

ABM Clinical Protocol #22: Guidelines for Management of Jaundice in the Breastfeeding Infant 35 Weeks or More of Gestation—Revised 2017

Valerie J. Flaherman,¹ M. Jeffrey Maisels,² and the Academy of Breastfeeding Medicine

A central goal of The Academy of Breastfeeding Medicine is the development of clinical protocols free from commercial interest or influence for managing common medical problems that may impact breastfeeding success. These protocols serve only as guidelines for the care of breastfeeding mothers and infants and do not delineate an exclusive course of treatment or serve as standards of medical care. Variations in treatment may be appropriate according to the needs of an individual patient.

Purpose

1. To provide guidance in determining whether and how breastfeeding may or may not be contributing to infant jaundice.
2. To review evidence-based strategies for ameliorating jaundice in the breastfeeding infant.
3. To provide protocols for supporting breastfeeding while infants are being evaluated and/or treated for jaundice.

Biologic Basis for Jaundice in the Newborn and Its Relationship to Breastfeeding

Some comprehensive reviews of bilirubin metabolism and jaundice in the newborn are listed in the references for a more complete discussion of the biology and pathobiology of jaundice in the newborn and its relationship to breastfeeding.^{1–3} Although the management of breastfeeding and jaundice varies in different countries,⁴ the following principles and recommendations should apply universally.

Hyperbilirubinemia of the newborn

Virtually all newborns have some elevation of their total serum bilirubin (TSB) (>90% of which is unconjugated or indirect reacting) relative to normal adult values, which are $\leq 17 \mu\text{mol/L}$ ($\leq 1.0 \text{ mg/dL}$).⁵ The catabolism of heme by heme oxygenase (HO) produces biliverdin. Biliverdin is reduced by biliverdin reductase to unconjugated bilirubin, which is conjugated in the liver and excreted through the gut. Newborns have higher TSB levels because of a combination of three factors: increased production of bilirubin due to postnatal heme degradation; decreased uptake and conjugation of bilirubin due to developmental hepatic immaturity; and increased intestinal reabsorption of bilirubin. In the first week of life, more than 80% of newborns appear jaundiced^{6,7} and,

depending on the racial and sociocultural population mix, about 75% have a transcutaneous bilirubin (TcB) of $>100\text{--}150 \mu\text{mol/L}$ ($>6\text{--}9 \text{ mg/dL}$) by 96 hours.^{8–10} Bilirubin is antioxidant and may protect infants from the relatively hyperoxygenic environment after birth. The term physiologic jaundice is often used to describe newborns with a TSB well above normal adult levels, but not attributable to a specific cause such as hemolytic disease; however, such terminology may be inappropriate because having an unknown etiology does not necessarily mean that a condition is physiologic.¹¹

Breastfeeding and jaundice

Although some early studies^{12,13} reported no differences in TSB concentrations between breastfed and formula-fed infants, subsequent studies using larger sample sizes and more robust research design demonstrated a strong association between hyperbilirubinemia and breastfeeding compared with formula feeding, especially when breastfeeding was exclusive.^{14–22} Nonetheless, in comparison with previous data,²³ Buitter et al.'s²⁴ study of the relationship between stool production and jaundice in healthy breastfed or formula-fed newborns found significantly less stool production in formula-fed infants and no difference in stool production or TcB concentrations in the first 4 days between breastfed and formula-fed infants. Based on this body of evidence, two broad categories of the association between breastfeeding and jaundice have been described. Jaundice, which occurs in the first week in association with ongoing weight loss, has been termed breastfeeding jaundice, breastfeeding-associated jaundice, breast-nonfeeding jaundice, or starvation jaundice.²⁵ However, as this jaundice is almost always associated with low enteral intake rather than breastfeeding per se, in this protocol, it will be called suboptimal intake jaundice. Jaundice that persists past the onset of robust weight gain is known as breast

¹Department of Pediatrics, School of Medicine, University of California, San Francisco, California.

²Department of Pediatrics, William Beaumont School of Medicine, Oakland University, Royal Oak, Michigan.

milk jaundice or the breast milk jaundice syndrome. Although this protocol focuses on breastfeeding and jaundice, it is important to note that early onset jaundice occurring within 24–48 hours of birth is unlikely to be related to breastfeeding and should be assessed and treated promptly without interruption of breastfeeding.

Suboptimal intake jaundice of the newborn

During the first days after birth, it is normal for colostrum volumes to be small; appropriate for the infant's stomach size and physiologic need. In the first 24 hours of life, exclusively breastfed infants may receive no more than 1–5 mL of milk per feeding^{26–29} or 5–37 mL in total.^{30,31} Encouraging breastfeeding within the first hour of birth and frequently thereafter maximizes caloric and fluid intake and stimulates breast milk production.

In normal adults, the absence of caloric intake, even for as brief a period as 24 hours and with good hydration, results in a small increase in unconjugated hyperbilirubinemia of about 17–34 $\mu\text{mol/L}$ (1–2 mg/dL),^{32–34} an effect due to an increase in the enterohepatic circulation of bilirubin.³⁵ Similarly, in newborns, breastfeeding difficulties or a delay in the onset of secretory activation (lactogenesis II)³⁶ may result in lower caloric intake, which may lead to an increase in enterohepatic circulation³⁵ and the development of hyperbilirubinemia. In addition, the mechanism for an increase in TSB is likely to include other developmental limitations in bilirubin metabolism and transport in the newborn.^{37–39} Because formula-fed infants are typically given volumes of milk much greater than physiologically normal (27 mL formula per feeding or about 150 mL/day), during that same period,⁴⁰ it is uncommon for them to become jaundiced. Oral intake equalizes for the groups once maternal secretory activation occurs around 2–5 days of age, and copious milk production begins.

