the WG's discussion of evidence in relation to midwifery values, equity considerations and the Ontario midwifery context.
- **Recommendations:** Action statements about the intervention based on the certainty of the evidence, clinical considerations, preferences and values.
- **No recommendation:** WG has deemed that there is insufficient evidence available to make a recommendation about the intervention.
- **Good practice statements:** Statements whereby the net benefit of the intervention is large and unequivocal and the WG has considered it useful to provide guidance to clinicians in this area. The evidence for good practice statements is typically difficult to collect and summarize and therefore no formal rating of the certainty of evidence is undertaken.
- **Summary statements:** WG has deemed a recommendation unnecessary according to standards of care.

STRENGTH OF RECOMMENDATION	The extent to which the CPG Work Group is confident that benefits of the recommended intervention outweigh its harms (or vice versa)
Strong	Benefits clearly outweigh risks and burdens (or vice versa). *Can be interpreted as:* • Most clients should be offered the intervention, assuming that they have been informed about and understand its benefits, harms and burdens. • Most clients would want the recommended course of action and only a small proportion would not.
Weak	Benefits, risks and burdens are closely balanced. *Can be interpreted as:* • The majority of clients would want the suggested course of action, but an appreciable proportion would not. • Values and preferences vary widely.

Literature Search

A search of the Pubmed and CINAHL databases and Cochrane library from 2001-2018 was conducted using a defined search strategy. Additional search terms and hand searching were used to provide more detail on individual topics as they related to severe hyperbilirubinemia. Older studies were accessed in cases of commonly cited statistics or significant impact on clinical practice. Systematic reviews were prioritized; if no systematic reviews were found, randomized controlled trials and observational studies were retrieved.

We included any English-language publications that contained data related to the prevention, screening and/or management of severe hyperbilirubinemia in healthy term and late preterm (gestational age ≥ 35 weeks) infants. We excluded research articles with a primary focus on pathologic jaundice, conjugated hyperbilirubinemia and neonates with comorbidities including but not limited to sepsis, cholestasis, G6PD deficiency or hemolytic disease. The management of infants with these complex conditions is not within the scope of midwifery care in Ontario.

Review

This CPG was reviewed using a modified version of the **AGREE instrument**, the AOM Values-based Approach to CPG Development, as well as consensus of the Hyperbilirubinemia Work Group; the CPG Committee; the Quality, Insurance and Risk Management Committee; the AOM Board of Directors; and member consultation.

WHAT ARE THE RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF SEVERE HYPERBILIRUBINEMIA?

Risk factors alone provide limited power to predict severe hyperbilirubinemia because the risk factors are common and the risk of developing severe hyperbilirubinemia is low. (2,3) However, understanding factors that may predispose an infant to develop severe hyperbilirubinemia can allow for timely and appropriate follow-up.

The risk factors discussed in this guideline are based on the National Institute for Health and Clinical Excellence's (NICE) guideline on neonatal jaundice. (1) Risk factor research included in the NICE guideline represents an exhaustive search of the literature and was rigorously evaluated using GRADE. The WG chose to adopt the risk factor list from NICE, as it was based on consistent, good quality evidence, which showed an independent significant association between the factor and the development of severe hyperbilirubinemia (see Table 1). Other guidelines were also consulted in the review of risk factors and are referred to below. (2,3) In addition to being of particular interest to midwifery practice, these risk factors were consistent with those of other guidelines on neonatal jaundice.

NICE also examined other commonly reported risk factors including cephalohaematoma, vacuum delivery, male sex and race. None of these risk factors were found to be significantly associated with hyperbilirubinemia. (5)

TABLE 1: RISK FACTORS FOR SEVERE HYPERBILIRUBINEMIA

RISK FACTOR	Reported odds ratios	Number of studies included in NICE evaluation
Gestational age under 38 weeks	0.6 to 20.79	6
Previous sibling with neonatal jaundice requiring phototherapy	2.3 to 6.0	3
Visible jaundice in the first 24 hours of life	2.9 to 10.1	2
Suboptimal feeding *(defined in description below)*	0.4 to 10.75	6

Source: (5)

Gestational age under 38 weeks

Gestational age less than 38 weeks is considered a significant independent risk factor in the development of severe hyperbilirubinemia. (1–4) Reduced enzyme function in earlier term infants is a major contributing factor to the increased risk of developing severe hyperbilirubinemia, as it can produce:

- a reduced ability to conjugate bilirubin due to a deficiency of the enzyme glucuronyl transferase and a reduction in albumin binding capacity; and
- a reduced survival time of red blood cells. (18)

Six studies included in the NICE guideline found that an infant's gestational age may be a strong predictor of an increased risk of developing severe hyperbilirubinemia (odds ratios (OR) ranging from 0.6 to 20.79). (5)

Previous sibling with neonatal jaundice requiring phototherapy

The link between a familial history of jaundice and a newborn's increased risk for hyperbilirubinemia is thought to be related to a number of genetic and environmental factors. These factors may help to explain why infants born in certain geographic regions or belonging to certain ethnic or racial groups are at higher risk of developing severe hyperbilirubinemia. (17–21)

Three studies summarized in the NICE guideline explored the association between a previous sibling with jaundice and an infant's increased risk for developing severe hyperbilirubinemia. Each of these studies reported a statistically significant association between the two factors, suggesting that not only is a previous sibling with jaundice a strong predictor of an infant's increased risk for hyperbilirubinemia, but that the severity of an infant's hyperbilirubinemia is associated with that of their sibling's (OR ranging from 2.3 to 6.0). (5)

Visible jaundice in the first 24 hours of life

Jaundice that appears within the first 24 hours may be abnormal and requires further assessment. (22) Two studies included in the NICE guideline found that an infant's elevated serum bilirubin level (OR 10.1) and

visible jaundice within the first 24 hours (OR 2.9) are predictors of an increased risk of developing severe hyperbilirubinemia. (5)

Visible jaundice within the first 24 hours can usually be attributed to an underlying condition in the newborn, such as a deficiency in the enzyme glucose-6-phosphate dehydrogenase (G6PD). A G6PD deficiency is the second most common cause, after ABO blood group incompatibility, in identifiable causes of severe hyperbilirubinemia, and is considered a risk factor for acute bilirubin encephalopathy and hyperbilirubinemia neurotoxicity. (7,9)

A G6PD deficiency can result in an infant's red blood cells becoming increasingly vulnerable to hemolysis, and subsequently, severe hyperbilirubinemia that is difficult to manage even with phototherapy. (1,7,8,23) This deficiency is common in infants of Asian, Mediterranean and African origins, although it is most commonly associated with jaundice of any severity among infants of African origin. (1,23)

Newborns who may be at an increased risk of a G6PD deficiency can be tested for the deficiency through a blood test. If a G6PD deficiency is suspected, prompt testing is important—particularly within the context of hyperbilirubinemia—as bilirubin levels can rise quickly and these infants require treatment at lower thresholds. (3)

G6PD is not screened for by the Newborn Screening Ontario panel, nor is it a test that a midwife may request in Ontario under R.R.O. 1990, Regulation 682, the Laboratory and Specimen Collection Centre Licensing Act. If a midwife suspects a G6PD deficiency, a pediatrician should be consulted for prompt testing and treatment.

Suboptimal feeding

Guidelines on hyperbilirubinemia include exclusive and partial human milk feeding as an independent risk factor for the development of severe hyperbilirubinemia. Six studies summarized in the NICE guideline found a positive association between an infant's risk for developing severe hyperbilirubinemia and exclusive breastfeeding (ORs ranging from 0.4 to 10.75). (5)

However, the factors that underlie the association between hyperbilirubinemia and human milk are not well understood. Suboptimal human milk intake, rather than the exclusivity of human milk feeding, may play an important role in increasing a newborn's risk for developing hyperbilirubinemia. First, suboptimal feeding can result in poor intake, which has the potential to delay the expulsion of meconium, which stores a large amount of bilirubin. Delayed expulsion can facilitate bilirubin moving from the meconium back into the newborn's blood stream, thereby increasing levels of unconjugated serum bilirubin. (19,24,25) Second, poor human milk intake resulting in dehydration may lead to newborn lethargy, thus resulting in fewer feeding sessions and less efficient sucking. (24,26,27) Third, human milk itself may be implicated in higher levels of unconjugated serum bilirubin. (19,27) A component of human milk, β-glucuronidase, is an enzyme that deconjugates intestinal bilirubin conjugates, which in turn, facilitates the intestinal absorption of bilirubin via enterohepatic circulation. (27)

While the role of human milk feeding in the development of severe hyperbilirubinemia is still not well understood, its relationship was influential in the development of hyperbilirubinemia guidelines, which included 'exclusive breastfeeding' as an independent risk factor. This association was particularly compelling as the AAP and CPS developed their guidelines for two interrelated reasons. First, evidence in the United States showed that as breastfeeding initiation rates increased in the 1980s and 1990s, so too did rates of kernicterus. (28,29) American kernicterus registries identified that the overwhelming majority of newborns who developed kernicterus were fed with human milk and that for one-third of these newborns, human milk feeding was the only independent risk factor associated with the newborn's development of severe hyperbilirubinemia. (27) Second, increased breastfeeding initiation rates coincided with a move towards earlier discharge from hospital. It has been suggested that many new parents—who prior to this transition would have remained longer in hospital with access to adequate lactation support—were now receiving limited lactation support and moving back into the community with little to no early postpartum follow-up, resulting in delayed detection and diagnosis of severe hyperbilirubinemia. (29–31) It is conceivable, then, that this move toward earlier discharge in the United States may have resulted in higher rates of suboptimal feeding and reduced detection of severe hyperbilirubinemia, thereby contributing to higher rates of kernicterus.

