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An AOM Clinical Practice Guideline Summary

HYPERBILIRUBINEMIA

This summary provides easy access to some of the most essential content of **AOM CPG No. 18–Management of Hyperbilirubinemia in Healthy Term and Late Preterm Neonates**, and is intended for use in conjunction with the full-length Clinical Practice Guideline (CPG). For a complete analysis of the research relevant to the management of hyperbilirubinemia, along with citations, refer to the full CPG.

DEFINITIONS

Hyperbilirubinemia: A condition caused by an excess of bilirubin in the blood and tissues of an infant's body. (1)*

Jaundice: The yellowing of the skin and the whites of the eyes because of a buildup of bilirubin. (1)*

Significant hyperbilirubinemia: An elevation of the serum bilirubin to a level requiring treatment. (1)

Severe hyperbilirubinemia: A total serum bilirubin (TSB) greater than 425 µmol/L or a need for blood exchange transfusion (BET). (2)

Acute bilirubin encephalopathy: The clinical manifestation of bilirubin toxicity. Clinical presentation can progress from lethargy, hypotonia and poor suck to hypertonia of extensor muscles (with opisthotonus, rigidity, and retrocollis), high-pitched cry, fever and irritability and eventually seizures, coma or apnea. (2,3)

Chronic bilirubin encephalopathy: The clinical sequelae of acute bilirubin encephalopathy, which includes athetoid cerebral palsy, hearing deficits, developmental delay and oculomotor disturbances. (3)

Kernicterus: A pathological finding of deep-yellow staining of the brain by bilirubin and evidence of neuronal injury. (4)

TYPES OF JAUNDICE

Physiologic jaundice: The most common form of jaundice; typically becomes apparent between 24 to 72 hours of life. There are no underlying pathological causes of physiologic jaundice. (1)

Pathologic jaundice: Jaundice that manifests as a symptom of an existing underlying condition. The appearance of jaundice within the first 24 hours may be an indication of pathologic jaundice, although not all presents early. Once identified, the underlying condition must be addressed in a timely manner. (2)

Prolonged jaundice: Clinically significant jaundice in term or late preterm infants, where TSB levels are within 35 µmol/L of the phototherapy threshold, persisting for more than 14 days. (2)

*The terms hyperbilirubinemia and jaundice are used interchangeably throughout this document.

RISK FACTORS

SIGNIFICANT HYPERBILIRUBINEMIA

What risk factors are associated with significant hyperbilirubinemia?

According to the National Institute for Health and Clinical Excellence (NICE), the most significant risk factors for significant hyperbilirubinemia are (1,5):

- gestational age under 38 weeks (OR 0.6 to 20.70)
- previous sibling with neonatal jaundice requiring phototherapy (OR 2.3 to 6.0)
- visible jaundice in the first 24 hours of life (OR 2.9 to 10.1)
- suboptimal feeding (OR 0.4 to 10.75)

The CPS identifies those same four risks and several additional factors as hyperbilirubinemia risk factors, which increase a neonate's baseline risk of developing this condition:

- lower gestational age at birth (<38 weeks)
- appearance of jaundice noted in the first 24 hours post-birth
- evidence of hemolysis, with suspicion based on positive results from specific testing (e.g., DAT, peripheral blood smear, hemoglobin levels, G6PD assay, pyruvate kinase assay, or others)
- need for phototherapy in the first 72 hours of age
- parent or sibling with a history of hyperbilirubinemia requiring phototherapy or exchange transfusion
- family history or genetic predisposition to inherited red blood cell disorders causing hemolysis
- suboptimal oral feeding volume or excessive weight loss (or both)
- significant bruising or cephalohematoma
- polycythemia (2)

Good Practice Statements:

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

   For all clients, include the following as part of an informed choice discussion:
   - Jaundice is common, short-lived and usually harmless; however, a small number of babies will develop significant hyperbilirubinemia, which can be harmful if not treated.
   - Provide instruction on how to detect visible jaundice, particularly within the first 24 hours: in lighter-skinned infants, visibly yellow tone and/or yellow sclera; in darker-skinned infants, blanched skin and/or yellow sclera.
   - Describe additional signs of hyperbilirubinemia, including poor suck, lethargy and reduced feeding, dark urine and pale, chalky stools.
   - Review how to contact their midwife if jaundice is suspected in the newborn. **[2025]**

2. Share with clients how risk factors, if present, may impact considerations for screening and management of significant hyperbilirubinemia. **[2019]**

Good practice statements

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

EVIDENCE OF HEMOLYSIS, WITH SUSPICION BASED ON POSITIVE TEST RESULTS

What factors are associated with an increased risk of hemolysis and subsequent development of significant hyperbilirubinemia?