The interaction between low enteral intake and other factors related to neonatal hyperbilirubinemia is the subject of recent investigation.^{18,24,41,42} Sato et al. found that the hyperbilirubinemia associated with the G71R mutation of UDP glucuronosyltransferase family 1 member A1 (*UGT1A1*) gene could be prevented by adequate enteral intake.^{41,42} People with Gilbert's syndrome have lower activity of UDP-glucuronosyltransferase and develop significantly higher TSB with fasting than the normal population.

Breast milk jaundice (prolonged jaundice associated with breast milk feeding)

Many breastfed infants have unconjugated hyperbilirubinemia that extends into the second and third week, but can

continue for as long as 2–3 months.^{43,44} At 28 days, 21% of predominantly breastfed infants were still visibly jaundiced and 34% had a TcB $\geq 85 \mu\text{mol/L}$ ($\geq 5 \text{ mg/dL}$).⁴³ Prolonged jaundice beyond the second to third week in healthy breastfeeding newborns has been called breast milk jaundice to distinguish it from suboptimal intake jaundice, which should resolve by 1–2 weeks.⁴⁵

The precise mechanism of breast milk jaundice remains unknown despite much investigation. Multiple factors appear to contribute to whether bilirubin is eliminated together with fecal fat⁴⁶ or reabsorbed into the blood stream (the enterohepatic circulation). The development of breast milk jaundice has been attributed to numerous processes involved in bilirubin excretion, including enhanced intestinal reabsorption of unconjugated bilirubin⁴³; increased concentrations of cytokines (including IL-1, IL-10, and TNF-) in human milk⁴⁷; low total antioxidant capacity in human milk⁴⁸; variations in the HO-1 gene promoter⁴⁹; variations in the *UGT1A1* gene^{18,41,42,50,51}; lower serum and milk levels of epidermal growth factor⁵²; higher serum alpha-fetoprotein levels⁵³; higher cholesterol levels⁵⁴; and lower abundance of *Bifidobacterium adolescentis*, *Bifidobacterium longum* and *Bifidobacterium bifidum*⁵⁵ in human milk and stool. The relative contribution of each of these factors, their potential interaction, and their precise mechanism of action remain unknown. Over time, the jaundice and elevated TSB decline at varying rates to normal adult values even while breastfeeding continues. Features that may distinguish suboptimal intake jaundice from breast milk jaundice are summarized in Table 1.

Whenever jaundice in a breastfed newborn is prolonged beyond the third week, it is important to rule out cholestasis by measuring the direct or conjugated bilirubin level and to evaluate for other causes of prolonged indirect hyperbilirubinemia such as congenital hypothyroidism. For indirect hyperbilirubinemia that extends beyond 2 months, conditions such as ongoing undiagnosed hemolysis, Gilbert's syndrome, or the very rare Crigler–Najjar syndrome (with an incidence of 1 per million births) should be considered.⁵⁶

Interaction of suboptimal intake jaundice and breast milk jaundice

Strong evidence suggests that increased serum bilirubin in the first few days is highly correlated with suboptimal enteral intake; serum bilirubin concentrations are highly associated with greater weight loss in breastfed infants.^{41,42,57–62} Ineffective suckling with inadequate caloric intake during the first days of life increases TSB levels because of relative starvation.^{32,35,37,38}

TABLE 1. CHARACTERISTICS DISTINGUISHING SUBOPTIMAL INTAKE JAUNDICE FROM BREAST MILK JAUNDICE

	<i>Typical time frame</i>	<i>Weight</i>	<i>Stool output</i>	<i>Urine output</i>	<i>Clinical findings</i>
Suboptimal intake jaundice	Onset 2–5 days of age and usually resolved by 2 weeks	Ongoing weight loss	<5/day with color black, brown, or green	<5/day with uric acid crystals (brick color)	Commonly <38 weeks and rarely ≥ 40 weeks gestation. May be fussy and difficult to settle between feedings or sleepy and difficult to wake for feeding
Breast milk jaundice	Onset 2–5 days and may last up to 3 months	Gaining $\geq 30 \text{ g/day}$ ¹⁰⁷	≥ 8 /day with yellow color	≥ 8 /day with yellow or clear color	Waking to feed 8–12 $\times$ /day

If jaundice continues beyond the second and third weeks, despite adequate milk intake and weight gain, it is likely that one or more of the factors listed above are contributing to the hyperbilirubinemia. Early optimizing of breastfeeding and consideration of additional enteral intake when there is clinical or laboratory evidence that breastfeeding is compromised might mitigate the development of subsequent hyperbilirubinemia. Options for additional enteral intake are discussed below.