The healthcare landscape in which the AAP and CPS

guidelines were created differ markedly from the midwifery context. The midwifery context is such that clients receive an average of six visits in the first six weeks postpartum (32), which take place in the hospital, home or clinic setting, along with on-call availability at all other times. Midwifery clients typically receive three of these visits in the first week after the birth in the setting of the clients' choice, usually at home. Those interested in exclusively nursing receive support from their midwives and are supported in optimally feeding their newborns. Furthermore, clinical assessments for signs of visible jaundice, weight gain/loss, output levels and/or testing of bilirubin levels are components of the midwifery postpartum/newborn visit and parents are informed about important risk factors and symptoms of jaundice. It is likely that midwifery clients — provided they receive consistent follow-up care in the community setting with adequate lactation support and teaching about jaundice — would be at a lesser risk for severe hyperbilirubinemia.

Research Gaps:

- Researchers have yet to identify the underlying factors that explain the association between human milk feeding and hyperbilirubinemia.

Good Practice Statements:

1. Identification of risk factors for severe hyperbilirubinemia typically occurs in an ongoing manner throughout the course of the prenatal and postpartum period in the context of Ontario midwifery care

   Regardless of risk factors, review the following as part of an informed choice discussion with clients:
   - that jaundice is common, short-lived and usually harmless; however, a small number of babies will develop severe hyperbilirubinemia, which can be harmful if not treated;
   - how to detect visible jaundice, particularly within the first 24 hours (visibly yellow in lighter-skinned infants and/or yellow sclera or with blanched skin in darker-skinned infants and/or yellow sclera) and signs of hyperbilirubinemia, including poor suck, lethargy and reduced feeding, dark urine and pale, chalky stools; and
   - how to contact the midwife if jaundice is suspected in the newborn.
2. Share with clients how risk factors, if present, may impact considerations for screening and management of severe hyperbilirubinemia.

   These good practice statements recognize the client as the primary decision-maker, the midwife's ability to identify emerging risk factors for severe hyperbilirubinemia and the need for timely decision-making.

WHAT ARE THE FACTORS ASSOCIATED WITH PROLONGED JAUNDICE?

Prolonged jaundice is any jaundice lasting more than 14 days in term infants and more than 21 days in preterm infants. (3) Prolonged jaundice accompanied by a conjugated bilirubin level greater than 18 µmol/L or greater than 20% of the TSB concentration warrants further investigation, as jaundice may be due to pathological causes including hemolysis, infection, congenital hypothyroidism and inherited metabolic conditions. (2,33) Early recognition and timely treatment of these conditions is essential to prevent morbidity.

Midwives should further be aware that prolonged jaundice may signify cholestasis and be associated with biliary atresia and liver disease. (33) Cholestasis should be suspected in all infants with prolonged jaundice, light stools and dark urine. (33)

Most cases of prolonged jaundice are caused by **breast milk jaundice**, a condition whereby infants who are exclusively fed with human milk experience elevated bilirubin levels, despite being otherwise healthy. (34) Breast milk jaundice appears late in the first to second week after birth, but is a benign condition that resolves spontaneously within the first 12 weeks of life and does not place infants at risk for acute or chronic bilirubin encephalopathy. (5,34–36) Infants with breast milk jaundice typically feed well, have normal weight gain, frequent urine output and frequent yellow stools, and do not require treatment for hyperbilirubinemia or supplementation with formula. (34)

Good Practice Statement:
3. In the otherwise well, human milk-fed infant with prolonged jaundice (jaundice lasting > 14 days), midwives may consider drawing TSB including the conjugated bilirubin to screen for the need for further investigation. If conjugated bilirubin level is > 18 µmol/L or greater than 20% of the TSB concentration, consult with a physician for further investigation of potential underlying causes of prolonged jaundice. *This good practice statement recognizes continuity of care and the ability of the midwife to assess the need for interprofessional collaboration as the neonate's clinical picture requires.*

WHAT ARE THE FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ACUTE AND/OR CHRONIC BILIRUBIN ENCEPHALOPATHY?

While the mechanisms between the factors listed below are not well understood, they are believed to increase the risk of acute bilirubin encephalopathy in infants who have severe hyperbilirubinemia. (2,3) Based on limited observational data, guideline groups suggest that infants with these risk factors are at greater risk of developing acute and/or chronic bilirubin encephalopathy at lower bilirubin levels:

- Isoimmune hemolytic disease
- G6PD deficiency
- Asphyxia
- Respiratory distress
- Significant lethargy
- Temperature instability
- Sepsis
- Acidosis

Many of these risk factors represent a pathologic form of jaundice. If a pathologic cause is suspected, further investigation to determine the underlying disease is required. Most of these risk factors would require that midwives consult with a physician, as they would necessitate more intensive monitoring, management and/or treatment from a specialist within a hospital setting.

Midwives who suspect the presence of hemolytic disease, however, can order a direct anti-globulin test (DAT). This test will identify whether an Rh or ABO blood group isoimmunization, due to Rh or ABO blood group incompatibility, is involved in the excessive breakdown of a newborn's red blood cells.

Direct anti-globulin (Coombs) test

Hemolytic disease of the newborn (HDN) is the most common pathological cause of neonatal hyperbilirubinemia, and typically occurs as a result of an Rh or ABO blood group incompatibility between the birthing parent and their fetus/newborn. (1,37)

HDN should be considered in the newborn when there is:

- rapidly developing or severe hyperbilirubinemia, not predicted by maternal antibody screening;
- a positive direct anti-globulin test (DAT);
- prolonged hyperbilirubinemia; or
- hemolysis detected on blood film examination. (38)

Infants affected by Rh-induced hemolysis, which includes those who have declined or who have not otherwise received Rh prophylaxis, do not typically appear jaundiced at birth. However, hyperbilirubinemia can develop quickly, as their livers and spleens work to destroy red blood cells adhered to parental antibodies. (8,37) Routine postnatal prophylactic anti-D immunoglobulin for Rh D negative birthing parents has significantly reduced this form of HDN. (38)

Hemolysis as a result of an ABO incompatibility is seen more commonly in infants, but is milder than hemolysis as a result of an Rh incompatibility. (8) In Canada, an ABO blood group incompatibility is the most common cause of severe neonatal hyperbilirubinemia. (7,9) Hyperbilirubinemia due to an ABO incompatibility typically presents at 24 to 72 hours after birth, which is later than that of an Rh incompatibility. (8) A direct anti-globulin test (DAT or direct Coombs) can be done on an infant's cord blood to identify isoimmunization (37). Having information about the infant's blood group and DAT may facilitate risk assessment for hemolysis and identify infants at greater risk of developing severe hyperbilirubinemia.

Good Practice Statement:

4. For O blood group birthing parents, midwives should consider drawing cord blood and storing it for processing in the event that jaundice presents in the first 24 hours or that a TSB is later drawn for that infant. Although community standards may vary, midwives can consider bringing (i) stored cord blood for DAT processing and (ii) the TSB sample from the infant's heel prick to the laboratory for processing at the same time. If cord blood has not previously been drawn and stored at birth, midwives may consider drawing a tube of blood for DAT and blood type in addition to the TSB by infant heel prick.
    - If the newborn's TSB level is normal and no further testing or treatment is required, cord blood does not need to be tested for isoimmunization.
    - If TSB level is high, have cord blood processed to aid in the identification of the cause of hyperbilirubinemia.

    This good practice statement recognizes cord blood as an aid in the identification of the cause of hyperbilirubinemia in cases where pathologic jaundice may be possible (e.g. when birthing parent has O blood group).

Considerations for Cord Blood Storage:

As midwives perform screening in community settings, there are important considerations related to proper storage and handling of cord blood in order to preserve its integrity for future lab processing:

- Samples should be collected in lavender or pink top tubes with EDTA.
- Samples should not be collected in a gel coagulant separator tube.
- Samples held under 24 hours can be stored at room temperature.
- Samples older than 24 hours should be refrigerated (1-10° C).
- Sample storage limits vary according to the methods used to process the sample; average storage times range from 24 hours to 20 days.

Although these are general guidelines for cord blood storage, local lab practices may vary. To ensure sample integrity and lab acceptance, it is best to check that the storage practices, tubes and age of the sample comply with the protocols of the local receiving lab.