G6PD deficiency is considered an important risk factor for acute bilirubin encephalopathy and hyperbilirubinemia neurotoxicity. (4,6) G6PD testing should be considered for any infant with significant or severe hyperbilirubinemia who does not respond to treatment or presents without identifiable risk factors.

A direct anti-globulin test (DAT or direct Coombs) can be done on an infant's cord blood or freshly collected capillary sample to identify isoimmunization (7). Information about the infant's blood group and DAT may facilitate risk assessment for hemolysis and identify infants at greater risk of significant hyperbilirubinemia caused by immune-mediated hemolysis. While a positive DAT indicates the presence of antibodies on the surface of red blood cells, it does not diagnose or measure the degree of hemolysis, if present. (2)

When hemolysis is suspected due to an early, rapidly rising TSB or severe hyperbilirubinemia, additional investigations – such as hemoglobin level, peripheral blood smear, reticulocyte count – should be considered. (2) Hemolysis may be suspected based on a rapid rate of increase in TSB ≥ 5 µmol/L/h (within 24 hours post-birth) or ≥ 3.5 µmol/L/h (beyond 24 hours post-birth). (2) In these cases, a pediatrician should be consulted for prompt testing and treatment considerations.

Good Practice Statement:

3. For birthing parents in the O blood group, midwives should consider collecting and storing cord blood for processing, in the event that jaundice presents in the first 24 hours or if a TSB is later required for the infant.

    - If the newborn's TSB level is below treatment thresholds and no further testing is required, cord blood will not need to be tested for blood group and DAT.
    - If the TSB level is elevated, cord blood may be processed by the lab to help identify the underlying cause of hyperbilirubinemia and determine the need for follow-up. **[2025]**

    Good practice statement
    This good practice statement recognizes the client as the primary decision-maker, midwives' ability to identify emerging risk factors and the need for timely decision-making.

JAUNDICE BEYOND 14 DAYS OF LIFE

What factors are associated with jaundice beyond 14 days of life?

Most cases are because of breast milk jaundice, a benign condition in which infants who are primarily fed with human milk experience elevated bilirubin levels, despite being otherwise healthy. (8)

Prolonged jaundice, defined as clinically significant jaundice in term or late preterm infants where TSB levels are within 35 µmol/L of the phototherapy threshold and persist for more than 14 days, may result from pathologic causes associated with elevated *unconjugated* bilirubin levels such as hemolytic diseases, infection, congenital hypothyroidism and inborn errors of metabolism). It can also occur in the presence of elevated *conjugated* bilirubin levels from underlying cholestatic liver diseases, such as biliary atresia). (9)

A conjugated (direct) bilirubin level greater than 17 µmol/L is considered abnormal and warrants further investigation. (2)

Good Practice Statement:

4. In the otherwise well, human milk–fed infant with persistent visual jaundice, midwives may consider drawing a TSB, including the conjugated fraction, to determine whether further investigation is needed.

   A conjugated bilirubin level above 17 µmol/L warrants consultation with a physician for further investigation of potential underlying causes. **[new 2025]**

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

SEVERE HYPERBILIRUBINEMIA AND/OR ACUTE BILIRUBIN ENCEPHALOPATHY

What factors are associated with severe hyperbilirubinemia and/or acute bilirubin encephalopathy?

While the exact mechanisms underlying some of the neurotoxicity risk factors listed below are not well understood, they are believed to increase the risk of acute bilirubin encephalopathy by increasing the toxic effects of bilirubin on the newborn brain: (2)

- lower gestational age at birth (< 38 weeks)
- hypoalbuminemia (serum albumin < 30 g/L)
- a suspected or diagnosed hemolytic condition [hemolysis may be suspected based on a rapid rate of increase in TSB ≥ 5 µmol/L/h (within 24 hours post-birth) or ≥ 3.5 µmol/L/h (beyond 24 hours post-birth)]
- suspected or culture-proven sepsis
- significant hemodynamic or respiratory instability (or both) in the preceding 24 hours.

Apart from lower gestational age at birth, many of these risk factors reflect a pathologic form of jaundice in which further investigation is indicated to determine the underlying condition. (7)

Good Practice Statement:

5. If midwives suspect a pathologic cause of hyperbilirubinemia, further investigation, which may include physician consultation, is required to determine the underlying condition. **[new 2025]**

   Good practice statement
   This good practice statement recognizes midwives' ability to identify emerging risk factors and assess the need for interprofessional collaboration as the neonate's clinical picture requires.