Kernicterus and bilirubin encephalopathy

The most recent studies in high-resource countries suggest that in the absence of significant comorbidities such as sepsis or Rh hemolytic disease, kernicterus or chronic bilirubin encephalopathy occurs in about 1 in 200,000 live births and only when TSB levels exceeded 600 $\mu\text{mol/L}$ (35 mg/dL).^{63–65} In lower resource countries, bilirubin encephalopathy and comorbidities are much more common so that kernicterus can and does occur more frequently and at lower bilirubin levels.⁶⁶ Even in high-resource countries, extreme hyperbilirubinemia in apparently healthy breastfeeding infants can cause kernicterus.^{67,68} In the U.S. Kernicterus Registry, a database of 125 cases of kernicterus in infants discharged as healthy newborns, 98% of these infants were fully or partially breastfed, highlighting the importance of appropriate breastfeeding support and follow-up from the prenatal period through to the early postpartum months. Whether hyperbilirubinemia, in the absence of the classic symptoms of bilirubin toxicity, produces subtle neurologic deficits is a controversial topic beyond the scope of this protocol. Recent studies suggest, however, if severe hyperbilirubinemia does cause subtle neurologic deficits, it is a rare occurrence.^{63–65}

Evidence-Based Strategies for Preventing or Ameliorating Jaundice in the Breastfeeding Infant

Management of jaundice once treatment thresholds for TSB are reached is discussed in the next section. The following measures are recommended to maintain TSB levels below those proposed for treatment while supporting the successful establishment of breastfeeding:

1. Initiate early breastfeeding.
 - a. Initiate breastfeeding as early as possible, preferably in the first hour after birth^{69–72} (I) (quality of evidence [levels of evidence IA, IB, IIA, IIB, III, and IV] is based on levels of evidence used for the National Guidelines Clearing House⁷³ and is noted in parentheses) even for infants delivered by cesarean section. In the vast majority of births, breastfeeding should be initiated in the first hour.
2. Encourage frequent exclusive breastfeeding.
 - a. Frequent breastfeeding (8–12 times or more in 24 hours) is crucial both to increase infant enteral intake and to maximize breast emptying, which is essential for the establishment of milk supply. Feeding anything before the onset of breastfeeding delays the establishment of good breastfeeding practices and may hinder milk production, increasing the risk of reduced enteral intake and exaggerated hyperbilirubinemia. There is a positive association between the number of breastfeeds a day and lower TSB.⁷⁴ (III) It is unnecessary to

give glucose water to test the infant's ability to swallow or avoid aspiration.

- b. Hand expression or pumping of colostrum or breast milk can provide extra milk to support intake in some infants at risk for suboptimal intake jaundice and exaggerated hyperbilirubinemia and assist in establishing a good milk supply. Although pumping is commonly used, it is noteworthy that hand expression may be better tolerated by mothers in the immediate postpartum period. Randomized trials have shown that the initiation of pumping may reduce milk transfer and eventual breastfeeding duration for some populations of infants.^{26,27} (IB)
3. Optimize early breastfeeding management.
 - a. Ensure comfortable positioning (that avoids nipple compression or rubbing), effective latch, and adequate milk transfer (swallowing) from the outset by having a healthcare provider trained in breastfeeding management (e.g., nurse, lactation consultant, midwife, or physician) and evaluate position and latch, providing recommendations as necessary.
 - b. Support skin-to-skin contact for all mothers and infants (in a safe manner when the mother is awake and alert), but particularly for those breastfeeding, starting immediately after birth and throughout the postpartum period as it helps with milk supply and makes mother's milk easily available to the infant in the first days and weeks of life.⁷² (I)
4. Provide education on early feeding cues.
 - a. Teach the mother to respond to the earliest cues of infant hunger, such as moving about or restlessness, lip smacking, hand movements toward the mouth, and vocalizing. Most newborns need to be fed every 2 ½ to 3 hours. Infants should be put to the breast before the onset of crying as crying is a late sign of hunger and often results in a poor start to the breastfeeding episode. Attention should also be paid to infants who are sleepy or do not show signs of hunger.
5. Identify mothers and infants at risk for hyperbilirubinemia.
 - a. Some maternal factors (e.g., diabetes, Rh sensitization, and past family history of jaundiced infants) increase the risk of hyperbilirubinemia in the newborn. Primiparous mothers are at risk for delayed secretory activation as are those who give birth through cesarean section or have a maternal body-mass index over 27 kg/m². Infants of these mothers are therefore at risk for suboptimal intake.⁷⁵ (III)
 - b. With the exception of infants with pathologic conditions such as Rh or ABO hemolytic disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency, the single most important clinical risk factor for hyperbilirubinemia in newborns is decreasing gestational age. For each week of gestation below 40 weeks, the odds of developing a TSB $\geq 428 \mu\text{mol/L}$ (25 mg/dL) increase by a factor of 1.7 (95% CI 1.4–2.5).¹⁹ Management of 34–37-week late preterm and early term infants who are not breastfeeding well can be found in the relevant ABM Clinical Protocol.⁷⁶ (IV)
 - c. Significant bruising or cephalohematoma can increase the risk of hyperbilirubinemia due to the

increased breakdown of heme. East Asian newborns also have a higher risk of jaundice, perhaps related to their ethnic or genetic background.⁵⁹ (III)