WHICH INTERVENTIONS PREVENT THE DEVELOPMENT OF SEVERE HYPERBILIRUBINEMIA?

Interventions aimed at preventing severe hyperbilirubinemia seek to manage bilirubin levels in order to avoid the need for phototherapy or other treatment alternatives.

Infant formula supplementation

One observational study *(very low certainty of evidence)* was identified that addressed the use of formula supplementation for the prevention of severe hyperbilirubinemia. (39) This study of 313 healthy term infants included two comparisons:

1. ***mixed feeding*** (feeding of human milk and formula) vs. ***exclusive breastfeeding***
2. ***exclusive formula supplementation*** vs. ***exclusive breastfeeding***

Among mixed fed infants, this study showed that the use of formula may reduce the incidence of **severe hyperbilirubinemia** (RR 0.40, 95% CI 0.19 to 0.87, p=0.02), may reduce the **need for phototherapy** (RR 0.39, 95% CI 0.18 to 0.84, p=0.02), and may result in lower **bilirubin levels on day four** (184.69 µmol/L vs. 225.72 µmol/L; MD -41.04, 95% CI -65.67 to -16.41, p=0.001), though we are uncertain of these results.

Among infants who received ***formula exclusively***, this study showed that the use of formula may reduce the incidence of **severe hyperbilirubinemia** (RR 0.19, 95% CI 0.06 to 0.60, p=0.005), may reduce the **need for phototherapy** (RR 0.19, 95% CI 0.06 to 0.59, p=0.004), and may result in lower **bilirubin levels on day four** (167.58 µmol/L vs. 225.72 µmol/L; MD -58.14, 95% CI -87.46 to -28.82), though we are uncertain of these results.

Work group remarks, clinical considerations, values and preferences

The results from this research study are not applicable to practice in Canada. The bilirubin levels used to diagnose 'severe hyperbilirubinemia' and initiate

[2] See Considerations for Cord Blood Storage in the community setting below.

phototherapy in the study were lower than current Canadian guidance on phototherapy management. Due to these differences in treatment thresholds, the association between formula supplementation and the prevention of hyperbilirubinemia cannot be elucidated.

The following recommendation is strong, although the evidence available was of very low certainty. The WG balanced the rare risk that an infant will develop severe hyperbilirubinemia against the substantial benefits that result from exclusive human milk feeding, such as reduced risk of gastrointestinal infection (40) and improved immunologic status. (41) This recommendation recognizes that midwives support human milk as the optimal physiological nutrition for infants.

Recommendation:

5. Midwives should not recommend the use of formula supplementation to prevent severe hyperbilirubinemia in the otherwise well, healthy, human milk-feeding neonate.

   Strong recommendation: very low certainty of evidence

   This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

Lactation support

We identified one cluster-randomized study *(moderate certainty of evidence)* that addressed lactation support for the prevention of severe hyperbilirubinemia among participants intending to breastfeed. (42) In this trial, lactation support consisted of four core components: extended skin to skin, frequent breastfeeding, good positioning and acknowledgement of both parents as equal parents with different roles. At seven days, fewer infants in the lactation support group **required phototherapy** (n = 27/1657) vs. usual care group (n = 42/1143; RR 0.44, 95% CI 0.28 to 0.71, p=0.0008).

Work group remarks, clinical considerations, values and preferences

Lactation support programs were identified as an important intervention in the development of severe hyperbilirubinemia, which may be associated with dehydration, weight loss and reduced caloric intake subsequent to suboptimal human milk intake. (19,25,43) Maintaining a frequency of 8-12 daily feedings has been identified as an important way to prevent the development of severe hyperbilirubinemia. (29) The WG acknowledged the role lactation support may play in improving human milk intake for the prevention of severe hyperbilirubinemia and there was moderate certainty of evidence that lactation support programs likely reduce the need for phototherapy among infants fed with human milk.

Summary Statement:

- Lactation support, provided by midwives as a standard of care, likely helps reduce the risk of requiring phototherapy.

Timing of cord clamping

Two systematic reviews which included three relevant meta-analyses were found that examined the timing of cord clamping, comparing delayed cord clamping (after 60 seconds or when cord pulsation stopped) and early cord clamping (within 60 seconds of birth) among healthy term infants.

A meta-analysis of seven randomized controlled trials *(high certainty of evidence)* enrolling 2324 healthy term infants showed delayed cord clamping increases the **need for phototherapy**; 16 more infants (from 1 more to 40 more) per 1000 would require phototherapy after delayed cord clamping (RR 1.59, 95% CI 1.03 to 2.46, p=0.04). (44)

A meta-analysis of six randomized controlled trials *(moderate certainty of evidence)* enrolling 2098 healthy term infants showed that delayed cord clamping likely increases the incidence of **clinical jaundice**, with 16 more infants (from 10 fewer to 49 more) per 1000 receiving a diagnosis of 'clinical jaundice' (RR 1.16, 95% CI 0.90 to 1.49, p=0.15). (44)

A meta-analysis of two randomized controlled trials *(high certainty of evidence)* enrolling 91 infants showed that delayed cord clamping does not result in an important increase in **bilirubin levels** at or after 72 hours of life (140.86 µmol/L vs. 122.59 µmol/L; MD 18.27 µmol/L higher, 95% CI -2.47 to 39.0, p=0.08). (45)

A recent observational study that investigated the timing of cord clamping among a cohort of caesarean-delivered late preterm and term infants with ABO isoimmunization (n = 336) found similar effects. In this high-risk population, delayed cord clamping may increase the **need for phototherapy**, increase **hospital readmission rates** and increase **bilirubin levels**, but we are very uncertain of these results due to the study's small sample size. (46)

Work group remarks, clinical considerations, values and preferences

In making the following recommendation, the WG balanced the finding that delayed cord clamping results in an increased need for phototherapy but also poses no increased risk of chronic or permanent harms and has a number of benefits, such as improved long-term iron stores, haematocrit values and hemoglobin concentrations. (44)

Recommendation:

6. Midwives may offer delayed cord clamping to all clients, taking into consideration hyperbilirubinemia risk factors.

   Informed choice discussions should include:

   - the risks and benefits of delayed cord clamping compared with early cord clamping;
   - how risk factors for hyperbilirubinemia, if present, increase the infant's risk of jaundice; and
   - the client's values and preferences.

   Weak recommendation: moderate certainty of evidence

   This recommendation recognizes the preference for and health benefits of delayed cord clamping while balancing the client's values and preferences.

Postpartum home visits

The body of evidence exploring the impact of one or more postpartum home visits vs. none on outcomes related to severe hyperbilirubinemia is drawn from three studies conducted in Canada, (47) the United States (48) and Syria. (49)

One randomized controlled trial *(low certainty of evidence)* enrolling 175 parent-infant dyads showed there may be a slightly lower incidence of **severe hyperbilirubinemia** with home visits than without: 25 fewer cases (from 46 fewer to 82 more) per 1000 (RR 0.52, 95% CI 0.10 to 2.59, p=0.42). These results lack precision, as there are very few participants in the study who received a diagnosis of severe hyperbilirubinemia. (47)

One observational study *(very low certainty of evidence)* enrolling 2967 infants showed that postpartum home visits may reduce **hospital readmissions** (RR 0.22, 95% CI 0.05 to 0.9, p=0.04). (48) However, we are uncertain of the applicability of these results because study participants in the intervention group received only one home visit. In Ontario, where midwifery clients typically receive three visits in the first week, the strength of the association may be even greater.

Evidence from one randomized controlled trial *(very low certainty of evidence)* conducted in Syria showed that postpartum home visits may make little to no difference on the **incidence of jaundice** (RR 0.97, 95% CI 0.77 to 1.23, p=0.81) in a population of 573 infants, though a lack of blinding among study personnel and participants, differences in health-care settings between Ontario and Syria and wide confidence intervals limit our certainty in these results. (49)

Two randomized controlled trials *(moderate certainty of evidence)* showed that postpartum home visits likely increase the rates of exclusive breastfeeding: 103 more participants (from 34 more to 187 more) per 1000 exclusively breastfeeding (RR 1.42, 95% CI 1.14 to 1.76, p=0.001). (47,49) This evidence is not directly applicable to the Ontario midwifery context because the research was conducted in Syria, where the care received and the scheduling of home visits differs from Ontario.

Work group remarks, clinical considerations, values and preferences

Postpartum home visits are an essential component of midwifery care in Ontario and are highly valued by midwives and clients. Although the evidence on home visits and hyperbilirubinemia is limited *(low and very low certainty)*, there is moderate certainty of evidence that home visits increase rates of exclusive breastfeeding. As suboptimal feeding may increase rates of jaundice, home visits with lactation support have the potential to play an important role in establishing and maintaining a healthy nursing relationship. This outcome was highly valued by the WG, as it identified the association between feeding difficulties and an increased risk of severe hyperbilirubinemia. (19,24,26,27)

Summary Statement:

- As a standard of midwifery care, early postpartum visits, along with home visiting are an important component of how midwives monitor for and detect neonatal hyperbilirubinemia.