PREVENTION

INFANT FORMULA SUPPLEMENTATION

Can infant formula supplementation prevent severe hyperbilirubinemia?

One observational study found that formula feeding (either mixed or exclusive) may reduce the incidence of significant hyperbilirubinemia, need for phototherapy, and lower bilirubin levels. (10) However, this research is not applicable to the Canadian health care context as it did not diagnose hyperbilirubinemia and initiate treatment in accordance with current Canadian guidance.

The work group balanced the rare risk that an infant develops significant hyperbilirubinemia against the substantial benefits of human milk feeding.

Recommendation:

6. Midwives should not recommend formula supplementation to prevent significant hyperbilirubinemia in the otherwise well, healthy neonate fed with human milk. **[2019]**

   Strong recommendation: very low certainty of evidence
   This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

TIMING OF CORD CLAMPING

Can the timing of cord clamping prevent severe hyperbilirubinemia?

Delayed cord clamping likely increases the risk of hyperbilirubinemia and the need for phototherapy among healthy term neonates and late preterm and term infants with ABO isoimmunisation. (11,12) However, delayed cord clamping poses no increased risk of chronic or permanent harms and has several benefits, such as improved long-term iron stores, haematocrit values, and hemoglobin concentrations. (11)

Recommendation:

7. 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. **[2019]**

   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.

SUNLIGHT

Can sunlight be used to prevent severe hyperbilirubinemia?

The quality of the available research on sunlight and hyperbilirubinemia was limited by several serious factors. (13) The work group considered how sunlight exposure cannot be measured accurately and poses risks of UV radiation and burns.

Recommendation:
8. There is insufficient evidence to support the use of sunlight as a means of preventing significant hyperbilirubinemia. **[2019]** **No recommendation: very low certainty of evidence**

SCREENING

VISUAL ASSESSMENT

Can visual assessment be solely relied on to detect significant hyperbilirubinemia?

Results from four observational studies show that the use of visual assessment to determine the severity of jaundice is not accurate and that there is variability among methods and providers. (14–17)

The work group affirmed that visual assessment is an important component of midwives' clinical assessment but should not be solely relied upon to determine a newborn's risk of significant hyperbilirubinemia.

Recommendation:
9. Visual assessment alone is not recommended when screening for significant hyperbilirubinemia. **[2019]** **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 it should not be solely relied upon to determine a newborn's risk of significant hyperbilirubinemia.*

RISK FACTOR SCORING SYSTEM

Should a risk factor scoring system be used to screen for significant hyperbilirubinemia?

One diagnostic cohort study determined that most infants would be incorrectly classified when screened with a risk factor scoring system which included birth weight, gestational age, oxytocin use during delivery, vacuum extraction, and feeding method. (18) Incorrect classification has the potential to result in either overtreatment of healthy infants or missed treatment for infants with significant hyperbilirubinemia.

Recommendation:
10. The use of risk factor scoring systems is not recommended when screening for significant hyperbilirubinemia. **[2019]** **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 they should not use a scoring system.*

TRANSCUTANEOUS BILIMETRE (TCB)

Should a transcutaneous bilimeter (TcB) be used to screen for significant hyperbilirubinemia?

One systematic review of eleven diagnostic cohort studies demonstrated that TcB measurements obtained from bilimeters cannot provide an exact estimation of an infants' bilirubin level. (19)

Limitations of bilimeters include:

- a tendency for overestimation among infants with darker skin tones (20–24)
- a tendency for underestimation with higher (more dangerous) serum bilirubin levels. (25,26)
- a tendency to be inaccurate during or soon after phototherapy treatment (27)

Despite these limitations, TcB generally shows good correlation with TSB measurements (25) and may be used as a screening tool to prompt a follow up TSB test when necessary. The CPS 2025 Position Statement recommends performing a TSB measurement if a TcB level is within 50 µmol/L of the hour-specific phototherapy threshold or above 250 µmol/L. (2)

Benefits of bilimeters for midwives include:

- keeping care in the community
- sparing clients from unnecessary travel and testing

Recommendation:

11. Where screening for hyperbilirubinemia is requested and/or recommended and bilimeters are available, midwives should offer TcB screening. **[2019]**

    Strong recommendation: very low certainty of evidence
    This recommendation recognizes the uneven access to bilimeters across practice groups and the province. However, it affirms the bilimeter as an effective screening tool to prompt TSB testing when required and as a promising way to improve community-based care.