- d. The above factors can be additive with suboptimal intake jaundice and/or breast milk jaundice and produce even higher bilirubin levels than would otherwise be seen. When risk factors are identified, it is prudent to seek assistance with breastfeeding in the early hours after birth to ensure optimal breastfeeding management. Mothers may benefit from early instruction about milk expression by hand or pump to protect the milk supply.
6. Do not supplement infants with anything other than mother's own expressed milk in the absence of a specific clinical indication. Indications for supplementation are discussed briefly below. Full details on indications for supplementation, choice of supplement, and methods of supplementation are available in ABM Clinical Protocol #3: Supplementary Feedings in the Healthy Term Breastfed Neonate, Revised 2017.⁷⁷ (IV)
7. While management of newborns varies from country to country, most infants discharged before 72 hours of age should be seen by a healthcare provider within 2 days of discharge from birth hospitalization. This is especially important for exclusively breastfed infants. Close follow-up of the breastfeeding newborn both facilitates prevention of excess weight loss that may contribute to hyperbilirubinemia^{17,20,57–60} (III) and ensures that elevated bilirubin concentrations are promptly treated.²¹ (IV) Individual clinical judgment regarding follow-up can be used, such as in the case of an experienced multiparous mother who has breastfed previous infants and is going home with an infant who has no hyperbilirubinemia risk factors.²¹ Protocols for monitoring bilirubin vary from country to country and within countries. While the U.K. guidelines do not recommend measuring bilirubin levels at follow-up unless the infant is visibly jaundiced, frequent monitoring using a TcB meter is recommended by the Japanese Society for Neonatal Health and Development.

Management of Breastfeeding in the Newborn with Jaundice

Consensus-based guidelines for the management of hyperbilirubinemia, including monitoring procedures, recommended treatment, and thresholds for treatment, have been developed in the United States, Canada, Norway, the United Kingdom, and some 14 other countries.^{1,21,78,79} (IV) For monitoring, guidelines from the United States,²¹ Canada,⁸⁰ and several other countries recommend a measurement of the TSB or TcB in every infant before discharge from the birth hospitalization, although this is not specifically recommended in the U.K. guidelines. Universal TcB measurement is also standard practice in Japan. Combining the TcB measurement with the infant's gestational age and plotting on an appropriate graph provide a prediction of the risk of hyperbilirubinemia that is as accurate as the combination of all other nonpathologic risk factors. When TSB levels rise above the thresholds stated in guidelines, despite adequate lactation support, phototherapy is recommended as the most effective treatment. Other therapeutic options,

which may be used either alone or in combination with phototherapy, depending on clinical circumstance, include (1) temporary additional feedings with expressed breast milk; (2) temporary supplementation with donor human milk if available; (3) temporary supplementation with infant formula; or (4) very rarely, temporary interruption of breastfeeding and replacement feeding with infant formula. These options are described in more detail below.

When discussing any treatment options with parents, healthcare providers should emphasize that all treatments are compatible with continuation of breastfeeding. Because parents may associate breastfeeding with the development of jaundice requiring special treatment or hospitalization, they may be reluctant to continue breastfeeding, particularly if infant formula supplementation or interrupting breastfeeding is suggested as treatment. Healthcare providers should offer special assistance to these mothers to ensure that they understand the importance of continuing to breastfeed and know how to maintain their milk supply if temporary interruption is necessary. Special care should be taken to address and discuss any guilt parents have about their feeding decisions, both because such guilt can be counterproductive to continued breastfeeding^{81–84} (III) and because many factors contribute to jaundice and the relative contribution of each factor is often unknown.^{85–88} (III, IV)

Treatment options

1. Phototherapy. Phototherapy is the most frequently used treatment option when TSB concentrations exceed treatment thresholds, especially when levels are rising rapidly. Phototherapy can be used while continuing full breastfeeding or it can be combined with supplementation of expressed breast milk or infant formula if maternal supply is insufficient. Only in extenuating circumstances is temporary interruption of breastfeeding with replacement feeding necessary.^{1,21,89} (IV) Phototherapy can be done in the hospital or at home. Home phototherapy is acceptable for low-risk infants provided TSB levels are monitored.⁹⁰ (IV) In the hospital, it is best done in the mother's room or a hospital room where the mother can also reside to minimize mother–infant separation and so that breastfeeding can be continued. Interruption of phototherapy for durations of up to 30 minutes or longer to permit breastfeeding without eye patches does not alter the effectiveness of the treatment.^{91–93} (III, IB) Although phototherapy increases insensible water loss to some degree, infants under phototherapy do not routinely require extra oral or intravenous fluids.⁹⁰ (IV) However, if newborns receiving phototherapy are too sleepy to breastfeed vigorously, or if breastfeeding appears ineffective, mothers should express milk to feed by syringe, bottle, or gavage until newborns are vigorous enough to transfer milk effectively. The routine provision of intravenous fluids is discouraged because they may inhibit thirst and diminish oral intake. However, they may be indicated in cases of infant dehydration, hyponatremia, or inability to ingest adequate milk.
2. In settings where phototherapy is not readily available, results in significant mother–infant separation, or has other potential negative consequences, physicians may consider recommending supplementary feedings at

levels of bilirubin approaching those recommended for initiating phototherapy. Such decisions should be individualized with the goal of keeping mother and infant together as well as preserving and optimizing breastfeeding while effectively preventing or treating the hyperbilirubinemia.