Sunlight

Important research from the 1950s discovered that when the unconjugated bilirubin molecule was exposed to light it would convert into a water-soluble form (via a process of photo-oxidation) and become easily excretable in urine. (46) Nurses from that same period also reported that visible jaundice would fade more quickly in infants exposed to direct sunlight. (50) Based on these observations, research was undertaken to investigate how light influences bilirubin levels in infants with hyperbilirubinemia, marking the first known use of phototherapy lamps. (50)

This research from the 1950s was the only study found that investigated the use of sunlight compared with conventional phototherapy. The observational study *(very low certainty of evidence)* included 22 preterm infants from one to 13 days old. This study showed that the **need for exchange transfusion** was lower among infants who received sunlight compared to phototherapy (RR 0.17, 95% CI 0.01 to 3.23, p=0.24). More specifically, none of the infants exposed to sunlight and two of the infants exposed to conventional phototherapy required an exchange transfusion. The two infants exposed to phototherapy had severe jaundice due to Rh isoimmunization and failed to respond to the light treatment, whereas none of the infants exposed to sunlight had any risk factors. The same study suggests that sunlight may result in a smaller mean decrease in **bilirubin levels** (65.8 µmol/L vs. 75.6 µmol/L; MD -9.80 µmol/L, 95% CI –40.03 to 20.43, p=0.53), though we are very uncertain of these results. (50)

Work group remarks, clinical considerations, values and preferences

The evidence for these outcomes is of very low certainty. We cannot be certain of these results, as this study did not control for confounding risk factors. The need for an exchange transfusion for the two infants in the phototherapy group was likely due to the presence of Rh isoimmunization and not due to the effect of phototherapy itself. Furthermore, exchange transfusion is a rare outcome and would require large sample sizes to provide precise results; in this study, there was a small sample size (n = 24). This research was also conducted with preterm infants only, which is not the focus of the current guideline.

Midwives considered this research in both the historical and present context. Phototherapy replaced the routine use of exchange transfusion and is now the standard treatment for hyperbilirubinemia. However, phototherapy is not without its own risks, such as temperature instability, intestinal hypermotility and interference with the parent-child dyad. (2,3,51) The risks associated with phototherapy extend to treatment with sunlight, and risks in use of sunlight are further compounded by additional risks related to exposure to UV radiation. (3) Moreover, and in contrast to phototherapy, sunlight exposure cannot be accurately measured and a consistent level of sunlight intensity cannot be maintained over time or across all contexts. Therefore, the WG agreed that there was insufficient evidence to support the use of sunlight as a form of prevention.

Recommendation:

7. There is insufficient evidence to support the use of sunlight as a means of preventing the development of severe hyperbilirubinemia.

   No recommendation: very low certainty of evidence

Infant massage

Infant massage appears to be associated with increased bowel movements, which may have a positive impact on the development of neonatal hyperbilirubinemia by increasing the volume of bilirubin excretion. (52–55) We identified three trials *(low certainty of evidence)* enrolling 135 infants that examined infant massage for the prevention of hyperbilirubinemia. (54–56)

Two of the three studies were meta-analyzed; pooled data showed that infant massage may slightly reduce **bilirubin levels** on day four (163.31 µmol/L vs. 194.60 µmol/L; MD - 31.55, 95% CI -43.48 to -19.63, p<0.00001). (54,56) Data from a third study (n = 43) could not be meta-analyzed, but results are consistent with the pooled data, suggesting that bilirubin levels on day four were slightly lower among infants who received infant massage than those who did not. (55)

Our confidence in these results is low because there were serious methodological flaws related to randomization, allocation and blinding in all three studies.

Work group remarks, clinical considerations, values and preferences

Infant massage may slightly lower bilirubin levels, but the bilirubin levels in the studies for all infants on day four were not clinically concerning. Little clinical significance should be placed on these findings, as we do not know if massage would result in fewer infants requiring phototherapy in accordance with established treatment thresholds. However, there are many peripheral benefits of infant massage, such as an increase in parental-infant bonding through skin to skin contact, as well as potential improvements in oxytocin production and parental/newborn stress levels. (52)

Summary Statement:

- Further research is required before the use of infant massage for the prevention of severe hyperbilirubinemia is recommended.

WHAT ARE EFFECTIVE SCREENING TOOLS FOR HYPERBILIRUBINEMIA?

The TSB measurement obtained from a blood sample is considered the gold standard for diagnosing severe hyperbilirubinemia. Midwives may also use other screening methods including transcutaneous (TcB) measurements and clinical assessment, which may include the use of both visual and risk-factor assessment.

Visual assessment

Four observational studies were identified that explored the use of visual assessment for detecting jaundice. It is important to note that none of the studies described below examined down-stream consequences of receiving a false positive or a false negative. In other words, these studies do not provide any information to quantify the risk if an infant is 'missed' by the practitioners' visual assessment (i.e., actually belonged to a treatment zone and was therefore delayed necessary treatment).

In one study, neonatologists visually assessed infants as appearing "clinically jaundiced" by answering "yes" or "no." For infants with low bilirubin levels (< 68 µmol/L and < 204 µmol/L), neonatologists often visually assessed these infants as appearing clinically jaundiced (63% and 29% false positive rates respectively). Conversely, 19% of infants with higher bilirubin levels (> 204 µmol/L) were assessed as not being clinically jaundiced (false negative rate). (57)

A second study examined nurses' ability to visually detect jaundice using cephalocaudal progression compared to actual TSB concentrations. Of the 102 included infants, 8.1% were incorrectly assessed as jaundiced by nurses' visual assessment (false positive rate). Conversely, 28.5% of infants who were assessed as not being jaundiced actually were (false negative rate). (58)

In a third study, TSB tests were performed when a nurse determined that jaundice reached the infants' mid-abdomen, representing a bilirubin concentration at or above the 75th percentile. For infants who had a TSB ≥ 75th percentile, almost all were correctly identified by the nurses; there was, however, a small percentage of false negatives (1.5%) representing 4/263 infants who were assessed as not being jaundiced. (59)

The fourth study asked providers to visually assess the severity of jaundice by categorizing infants into four different risk zones (Zones A to D, whereby A is the lowest risk zone and D is the highest risk zone). Each infant's bilirubin level was then verified by a TSB measurement. The agreement between the zone that the infant was placed in by visual assessment and the zone that matched their actual TSB level was assessed. About 8% (230/2857) of infants who were visually categorized into the lowest risk zone (Zone A) should have been categorized into one of three higher zones (Zone B, C or D) according to their actual TSB levels. Conversely, 86% (13/15) of infants whose TSB concentrations placed them in the highest risk zone (Zone D) were visually categorized to lower zones (Zone A, B or C), which could result in many infants being missed, introducing the potential for serious consequences. (60)

Work group remarks, clinical considerations, values and preferences

Our confidence in these results is limited by concerns about the variability in accuracy of visual assessment of jaundice. The above studies suggest that visual assessment cannot detect all babies with higher bilirubin levels; however, practitioners in some of the studies performed relatively better than others. For example, in the one study that asked nurses to visually detect jaundice at the mid-abdomen (cephalocaudal progression), only 1.5% of infants were missed by visual assessment, suggesting that practitioners can see a progression of jaundice. (59) In light of the evidence, the WG affirmed that visual assessment is an important component of midwives' clinical assessment, but should not be used in isolation to discern an infant's risk for hyperbilirubinemia.

Recommendation:

8. The use of visual assessment alone is not recommended for screening for severe hyperbilirubinemia.

   Weak recommendation: very low certainty of evidence

   This recommendation recognizes that visual assessment for hyperbilirubinemia is an important part of the overall clinical assessment of a newborn but should not be relied on alone to determine a newborn's risk of severe hyperbilirubinemia.

Risk factor scoring system

One diagnostic cohort study *(low certainty of evidence)* of 884 infants was identified that examined how accurately different thresholds on a clinical risk factor scoring system identified infants with a significant risk for hyperbilirubinemia (confirmed with TSB). (61) The system assigned each identified risk factor (birth weight, gestational age < 38 weeks, oxytocin use during delivery, vacuum extraction, breastfeeding, and combination breast and bottle feeding) a score and an overall score was determined based on the number of risk factors present and their severity. Lower scores suggest that the infant had fewer risk factors. Higher scores suggest that the infant had more, or more severe, risk factors, which was assumed to be associated with a greater risk of developing hyperbilirubinemia. (61)

Using the lowest threshold (≥ 8) to determine a clinical risk factor score, 87% of infants were incorrectly classified as being at risk for significant hyperbilirubinemia (false positives). These infants all had bilirubin concentrations less than 342 µmol/L and may have been unnecessarily treated as a result of the use of this scoring system. (61) Conversely, when using a threshold of ≥ 24, almost all infants at significant risk were missed (false negative); 98% of infants who had a TSB ≥ 342 µmol/L were incorrectly classified as not being at risk. (61) The use of a high threshold on this scoring system could result in a large number of infants being missed, introducing the potential for serious consequences.