UNIVERSAL BILIRUBIN SCREENING

Should all neonates be screened for severe hyperbilirubinemia within 24-72 hours of life regardless of risk factors?

Available research (eight observational studies) on universal bilirubin screening suggests some benefits associated with universal screening including a lower incidence of high bilirubin concentrations and lower rates of hospital readmission. However, this research also demonstrates that universal screening may have no impact on the need for phototherapy. (28–35)

The work group recognized limited potential benefits from universal screening within the context of regular, timely and close follow-up care provided to newborns by midwives.

Midwives also face structural and systemic barriers to offering screening including:

- limited funding to maintain and replace bilimeters
- laboratories may reject blood samples drawn in the community setting

Universal screening may have consequences for clients including:

- longer hospital stays
- travel to clinic or hospital for testing

Recommendations:

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

    This discussion may include:

    - what is known about risk factors for significant hyperbilirubinemia, if present
    - how visible jaundice, poor feeding, dehydration and weight loss can increase an infant's risk
    - the limitations of relying on visual assessment alone to detect jaundice
    - timing of screening
    - barriers to and enablers of screening within the client's community context
    - the client's values and preferences and risk tolerance **[2025]**

    Weak recommendation: very low certainty of evidence
    This recommendation recognizes the lack of high-certainty evidence for the effectiveness of universal screening, the uniqueness of the midwifery context, and structural barriers that impact midwives' ability to offer community-based bilirubin screening.

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

    For neonates who have previously had a TcB or TSB result that required no repeat testing or treatment and in whom visible jaundice subsequently develops, midwives may use their clinical judgment in determining the need for re-screening. Consider presence or absence of other clinical factors associated with significant or pathologic hyperbilirubinemia (e.g., suboptimal feeding, lethargy, dark urine, pale chalky stools). **[2025]**

    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 a clinical manifestation of hyperbilirubinemia.

TREATMENT/MANAGEMENT

FIBREOPTIC PHOTOTHERAPY

Is fibreoptic phototherapy an effective treatment for significant hyperbilirubinemia?

One systematic review comparing fibreoptic phototherapy to conventional phototherapy found that fibreoptic phototherapy may increase the duration of phototherapy and is slightly less effective at lowering bilirubin concentrations within 24 hours of starting treatment. (36)

The work group considered the benefits of fibreoptic phototherapy, such as skin-to-skin contact and more frequent nursing. Although fibreoptic phototherapy may not be acceptable to clients who prefer a shorter duration of treatment, it is the preferred method of treatment in the home and community setting.

Recommendation:

14. Where available, midwives may offer fibreoptic phototherapy using their clinical experience and the clinical context of the client to guide decision-making. **[2019]**

    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 that it has benefits such as an increase in skin-to-skin contact.

Recommendation:

15. Midwives may offer fibreoptic phototherapy in the home as an option for treatment where community-based health infrastructure exists. **[2019]**

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

FORMULA SUPPLEMENTATION DURING PHOTOTHERAPY

Is the use of formula supplementation during phototherapy an effective adjunct when managing significant hyperbilirubinemia?

One observational study showed that formula supplementation in conjunction with phototherapy may reduce the duration of phototherapy and result in a faster average decrease of bilirubin levels within a 24-hour period. (37)

The work group recognized the various benefits of human milk feeding, such as improved bonding between parent and newborn, (38,39) improved immunologic status (40), and reduced risk of gastrointestinal infection. (39) Therefore, clients should not be deterred from nursing while an infant is undergoing phototherapy and should receive ongoing lactation support as indicated.

Recommendation:

16. Midwives should not routinely recommend formula supplementation for otherwise healthy infants undergoing phototherapy, discussing the risks and benefits with clients. **[2019]**

Strong recommendation: very low certainty of evidence
This recommendation recognizes midwifery support of human milk as the optimal physiological nutrition for infants.

CLIENT EXPERIENCES

What are the experiences of clients who have newborns with significant hyperbilirubinemia and how can they be supported by midwives?

Research involving families whose newborns required phototherapy suggests that phototherapy can be an uncomfortable experience for parents, both physically and emotionally. (41–43) Some parents may be disproportionately affected by the stress associated with phototherapy, including those with limited social support Midwives can provide ongoing educational and emotional support for clients before, during and following the management of significant hyperbilirubinemia.

Good Practice Statement:

17. Midwifery clients would benefit from discussions with their midwife about:
    - 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 **[2019]**

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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