- a. First and best supplement is expressed own mother's milk. It can be hand expressed into a small cup or spoon and directly fed to the infant with help from staff who are knowledgeable in this technique. In this way, breastfeeding is best supported.
 - b. If own mother's milk is not available, supplementing with donor human milk will increase enteral intake. Breastfeeding infants supplemented only with donor milk meet the World Health Organization definition of exclusive breastfeeding. The specific effect of donor milk supplementation on bilirubin levels has not been studied.
 - c. It may be necessary to supplement with infant formula if neither own mothers' milk nor donor human milk is available. The impact of introducing formula to an exclusively breastfed infant must be considered. The effect of supplementation with donor human milk versus infant formula is not well studied.
 - d. Supplementation with water or glucose water is contraindicated because it does not reduce serum bilirubin,^{94,95} (IIA, III) interferes with breastfeeding, and might cause hyponatremia.
 - e. Supplementation of breastfeeding should preferably be undertaken using a cup, spoon, syringe, or supplemental nursing system (if infant is latching) simultaneously with or immediately following each breastfeed. Nipples/teats and bottles should be avoided where possible. However, there is no evidence that any of these methods are unsafe or that one is necessarily better than the other.^{77,96} (IA)
3. When TSB levels are very high or associated with evidence of poor breast milk intake despite appropriate intervention, supplementation with infant formula can eliminate the deleterious effect of *UGT1A1* polymorphisms on serum bilirubin and is a reasonable addition if it can be done in a way that is supportive of breastfeeding.⁵¹ (IIA) Depending on the TSB level, follow-up TSB measurements within 4–24 hours are needed. Supplementation cannot be substituted for phototherapy in the treatment of infants with hemolytic hyperbilirubinemia.
- a. Supplementation of breastfeeding with infant formula. As infant formula inhibits the intestinal reabsorption of bilirubin,⁹⁷ (IV) it may sometimes be used to lower TSB in breastfeeding infants.⁷⁷ Small-volume (10–15 mL) feedings of formula immediately following a breastfeeding may be preferred to intermittent large-volume (30–60 mL) supplementation so as to maintain frequent breastfeeding and preserve maternal milk production at a high level.⁹⁸ (IA) Larger volumes may be required if the infant is not receiving sufficient milk at the breast (i.e., low milk supply or poor milk transfer).
 - b. Temporary interruption of breastfeeding. Temporary interruption of breastfeeding is very rarely needed, but may be considered for specific clinical scenarios in

which rapid reduction in TSB is urgently needed or if phototherapy is unavailable.⁹⁹ (IIA) If urgent clinical needs necessitate the temporary interruption of breastfeeding, it is critical to maintain maternal milk production by teaching the mother to effectively and frequently express milk by hand or pump. The infant needs to return to a good supply of milk when breastfeeding resumes, or poor milk supply may result in a return of higher TSB concentrations.

Post-treatment follow-up and evaluation

Infants who have had any of the above treatments for excessive hyperbilirubinemia need to be carefully followed with repeat TSB determinations and support of breastfeeding because suboptimal breast milk intake may result in recurrence of hyperbilirubinemia.

Encouragement to continue breastfeeding is of the greatest importance since many parents will be fearful that continued breastfeeding may result in more jaundice or other problems. Parents can be reassured that almost all hyperbilirubinemia requiring treatment resolves within the first 5 days after birth. Even those infants with more prolonged breast milk jaundice who required and received treatment rarely have sufficient rise in bilirubin with continued breastfeeding to require further intervention.

Summary and Conclusions

Breastfeeding and some degree of hyperbilirubinemia are normal and expected aspects of neonatal development.⁴⁵ Managing the confluence of jaundice and breastfeeding in a physiologic and supportive manner to ensure optimal health, growth, and development of the infant is the responsibility of all healthcare providers. A complete understanding of normal and abnormal states of both bilirubin and breastfeeding is essential if optimal care is to be provided and the best outcome achieved for the child. We provide guidelines for managing this problem while recognizing the need for adjusting the guidelines to the individual needs of each infant.

Research Needs

The recommendations above are based on the most current research and clinical experience available. Identifying the components in human milk that increase total serum bilirubin and whether and to what extent these components interact with genetic variation to increase jaundice might substantially improve risk-based strategies to prevent and treat hyperbilirubinemia. Because both commercial and noncommercial sources of banked donor milk are increasingly available,^{100–104} further research on the effect of supplementing breastfed infants with banked donor milk on TSB levels is urgently needed. Small volumes of L-aspartic acid, enzymatically hydrolyzed casein or whey/casein, immediately after breastfeeding show potential promise in reducing TSB without interfering with breastfeeding or milk supply, but such interventions need further evaluation before they can be recommended for use.¹⁰⁵ In addition, widely generalizable research is also needed to evaluate specific strategies for feeding management of the breastfed infant with hyperbilirubinemia that allow uninterrupted breastfeeding while reducing serum bilirubin concentrations to safe levels. Additional strategies to maximize maternal milk intake and

shorten the duration of phototherapy need to be further explored and considered.¹⁰⁶