Work group remarks, clinical considerations, values and preferences

While the identification of risk factors is an important part of midwives' overall clinical assessment, the use of this risk factor scoring system has been shown to be highly inaccurate. It is not typical practice for midwives in Ontario to limit their assessment of risk factors to those defined as part of this clinical scoring system and calculate a risk factor score alone to determine a course of action. Moreover, this particular clinical risk factor scoring system could result in harm, as it incorrectly identified infants, resulting in large numbers of false positive and false negative results.

Recommendation:

9. The use of risk factor scoring systems is not recommended for screening for severe hyperbilirubinemia.

   Weak recommendation: very low certainty of evidence

   This recommendation recognizes that midwives routinely assess for hyperbilirubinemia risk factors as part of an infant's clinical assessment in the postpartum period but should not use a scoring system.

Transcutaneous bilimetre

One systematic review of 11 diagnostic cohort studies *(very low certainty of evidence)* contributed results to this body of evidence on the use of transcutaneous bilimetres which measure TcB. In the systematic review hyperbilirubinemia was expressed in two ways:

1. value-based hyperbilirubinemia
2. percentile-based hyperbilirubinemia

The sensitivity and specificity of the TcB measurement compared with a TSB measurement was reported. The sensitivity of a test correlates to its ability to correctly identify people with a disease; a highly sensitive test (sensitivity of 100%) would identify all people with the disease. The specificity of a test correlates to its ability to correctly identify all people without the disease; a highly specific test (specificity of 100%) would identify all people who do not have the disease. (62)

To effectively detect severe hyperbilirubinemia, a test should maximize ***sensitivity*** to ensure that all infants with the condition are correctly identified.

Predicting TSB value-based hyperbilirubinemia

Six studies (n = 1946 participants) reported on the TcB thresholds that were necessary to ensure all infants with a TSB concentration > 256.5 µmol/L were identified. The results were variable: the TcB thresholds necessary to achieve 100% **sensitivity** (the identification of *all* infants with a TSB > 265 µmol/L) ranged from 136.8 µmol/L to 205.2 µmol/L. (63)

Predicting TSB percentile-based hyperbilirubinemia

Five studies (n = 1935 participants) reported the sensitivity and specificity of using a TcB cut-off of the 75th percentile to predict a TSB concentration greater than the 95th percentile of hour- specific values. The sensitivity of a TcB cut-off of the 75th percentile ranged from 87% to 100%. These results suggest that using a TcB cut-off of the 75th percentile may fail to identify all infants who had a TSB concentration greater than the 95th percentile, introducing the potential for serious consequences. (63)

Work group remarks, clinical considerations, values and preferences

The research evidence demonstrates that TcB measurements obtained from bilimetres will not provide an exact estimation of an infant's bilirubin level. In general, TcB shows good correlation with TSB measurements, (64) but does have some important limitations, including a tendency for overestimation amongst infants of darker skin tones (65–69) and those with higher serum bilirubin levels. (64,70) TcB measurements may also be inaccurate during or after phototherapy treatment. (71) In light of this evidence, TcB measurements should be used as an initial screening prompt to determine an infant's need for a follow-up serum bilirubin test, and should not be used during or after phototherapy treatment. Furthermore, Ontario's 2017 *Clinical Pathway Handbook for Hyperbilirubinemia in Term and Late Pre-Term Infants (≥ 35 weeks)* recommends performing a TSB measurement when a TcB result is within 50 µmol/L of the phototherapy treatment line. (72)

Although bilimetres cannot replace TSB testing, they can effectively allow midwives to perform efficient and preventative care in the home and the community. In contrast to TSB tests, bilimetres offer midwives the ability to obtain a bilirubin measurement immediately at point of care and without additional lab analysis. In the cases where clients are required to visit a hospital if they wish to receive TSB screening, a bilimetre can spare these clients from the increased stress and cost associated with travel. This is particularly important for reducing inequities for families that live in rural and remote settings where access to labs and hospitals are limited both by number and substantial geographic distance, and for families with lower socioeconomic status that may have limited access to transportation or are unable to afford taking time off work or hiring childcare.

Research has also shown that a TcB test reduces the need for blood sampling, thereby sparing infants from invasive TSB testing and associated harms, including pain and repeat testing. (64) These factors are likely to increase clients' acceptance of hyperbilirubinemia screening and may reduce midwifery workload associated with drawing and processing a TSB sample.

Despite the many benefits of bilimeters, the number one barrier to their widespread uptake among Ontario midwives is the up-front purchasing cost of the device and the additional costs associated with maintenance and calibration. (5)

Recommendation:

10. Where screening for hyperbilirubinemia is requested and/or recommended and bilimetres are available to the midwife, TcB screening should be offered.

    Strong recommendation: very low certainty of evidence

    This recommendation recognizes the unequal access to bilimetres across practice groups and the province but affirms the use of bilimetres as an effective screening tool to prompt TSB testing when required and as a promising way to increase community-based care.

Universal bilirubin screening

Eight observational studies were identified that compared a universal screening program described as screening all infants in the first 72 hours of life using either TcB or TSB measurement vs. no universal screening program. In each study, all infants born after the implementation of a universal TcB and/or TSB screening program received screening, whereas infants born prior to the implementation of universal screening received selective bilirubin testing on the basis of clinical judgement.

Two retrospective-cohort studies *(very low certainty of evidence)* enrolling 49 726 infants showed universal TSB or TcB bilirubin measurement may increase the need for exchange transfusion (RR 1.31, 95% CI 0.35 to 4.86, p=0.69), although the results are limited by the small number of infants who required an exchange transfusion. (73,74)

Three observational studies *(very low certainty of evidence)* limited by indirect evidence showed a lower incidence of a bilirubin concentration ≥ 513 µmol/L among infants (n = 1 418 759) who were born after the implementation of universal bilirubin measurement (RR 0.35, 95% CI 0.19 to 0.65, p=0.0009). These results were considered indirect because the population of infants included did not represent healthy term or late-preterm neonates. (74–76)

Pooled results from four observational studies *(very low certainty of evidence)* including 1 510 040 infants showed a lower incidence of bilirubin concentrations ≥ 427 µmol/L among infants who were born after the implementation of universal bilirubin measurement (RR 0.42, 95% CI 0.25 to 0.70, p=0.0009), though we are uncertain of these results because results were not consistent across all of the studies; some studies reported a higher incidence of bilirubin concentrations ≥ 427 µmol/L among infants who were universally screened. (74–77)

Three observational studies *(very low certainty of evidence)* enrolling 481 223 infants examined the incidence of bilirubin concentrations ≥ 342 µmol/L. Results were inconsistent across studies, though meta-analysis showed a lower incidence of bilirubin concentration ≥ 342 µmol/L among infants who were

born after the implementation of universal bilirubin screening (RR 0.58, 95% CI 0.47 to 0.71, p<0.00001). (74,76,77)

Six observational studies *(very low certainty of evidence)* enrolling 942 405 infants showed a universal screening program may make little to no difference in the need for phototherapy (RR 1.10, 95% CI 0.64 to 1.90, p=0.73), though we are very uncertain of these results due to inconsistent findings across studies as well as methodological flaws in all three studies, including lack of control for confounding factors such as the age of infants, presence of risk factors and rates of human milk feeding. (73,74,78,79)

Three retrospective-cohort studies *(very low certainty of evidence)* including 649 305 infants reported on hospital readmissions. Results were inconsistent across studies; pooled data from two studies showed that implementation of the universal screening program may make little to no difference on hospital readmission rates (RR 0.58, 95% CI 0.30 to 1.12, p=0.10) (76,80), whereas the third study reported an increase in hospital readmission after implementation of universal screening (RR 1.21, 95% CI not reported). (81)

Work group remarks, clinical considerations, values and preferences

In making this weak recommendation, the WG considered the paucity of high-certainty evidence on the effectiveness of universal screening as well as the limitations of visual assessment, such as provider variability in recognizing the presence or severity of jaundice. The WG also considered evidence from the CPSP which demonstrated that after the introduction of the 2007 Canadian-specific guideline recommending universal bilirubin screening, the incidence of critical hyperbilirubinemia amongst newborns declined significantly, from 1 in 2400 live births in 2002-2004 to 1 in 8600 live births in 2011-2013. (9) This reduction indicates that universal screening may prevent the development of critical hyperbilirubinemia.

However, within the context of regular, timely and close follow-up care, the WG recognized that there may be limited benefit to performing universal screening in the midwifery context, particularly for the approximately 40% of healthy term infants who do not develop visible jaundice and who meet developmental and feeding milestones. For these infants, the WG recognized the small harms associated with TSB sampling, including infant pain and additional stress on parents in the early postpartum period. These harms may disproportionately affect midwifery clients who receive serum blood screening in the community setting, as so few midwives have access to bilimetres to perform TcB screening.

Midwives also face a number of structural and systemic barriers to offer screening. First, midwives do not have access to specific funding which would allow for the purchase of bilimetres. Second, midwives face barriers when submitting blood samples to community and hospital-based labs that in some cases will not accept a sample which has been drawn in the community. Labs must be instructed to accept and process midwifery samples in a timely way. Third, midwives have not been adequately compensated for the increased workload associated with screening, including the time required to commute samples from the home to lab or clinic setting. Universal midwifery access to bilimetres and labs would help facilitate equitable access to bilirubin screening among infants born in midwifery care and between midwifery and non-midwifery cohorts.

These barriers also impact midwifery clients in a myriad of ways. Midwifery clients who have home or birth centre births and who choose screening but are unable to receive screening in the home setting will need to travel to the nearest out-patient clinic or emergency room. This problem is exacerbated in rural and remote communities, where access to labs and hospitals may be severely limited by geographic distance, and for families with lower socioeconomic status that may be limited by unstable housing and a lack of adequate transportation. Research has demonstrated that universal screening in Ontario appears to have the unintended consequence of increasing health disparities when barriers to health care access for disadvantaged populations are left unaddressed. (82)

For those midwifery clients who have a hospital birth, midwives may be more inclined to recommend a 24-hour postpartum stay to facilitate screening. This lengthens midwifery discharge times, thereby increasing nursing workload and the financial burden on the health-care system overall. Given these considerations, the WG recognized that the values, preferences and risk tolerance for screening among midwifery clients may differ.

Recommendations:

11. The risks and benefits of universal screening should be discussed with all clients as part of an informed choice discussion.

    This discussion may address:
    - what is known about risk factors, if present;
    - how visible jaundice, poor feeding, dehydration and weight loss impacts the risk of developing severe hyperbilirubinemia;
    - what is known about the limitations of visual assessment of jaundice;
    - optimal timing of screening: between 24 to 72 hours of age;
    - barriers to and enablers of screening within the client's community context; and
    - the client's values and preferences and risk tolerance.

    Weak recommendation: very low certainty of evidence

    This recommendation recognizes the paucity of high-certainty evidence on the effectiveness of universal screening, the uniqueness of the midwifery context and structural barriers which impact midwives' ability to offer community-based bilirubin screening.

12. If visible jaundice develops, obtaining a bilirubin measurement is recommended.

    For neonates who have previously had a negative TSB screen and in whom visible jaundice subsequently develops, midwives may use their clinical judgement in determining the need to re-screen. Consider presence or absence of other clinical factors associated with severe hyperbilirubinemia (e.g. suboptimal feeding, lethargy, dark urine, pale chalky stools).

    Weak recommendation: very low certainty of evidence

    This recommendation recognizes that the timely, frequent and close follow-up of neonates as a standard of midwifery care limits the benefits associated with universal screening while acknowledging the importance of the clinical manifestation of hyperbilirubinemia.

Research Gaps:

- Midwives may be unique among health-care providers in the extent to which they provide ongoing, timely and in-person clinical assessment throughout the first days and weeks postpartum, including home visiting. Studies of the efficacy of universal screening within this model are lacking; this information would be more useful to inform midwifery practice.

Considerations for Bilirubin Transport:

As midwives perform TSB screening in community settings, there are important considerations related to the proper transport and handling of samples in order to preserve integrity:

Optimal microtainers

- Optimal microtainers for bilirubin samples include Lithium Heparin (Green) and the SST-Serum Separator Gel (Gold) amber microtainers (as is suggested by Sunnybrook Hospital and the Department of Pathology and Laboratory Medicine at the University of California). (83,84)

Protection from light

- To ensure that samples are protected from light degradation, they can be wrapped in aluminum foil, stored in an opaque box or placed in a brown paper bag. (85,86) Amber coloured microtubes can also be used to protect bilirubin samples from light. (87)

Protection from hot or cold temperatures

- Research has tested bilirubin samples at temperatures between + 3°C and + 35°C and found this entire range to be acceptable for maintaining bilirubin level stability with light protection. (88–90) To ensure sample integrity, midwives may consider transporting bilirubin samples with ice or cold packs dependent on weather and transport conditions. (86)

Time for transportation

- Where possible, blood samples should be delivered to a lab within two hours of the blood draw. (4)

WHAT INTERVENTIONS EFFECTIVELY MANAGE AND TREAT SEVERE HYPERBILIRUBINEMIA?

Interventions such as phototherapy aim to manage hyperbilirubinemia in order to avoid more serious consequences of bilirubin toxicity.

Fibreoptic phototherapy

One Cochrane review was identified that addressed the use of fibreoptic phototherapy vs. conventional phototherapy for the treatment of hyperbilirubinemia. (91) This Cochrane review found evidence on the effects of fibreoptic phototherapy on **duration of phototherapy** (four randomized or quasi-randomized trials), **change in bilirubin concentration over total treatment period** (five randomized trials), and **change in bilirubin levels at 24 hours** (four randomized trials).

A meta-analysis of four randomized or quasi-randomized controlled trials *(low certainty of evidence)*, with serious methodological flaws related to randomization, allocation and blinding, showed fibreoptic phototherapy may increase the **duration of phototherapy** (73.4 hours vs. 53.8 hours; MD 21.45 hours, 95% CI 16.92 to 25.99, p<0.00001) in a population of 330 healthy term infants. (91)

A meta-analysis of five randomized controlled trials *(moderate certainty of evidence)* enrolling 345 healthy infants examined **change in bilirubin concentration over the total treatment period**, calculated as the percent change per day. Results were inconsistent across studies, though the change in bilirubin concentration was 4.82% (p<0.0005) greater in the conventional phototherapy group. (91)

A meta-analysis of four randomized controlled trials *(high certainty of evidence)* enrolling 183 healthy infants showed fibreoptic phototherapy is slightly less effective at lowering bilirubin **concentrations within 24 hours** of starting treatment. The percent change in bilirubin concentration was 4.35% (p=0.002) greater in the conventional phototherapy group, however, these differences are not clinically significant. (91)

Work group remarks, clinical considerations, values and preferences

The WG balanced the benefits of fibreoptic phototherapy, such as skin to skin contact and more frequent human milk feeding, against the finding that fibreoptic therapy is slower at lowering bilirubin concentrations, which may increase treatment duration. The WG recognized that fibreoptic phototherapy may be less acceptable to clients who would prefer a shorter duration of treatment, but more acceptable to clients who value the opportunity for skin to skin contact and/or the potential for less disruption of human milk feeding.

The WG further identified fibreoptic phototherapy as the preferred method of treatment in the home and community setting. Home phototherapy may prevent prolonged hospitalization, promote the parent-child dyad, and provide cost savings to the health-care system. (92) The WG discussed the use of fibreoptic phototherapy in the home, balancing the potential increased treatment duration with the benefit of supporting the parent-infant bond and client values regarding treatment at home. Home phototherapy may also reduce the burden of treatment (travel) for rural and remote clients.

Importantly, the management of conventional phototherapy in many communities remains hospital-based and access to fibreoptic phototherapy varies across the province. Although midwives support community and home-based care, home phototherapy treatment is largely unavailable due to the inaccessibility of equipment and the potential time constraints on midwives. The WG valued offering this intervention in communities where fibreoptic phototherapy is available as part of an informed choice discussion, recognizing variability in clients' access, preferences and values.

Recommendations:

13. Where available, midwives may offer fibreoptic phototherapy using their clinical experience and the clinical context of the client to guide decision-making.

    Weak recommendation: low certainty of evidence

    This recommendation recognizes that fibreoptic phototherapy may increase the duration of treatment and therefore may not be appropriate in all cases, but has benefits such as an increase in skin to skin contact.

14. Midwives may offer fibreoptic phototherapy in the home as an option for treatment where community-based health infrastructure exists.

    Weak recommendation: low certainty of evidence

    This recommendation recognizes midwives' scope of practice to manage phototherapy, provided midwives have the knowledge, skills, experience and community-based health infrastructure to do so.

Research and implementation Gaps:

- No direct research was found that examined the use of fibreoptic phototherapy in the home setting.
- Improvements in community-based health care infrastructure are required in order to fund and support midwifery initiation and management of phototherapy in the home and community setting.

Considerations for Implementation: Midwifery Management of Phototherapy

Improvements to community-based health care infrastructure that would facilitate midwifery management of phototherapy include but are not limited to:

- Funding that allows midwifery practice groups to purchase home phototherapy equipment (fibreoptic phototherapy units e.g., bili blankets).
- Development of continuing education specific to midwives managing phototherapy.
- Increased access to community-based laboratories for processing blood samples (intake of blood samples from the community, laboratories that operate during the weekends and overnight). (4)
- Seamless consultation or transfer of care if necessary.
- Change in reimbursement policies that reflect additional daily assessments, laboratory sampling and travel costs required during phototherapy.

Formula supplementation during phototherapy

One observational study *(very low certainty of evidence)* was identified that explored the use of formula supplementation during phototherapy. In the study, 53 healthy term neonates were enrolled and divided into two groups according to feeding type at time of re-admission to hospital: mixed fed (supplemented with 75 mL/kg/d of formula) and exclusively human milk-fed.