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References

1. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics* 2004;114:297–316.
2. Maisels MJ. Managing the jaundiced newborn: A persistent challenge. *CMAJ* 2015;187:335–343.
3. Preer GL, Philipp BL. Understanding and managing breast milk jaundice. *Arch Dis Child Fetal Neonatal Ed* 2011;96:F461–F466.
4. Olusanya BO, Osibanjo FB, Slusher TM. Risk factors for severe neonatal hyperbilirubinemia in low and middle-income countries: A systematic review and meta-analysis. *PLoS One* 2015;10:e0117229.
5. VanWagner LB, Green RM. Evaluating elevated bilirubin levels in asymptomatic adults. *JAMA* 2015;313:516–517.
6. Bhutani VK, Stark AR, Lazzaroni LC, et al. PredischARGE screening for severe neonatal hyperbilirubinemia identifies infants who need phototherapy. *J Pediatr* 2013;162:477–482 e471.
7. Keren R, Luan X, Friedman S, et al. A comparison of alternative risk-assessment strategies for predicting significant neonatal hyperbilirubinemia in term and near-term infants. *Pediatrics* 2008;121:e170–e179.
8. Fouzas S, Mantagou L, Skylogianni E, et al. Transcutaneous bilirubin levels for the first 120 postnatal hours in healthy neonates. *Pediatrics* 2010;125:e52–e57.
9. De Luca D, Romagnoli C, Tiberi E, et al. Skin bilirubin nomogram for the first 96 h of life in a European normal healthy newborn population, obtained with multiwavelength transcutaneous bilirubinometry. *Acta Paediatr* 2008;97:146–150.
10. Bhutani VK, Vilms RJ, Hamerman-Johnson L. Universal bilirubin screening for severe neonatal hyperbilirubinemia. *J Perinatol* 2010;30 Suppl:S6–S15.
11. Maisels MJ. What's in a name? Physiologic and pathologic jaundice: The conundrum of defining normal bilirubin levels in the newborn. *Pediatrics* 2006;118:805–807.
12. Bertini G, Dani C, Tronchin M, et al. Is breastfeeding really favoring early neonatal jaundice? *Pediatrics* 2001;107:E41.
13. Dahms BB, Krauss AN, Gartner LM, et al. Breast feeding and serum bilirubin values during the first 4 days of life. *J Pediatr* 1973;83:1049–1054.
14. Jangaard KA, Fell DB, Dodds L, et al. Outcomes in a population of healthy term and near-term infants with serum bilirubin levels of ≥ 325 micromol/L (≥ 19 mg/dL) who were born in Nova Scotia, Canada, between 1994 and 2000. *Pediatrics* 2008;122:119–124.
15. Kaplan M, Herschel M, Hammerman C, et al. Neonatal hyperbilirubinemia in African American males: The importance of glucose-6-phosphate dehydrogenase deficiency. *J Pediatr* 2006;149:83–88.
16. Kuzniewicz MW, Escobar GJ, Wi S, et al. Risk factors for severe hyperbilirubinemia among infants with borderline bilirubin levels: A nested case-control study. *J Pediatr* 2008;153:234–240.
17. Chen CF, Hsu MC, Shen CH, et al. Influence of breastfeeding on weight loss, jaundice, and waste elimination in neonates. *Pediatr Neonatol* 2011;52:85–92.
18. Yang H, Wang Q, Zheng L, et al. Multiple genetic modifiers of bilirubin metabolism involvement in significant neonatal hyperbilirubinemia in patients of Chinese descent. *PLoS One* 2015;10:e0132034.
19. Newman TB, Xiong B, Gonzales VM, et al. Prediction and prevention of extreme neonatal hyperbilirubinemia in a mature health maintenance organization. *Arch Pediatr Adolesc Med* 2000;154:1140–1147.
20. Huang MS, Lin MC, Chen HH, et al. Risk factor analysis for late-onset neonatal hyperbilirubinemia in Taiwanese infants. *Pediatr Neonatol* 2009;50:261–265.
21. Maisels MJ, Bhutani VK, Bogen D, et al. Hyperbilirubinemia in the newborn infant ≥ 35 weeks' gestation: An update with clarifications. *Pediatrics* 2009;124:1193–1198.
22. Itoh S, Kondo M, Kusaka T, et al. Differences in transcutaneous bilirubin readings in Japanese term infants according to feeding method. *Pediatr Int* 2001;43:12–15.
23. De Carvalho M, Robertson S, Klaus M. Fecal bilirubin excretion and serum bilirubin concentrations in breast-fed and bottle-fed infants. *J Pediatr* 1985;107:786–790.
24. Buiter HD, Dijkstra SS, Oude Elferink RF, et al. Neonatal jaundice and stool production in breast- or formula-fed term infants. *Eur J Pediatr* 2008;167:501–507.
25. Gartner LM. Breastfeeding and jaundice. *J Perinatol* 2001;21 Suppl 1:S25–S29.
26. Flaherman VJ, Gay B, Scott C, et al. Randomised trial comparing hand expression with breast pumping for mothers of term newborns feeding poorly. *Arch Dis Child Fetal Neonatal Ed* 2012;97:F18–F23.
27. Chapman DJ, Young S, Ferris AM, et al. Impact of breast pumping on lactogenesis stage II after cesarean delivery: A randomized clinical trial. *Pediatrics* 2001;107:E94.
28. Evans KC, Evans RG, Royal R, et al. Effect of caesarean section on breast milk transfer to the normal term newborn over the first week of life. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F380–F382.
29. Santoro W, Jr, Martinez FE, Ricco RG, et al. Colostrum ingested during the first day of life by exclusively breastfed healthy newborn infants. *J Pediatr* 2010;156:29–32.
30. Aaltonen T, Alvarez Gonzalez B, Amerio S, et al. Measurement of b hadron lifetimes in exclusive decays containing a J/ψ in pp collisions at $\sqrt{s} = 1.96$ TeV. *Phys Rev Lett* 2011;106:121804.
31. Saint L, Smith M, Hartmann PE. The yield and nutrient content of colostrum and milk of women from giving birth to 1 month post-partum. *Br J Nutr* 1984;52:87–95.
32. Whitmer DI, Gollan JL. Mechanisms and significance of fasting and dietary hyperbilirubinemia. *Semin Liver Dis* 1983;3:42–51.
33. White GL, Jr, Nelson JA, Pedersen DM, et al. Fasting and gender (and altitude?) influence reference intervals for serum bilirubin in healthy adults. *Clin Chem* 1981;27:1140–1142.
34. Bloomer JR, Barrett PV, Rodkey FL, et al. Studies on the mechanism of fasting hyperbilirubinemia. *Gastroenterology* 1971;61:479–487.
35. Fevery J. Fasting hyperbilirubinemia: Unraveling the mechanism involved. *Gastroenterology* 1997;113:1798–1800.
36. Pang WW, Hartmann PE. Initiation of human lactation: Secretory differentiation and secretory activation. *J Mammary Gland Biol Neoplasia* 2007;12:211–221.