This study showed that mixed feeding may reduce the **duration of phototherapy** (26.8 hours vs. 38.6 hours; MD -11.8 hours, 95% CI -17.75 to -5.85, p=0.0001) and result in a faster average decrease of **bilirubin levels** within a 24 hour period (92.34 µmol/L/24 hours vs. 68.40 µmol/L/24 hours; MD 23.94 µmol/L, 95% CI 7.05 to 40.83, p=0.005), but we are uncertain of these results. (93)

Work group remarks, clinical considerations, values and preferences

Formula supplementation may reduce the duration of phototherapy but we are very uncertain about these results, as the study did not control for confounding factors. In making the following recommendation, the WG balanced a longer duration of phototherapy against the substantial benefits that result from exclusive human milk feeding, such as improved bonding between parent and newborn, (40,94) reduced risk of gastrointestinal infection (40) and improved immunologic status. (41) Clients should not be deterred from nursing while an infant is undergoing phototherapy. Rather than formula supplementation, nursing parents should be encouraged to frequently feed their infant and receive ongoing lactation support, as required for the clinical picture.

Recommendation:

15. Midwives should not routinely recommend use of formula supplementation for otherwise healthy infants undergoing phototherapy, discussing the risks and benefits with clients.

    Strong recommendation: very low certainty of evidence

    This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

Infant massage during phototherapy

We identified two randomized controlled trials *(moderate certainty of evidence)* examining the use of infant massage as an adjunct to phototherapy. A meta-analysis of the two studies (n = 142) showed that infant massage likely results in lower **bilirubin levels on day three** (MD -31.03, 95% CI -41.1 to -20.96, p<0.00001). (95,96)

Work group remarks, clinical considerations, values and preferences

Available evidence on massage and phototherapy includes moderate certainty of evidence that massage may result in lower bilirubin levels on day three of phototherapy, though this difference is not clinically significant. Confidence in the results is limited by uncertainty about the randomization process and a small, inadequately powered sample size. The WG considered the other potential benefits of infant massage, such as improved elimination and weight gain, improved sleep patterns, growth and development, reduced rates of colic, constipation, and stress, as well as the promotion of parent-infant bonding. (52,95,97)

Summary Statement:

- Infant massage as an adjunct to phototherapy is unlikely to affect bilirubin levels in a clinically meaningful way.

Skin to skin contact

We identified one observational study *(very low certainty)* and one randomized controlled trial *(moderate certainty of evidence)* examining the use of skin to skin contact in conjunction with phototherapy for the treatment of severe hyperbilirubinemia.

Results from the observational study, in which skin to skin was done for one hour three times daily, showed that skin to skin may reduce the **duration of phototherapy** (68.14 hours vs. 100.86 hours; MD -32.72 hours, 95% CI -52.54 to -12.9. p=0.001), but may result in little to no difference in peak serum **bilirubin levels** (261.6 µmol/L vs. 263.6 µmol/L; MD -2 µmol/L, 95% CI -20.14 to 16.14, p=0.83). (98)

Results from the randomized controlled trial, in which intermittent skin to skin was done every three hours, showed shorter **duration of hospitalization** (2.09 days vs. 3.03 days, p=<0.001). Small sample sizes and wide confidence intervals as well as missing outcome data limit our confidence in these results. (99)

Work group remarks, clinical considerations, values and preferences

Research suggests that continuous skin to skin contact (> 20 hours/day) reduces mortality and risk of hypothermia, hypoglycemia and sepsis, and increases weight, length and head circumference gain. (100) The certainty of evidence for intermittent skin to skin is very low; we are uncertain whether this intervention reduces the duration of phototherapy and/or is more effective at lowering bilirubin levels. It is important to note that the peak serum bilirubin levels in this study were not clinically meaningful and skin to skin may not always be able to be maintained if the infant's bilirubin levels are more critical. While there are no known harms of intermittent skin to skin contact, there are a number of benefits, including lactation support, reduction of parental anxiety, improvement of respiration and oxygen saturation of the infant. (98,101,102)

Summary Statement:

- Midwives support skin to skin contact as a standard component of normal, physiologic postpartum care for infants, including infants undergoing standard phototherapy treatment.

Other treatments

There are other more rarely used treatments for severe hyperbilirubinemia. These treatments are typically used among preterm infants or in cases of pathological jaundice resulting from G6PD deficiency or other hemolysis disease. While outside of midwifery scope, the WG identified the need to identify these therapies so that midwives may provide information to clients who receive these treatments.

Treatment: Intravenous immunoglobulin infusion

Intravenous immunoglobulin (IVIG) infusion is the process of administering a blood product comprised of antibodies to treat autoimmune conditions. It has been used in infants who demonstrate Rh, ABO or other blood group incompatibilities. It is particularly indicated for infants with pathologic jaundice, as a result of underlying hemolytic disease, as it is considered to be safer and a more well-tolerated treatment than exchange transfusion. Results from one Cochrane review (n = 189) on the use of IVIG among infants experiencing severe hyperbilirubinemia as a result of isoimmune hemolytic disease suggest that IVIG is associated with a reduced need for exchange transfusion; however, further research is required before its routine use is recommended. (103)

Treatment: Phenobarbitone

Phenobarbitone is a barbiturate used in the management of physiologic jaundice. It can be administered to neonates either orally or parenterally, and enhances enzymatic activity of glucuronyl transferase in the liver. Liver metabolism of phenobarbitone increases the conversion of unconjugated bilirubin to conjugated bilirubin, allowing for greater excretion of the conjugated bilirubin from the body. Results from a meta-analysis of three studies (n = 497) focused solely on preterm infants with very low birth weight suggest that the use of phenobarbitone may result in lower peak serum bilirubin levels and a reduced need for phototherapy or exchange transfusion. Further research on phenobarbitone is required for a full understanding of its adverse effects, such as survival without major disability at 18-24 months, duration of NICU stay, and duration of hospital stay, among other outcomes, before its routine use is recommended. (104)

Treatment: Metalloporphyrins (SnMP)

Metalloporphyrins are heme analogues involved in the regulation of hepatic heme oxygenase, an enzyme that actively catabolizes heme into bilirubin during the neonatal period. Specifically, metalloporphyrins prevent the conversion of heme to bilirubin by inhibiting enzymatic activity of heme oxygenase and can be administered to neonates orally or parenterally. A Cochrane review of three studies (n = 170) suggested that metalloporphyrins may prevent the buildup of bilirubin levels and the need for phototherapy among preterm and term neonates; however, the review authors concluded that evidence reviewed neither supports or refutes that metalloporphyrins decrease the risk of neonatal kernicterus or long-term neurodevelopmental impairment. (105)

Treatment: Clofibrate

Clofibrate is administered orally to neonates as a treatment for hyperbilirubinemia. It enhances enzymatic activity of glucuronyl transferase in the liver to increase the conversion of unconjugated bilirubin to conjugated bilirubin which can then be excreted. A Cochrane review examined the effect of two different doses of clofibrate (100 mg/kg and 50 mg/kg) in combination with phototherapy compared to phototherapy alone on mean TSB levels at 48 hours after treatment, and duration of phototherapy among term neonates. (106)

Results for the pooled outcome of mean TSB levels suggested that the use of combination treatment (dose: 100mg/kg or 50 mg/kg) lowered bilirubin levels slightly more than phototherapy alone at 48 hours after the initiation of treatment. The effect of combination treatment was significantly associated with a reduction in the duration of phototherapy compared to treatment with phototherapy alone (WMD: -25.40 hours; 95% CI: -28.94 to -21.86; n = 4 studies). However, there were significant inconsistencies in the findings across studies.

Review authors concluded that the evidence was insufficient to make recommendations for practice since the included studies showed a high risk of bias and inconsistent results. Further research on clofibrate and its effects on long-term health outcomes, such as reductions in the incidence of bilirubin encephalopathy and adverse sequelae is required before its routine use can be recommended. (106)

Midwifery Clinical Pathway for Screening and Management:

Screening for hyperbilirubinemia and management of phototherapy, as required, is within the midwifery scope of practice. A clinical pathway titled: Clinical Pathway for Midwifery Screening (≥ 35 weeks) and Management of Phototherapy in Term Infants (≥ 37 weeks) has been developed to complement this CPG.

The clinical pathway has been adapted for midwives from Ontario's Clinical Pathway Handbook for Hyperbilirubinemia in Term and Late Pre-term Infants. The midwifery pathway was adapted to reflect midwives' scope of practice and guidance in this CPG, integrate midwifery values, and incorporate the midwifery philosophy and model of care.

The midwifery screening and management of hyperbilirubinemia clinical pathway:

- Provides midwives with a clinical pathway for hyperbilirubinemia screening, following recommendations from this CPG.
- Provides midwives with a clinical pathway for midwifery management of phototherapy, if applicable to the individual midwife's practice.

To access the clinical pathway, visit the AOM website.

WHAT ARE THE EXPERIENCES OF CLIENTS WHOSE NEWBORNS REQUIRE MANAGEMENT OF SEVERE HYPERBILIRUBINEMIA?