37. De Carvalho M, Klaus MH, Merkatz RB. Frequency of breast-feeding and serum bilirubin concentration. *Am J Dis Child* 1982;136:737–738.
38. Yamauchi Y, Yamanouchi I. Breast-feeding frequency during the first 24 hours after birth in full-term neonates. *Pediatrics* 1990;86:171–175.
39. Wu PY, Hodgman JE, Kirkpatrick BV, et al. Metabolic aspects of phototherapy. *Pediatrics* 1985;75(2 Pt 2):427–433.
40. Davila-Grijalva H, Troya AH, Kring E, et al. How much do formula-fed infants take in the first 2 days? *Clin Pediatr* 2016;pii: 0009922816637647.
41. Sato H, Uchida T, Toyota K, et al. Association of neonatal hyperbilirubinemia in breast-fed infants with UGT1A1 or SLCOs polymorphisms. *J Hum Genet* 2015;60:35–40.
42. Sato H, Uchida T, Toyota K, et al. Association of breast-fed neonatal hyperbilirubinemia with UGT1A1 polymorphisms: 211G>A (G71R) mutation becomes a risk factor under inadequate feeding. *J Hum Genet* 2013;58:7–10.
43. Maisels MJ, Clune S, Coleman K, et al. The natural history of jaundice in predominantly breastfed infants. *Pediatrics* 2014;134:e340–e345.
44. Kivlahan C, James EJ. The natural history of neonatal jaundice. *Pediatrics* 1984;74:364–370.
45. American Academy of Pediatrics. Breastfeeding and the use of human milk. *Pediatrics* 2012;129:e827–e841.
46. Verkade HJ. A novel hypothesis on the pathophysiology of neonatal jaundice. *J Pediatr* 2002;141:594–595.
47. Apaydin K, Ermis B, Arasli M, et al. Cytokines in human milk and late-onset breast milk jaundice. *Pediatr Int* 2012;54:801–805.
48. Uras N, Tonbul A, Karadag A, et al. Prolonged jaundice in newborns is associated with low antioxidant capacity in breast milk. *Scand J Clin Lab Invest* 2010;70:433–437.
49. Bozkaya OG, Kumral A, Yesilirmak DC, et al. Prolonged unconjugated hyperbilirubinaemia associated with the haem oxygenase-1 gene promoter polymorphism. *Acta Paediatr* 2010;99:679–683.
50. Zaja O, Tiljak MK, Stefanovic M, et al. Correlation of UGT1A1 TATA-box polymorphism and jaundice in breastfed newborns-early presentation of Gilbert's syndrome. *J Matern Fetal Neonatal Med* 2014;27:844–850.
51. Chou HC, Chen MH, Yang HI, et al. 211 G to a variation of UDP-glucuronosyl transferase 1A1 gene and neonatal breastfeeding jaundice. *Pediatr Res* 2011;69:170–174.
52. Kumral A, Ozkan H, Duman N, et al. Breast milk jaundice correlates with high levels of epidermal growth factor. *Pediatr Res* 2009;66:218–221.
53. Manganaro R, Marseglia L, Mami C, et al. Serum alpha-fetoprotein (AFP) levels in breastfed infants with prolonged indirect hyperbilirubinemia. *Early Hum Dev* 2008;84:487–490.
54. Nagao Y, Ohsawa M, Kobayashi T. Correlation between unconjugated bilirubin and total cholesterol in the sera of 1-month-old infants. *J Paediatr Child Health* 2010;46:709–713.
55. Tuzun F, Kumral A, Duman N, et al. Breast milk jaundice: Effect of bacteria present in breast milk and infant feces. *J Pediatr Gastroenterol Nutr* 2013;56:328–332.
56. Watchko JF, Lin Z. Genetics of neonatal jaundice. In: Care of the Jaundiced Neonate, Stevenson DK, Maisels MJ, Watchko JF, eds. New York, NY: McGraw Hill, 2012, pp. 1–27.
57. Chang RJ, Chou HC, Chang YH, et al. Weight loss percentage prediction of subsequent neonatal hyperbilirubinemia in exclusively breastfed neonates. *Pediatr Neonatol* 2012;53:41–44.
58. Chen YJ, Chen WC, Chen CM. Risk factors for hyperbilirubinemia in breastfed term neonates. *Eur J Pediatr* 2012;171:167–171.
59. Huang A, Tai BC, Wong LY, et al. Differential risk for early breastfeeding jaundice in a multi-ethnic Asian cohort. *Ann Acad Med Singapore* 2009;38:217–224.
60. Huang HC, Yang HI, Chang YH, et al. Model to predict hyperbilirubinemia in healthy term and near-term newborns with exclusive breast feeding. *Pediatr Neonatol* 2012;53:354–358.