Perspectives and needs of clients whose newborns require management of severe hyperbilirubinemia

Compared to clinical management of hyperbilirubinemia, there is less information available to guide midwives in providing care to meet the psychosocial needs of clients whose infants require treatment for jaundice.

Research involving families whose newborns required phototherapy suggests that phototherapy can be a discomforting experience for parents, both physically and emotionally. (107–109) Many parents feel anxious about the immediate and long-term implications of severe hyperbilirubinemia for their newborns, particularly as the timing of this diagnosis can seem sudden to parents, leaving many feeling unprepared. (107,110) Some parents may be disproportionately impacted by the stress associated with phototherapy, including those with limited social support and inadequate access to transportation to and from the hospital.

Research on the parental experience with neonatal jaundice provides important insight into the ways that health-care providers can support the physical, emotional and learning needs of parents. Through the provision of consistent guidance and support, health-care providers can address concerns parents have about severe hyperbilirubinemia, help them navigate the phototherapy experience and mediate potential difficulties presented by the management of severe hyperbilirubinemia. (107–110) Parents also greatly benefit from the support and information they receive from health-care providers in helping them best meet the nutritional needs of their newborns during this period. (41,109)

For more information on Ontario midwifery client experiences, see the client-directed resources: *What is Jaundice?*, and *What is Phototherapy and Why does my Baby Need it?*

Practice points for communication during management of severe hyperbilirubinemia

The practice points in **Figure 1** have the potential to lessen the psychosocial impacts of phototherapy and other forms of managing severe hyperbilirubinemia.

FIGURE 1: PRACTICE POINTS FOR COMMUNICATION AND CARE BEFORE, DURING AND FOLLOWING THE MANAGEMENT OF SEVERE HYPERBILIRUBINEMIA

Good Practice Statement:

16. Midwifery clients would benefit from discussions with their midwife on:
    - The results of bilirubin testing and their clinical significance, if any.
    - Treatment options and alternatives, including what to expect regarding the impact of treatment on skin to skin and feeding.
    - How to access psychosocial and emotional support during and after their experience of treatment.

    This good practice statement recognizes continuity of care and the skill of midwives in providing health information to clients.

SUMMARY OF GOOD PRACTICE STATEMENTS & RECOMMENDATIONS

1. Identification of risk factors for severe hyperbilirubinemia typically occurs in an ongoing manner throughout the course of the prenatal and postpartum period in the context of Ontario midwifery care.

   Regardless of risk factors, review the following as part of an informed choice discussion with clients:
   - that jaundice is common, short-lived and usually harmless; however, a small number of babies will develop severe hyperbilirubinemia, which can be harmful if not treated;
   - how to detect visible jaundice, particularly within the first 24 hours (visibly yellow in lighter-skinned infants and/or yellow sclera or with blanched skin and/or yellow sclera in darker-skinned infants) and signs of hyperbilirubinemia including poor suck, lethargy and reduced feeding, dark urine and pale, chalky stools; and
   - how to contact the midwife if jaundice is suspected in the newborn.

2. Share with clients how risk factors, if present, may impact considerations for screening and management of severe hyperbilirubinemia.

   ### Good practice statements

   These good practice statements recognize the client as the primary decision-maker, the midwife's ability to identify emerging risk factors for severe hyperbilirubinemia and the need for timely decision-making.

3. In the otherwise well, human milk-fed infant with prolonged jaundice (jaundice lasting > 14 days), midwives may consider drawing TSB including the conjugated bilirubin to screen for the need for further investigation.

   If conjugated bilirubin level is > 18 µmol/L or greater than 20% of the TSB concentration, consult with a physician for further investigation of potential underlying causes of prolonged jaundice.

   ### Good practice statement

   This good practice statement recognizes continuity of care and the ability of the midwife to assess the need for interprofessional collaboration as the neonate's clinical picture requires.

4. For O blood group birthing parents, midwives should consider drawing cord blood and storing it for processing in the event that jaundice presents in the first 24 hours or that a TSB is later drawn for that infant. Although community standards may vary, midwives can consider bringing (i) stored cord blood for DAT processing and (ii) the TSB sample from the infant's heel prick to the laboratory for processing at the same time. If cord blood has not previously been drawn and stored at birth, midwives may consider drawing a tube of blood for DAT and blood type in addition to the TSB by infant heel prick.
   - If the newborn's TSB level is normal and no further testing or treatment is required, cord blood does not need to be tested for isoimmunization.
   - If TSB level is high, have cord blood processed to aid in the identification of the cause of hyperbilirubinemia.

   ### Good practice statement

   This good practice statement recognizes cord blood as an aid in the identification of the cause of hyperbilirubinemia in cases where pathologic jaundice may be possible (e.g. when birthing parent has O blood group).

5. Midwives should not recommend the use of formula supplementation to prevent severe hyperbilirubinemia in the otherwise well, healthy, human milk-feeding neonate.

   ### Strong recommendation: very low certainty of evidence

   This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

6. Midwives may offer delayed cord clamping to all clients, taking into consideration hyperbilirubinemia risk factors.

   Informed choice discussions should include:
   - the risks and benefits of delayed cord clamping compared with early cord clamping;
   - how risk factors for hyperbilirubinemia, if present, increase the infant's risk of jaundice; and

- the client's values and preferences.

Weak recommendation: moderate certainty of evidence

This recommendation recognizes the preference for and health benefits of delayed cord clamping while balancing the client's values and preferences.

7. There is insufficient evidence to support the use of sunlight as a means of preventing the development of severe hyperbilirubinemia.

No recommendation: very low certainty of evidence

8. The use of visual assessment alone is not recommended for screening for severe hyperbilirubinemia.

Weak recommendation: very low certainty of evidence

This recommendation recognizes that visual assessment for hyperbilirubinemia is an important part of the overall clinical assessment of a newborn but should not be relied on alone to determine a newborn's risk of severe hyperbilirubinemia.

9. The use of risk factor scoring systems is not recommended for screening severe hyperbilirubinemia.

Weak recommendation: low certainty of evidence

This recommendation recognizes that midwives routinely assess for hyperbilirubinemia risk factors as part of an infant's clinical assessment in the postpartum period but should not use a scoring system.

10. Where screening for hyperbilirubinemia is requested and/or recommended and bilimetres are available to the midwife, TcB screening should be offered.

Strong recommendation: very low certainty of evidence

This recommendation recognizes the unequal access to bilimetres across practice groups and the province but affirms the use of bilimetres as an effective screening tool to prompt TSB testing when required and as a promising way to increase community-based care.

11. The risks and benefits of universal screening should be discussed with all clients as part of an informed choice discussion.

This discussion may address:

- what is known about risk factors, if present;
- how visible jaundice, poor feeding, dehydration and weight loss impact risk of developing severe hyperbilirubinemia;
- what is known about the limitations of visual assessment of jaundice;
- optimal timing of screening: between 24 to 72 hours of age;
- barriers to and enablers of screening within the client's community context; and
- the client's values and preferences and risk tolerance.

Weak recommendation: very low certainty of evidence

This recommendation recognizes the paucity of high-certainty evidence on the effectiveness of universal screening, the uniqueness of the midwifery context and structural barriers which impact midwives' ability to offer community-based bilirubin screening.

12. If visible jaundice develops, obtaining a bilirubin measurement is recommended.

For neonates who have previously had a negative TSB screen and in whom visible jaundice subsequently develops, midwives may use their clinical judgement in determining the need to re-screen. Consider presence or absence of other clinical factors associated with severe hyperbilirubinemia (e.g. suboptimal feeding, lethargy, dark urine, pale chalky stools).

Weak recommendation: very low certainty of evidence

This recommendation recognizes that the timely, frequent and close follow-up of neonates as a standard of midwifery care limits the benefits associated with universal screening while acknowledging the importance of the clinical manifestation of hyperbilirubinemia.

13. Where available, midwives may offer fibreoptic phototherapy using their clinical experience and the clinical context of the client to guide decision-making.

Weak recommendation: low certainty of evidence

This recommendation recognizes that fibreoptic phototherapy may increase the duration of treatment and therefore may not be appropriate in all cases, but has benefits such as an increase in skin to skin contact.

14. Midwives may offer fibreoptic phototherapy in the home as an option for treatment where community-based health infrastructure exists.

Weak recommendation: low certainty of evidence

This recommendation recognizes midwives' scope of practice to manage phototherapy, provided midwives have the knowledge, skills, experience and community-based health infrastructure to do so.

15. Midwives should not routinely recommend use of formula supplementation for otherwise healthy infants undergoing phototherapy, discussing the risks and benefits with clients.

Strong recommendation: very low certainty of evidence

This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

16. Midwifery clients would benefit from discussions with their midwife on:

- The results of bilirubin testing and their clinical significance, if any.
- Treatment options and alternatives, including what to expect regarding the impact of treatment on skin to skin and feeding.
- How to access psychosocial and emotional support during and after their experience of treatment.

Good practice statement

This good practice statement recognizes continuity of care and the skill of midwives in providing health information to clients.

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