61. Salas AA, Salazar J, Burgoa CV, et al. Significant weight loss in breastfed term infants readmitted for hyperbilirubinemia. *BMC Pediatr* 2009;9:82.
62. Yang WC, Zhao LL, Li YC, et al. Bodyweight loss in predicting neonatal hyperbilirubinemia 72 hours after birth in term newborn infants. *BMC Pediatr* 2013;13:145.
63. Ebbesen F, Bjerre JV, Vandborg PK. Relation between serum bilirubin levels $\geq 450 \mu\text{mol/L}$ and bilirubin encephalopathy; a Danish population-based study. *Acta Paediatr* 2012;101:384–389.
64. Kuzniewicz MW, Wickremasinghe AC, Wu YW, et al. Incidence, etiology, and outcomes of hazardous hyperbilirubinemia in newborns. *Pediatrics* 2014;134:504–509.
65. Newman TB, Kuzniewicz MW. Follow-up of extreme neonatal hyperbilirubinaemia: More reassuring results from Denmark. *Dev Med Child Neurol* 2015;57:314–315.
66. Bhutani VK, Zipursky A, Blencowe H, et al. Neonatal hyperbilirubinemia and Rhesus disease of the newborn: Incidence and impairment estimates for 2010 at regional and global levels. *Pediatr Res* 2013;74 Suppl 1:86–100.
67. Bhutani VK, Johnson LH, Jeffrey Maisels M, et al. Kernicterus: Epidemiological strategies for its prevention through systems-based approaches. *J Perinatol* 2004;24:650–662.
68. Maisels MJ, Newman TB. Kernicterus in otherwise healthy, breast-fed term newborns. *Pediatrics* 1995;96(4 Pt 1):730–733.
69. Righard L, Alade MO. Effect of delivery room routines on success of first breast-feed. *Lancet* 1990;336:1105–1107.
70. Mikiel-Kostyra K, Mazur J, Boltrusko I. Effect of early skin-to-skin contact after delivery on duration of breastfeeding: A prospective cohort study. *Acta Paediatr* 2002;91:1301–1306.
71. Bramson L, Lee JW, Moore E, et al. Effect of early skin-to-skin mother–infant contact during the first 3 hours following birth on exclusive breastfeeding during the maternity hospital stay. *J Hum Lact* 2010;26:130–137.
72. Moore ER, Bergman N, Anderson GC, et al. Early skin-to-skin contact for mothers and their healthy newborn infants. *Cochrane Database Syst Rev* 2016. DOI:10.1002/14651858.CD003519.pub4
73. Shekelle PG, Woolf SH, Eccles M, et al. Developing guidelines. *BMJ* 1999;318:593–596.
74. Boskabadi H, Zakerihamidi M. The correlation between frequency and duration of breastfeeding and the severity of neonatal hyperbilirubinemia. *J Matern Fetal Neonatal Med* 2017. DOI:10.1080/14767058.2017.1287897
75. Dewey KG, Nommsen-Rivers LA, Heinig MJ, et al. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. *Pediatrics* 2003;112(3 Pt 1):607–619.
76. Boies EG, Vaucher YE, The Academy of Breastfeeding Medicine. ABM Clinical Protocol #10: Breastfeeding the

- late preterm (34–36 6/7 weeks of gestation) and early term infants (37–38 6/7 weeks of gestation), second revision 2016. *Breastfeed Med* 2016;11:494–500.
77. Kellams A, Harrel C, Omage S, et al. ABM clinical protocol #3: Supplementary feedings in the healthy term breastfed neonate. *Breastfeed Med* 2017;12:188–198.
 78. National Institute for Health and Care Excellence (NICE). Jaundice in Newborn Babies Under 28 Days. NICE, London, 2016.
 79. Bratlid D, Nakstad B, Hansen TW. National guidelines for treatment of jaundice in the newborn. *Acta Paediatr* 2011;100:499–505.
 80. Guidelines for detection, management and prevention of hyperbilirubinemia in term and late preterm newborn infants (35 or more weeks' gestation)—Summary. *Paediatr Child Health* 2007;12:401–418.
 81. Flaherman VJ, Hicks KG, Cabana MD, et al. Maternal experience of interactions with providers among mothers with milk supply concern. *Clin Pediatr* 2012;51:778–784.
 82. Kair LR, Flaherman VJ, Newby KA, et al. The experience of breastfeeding the late preterm infant: A qualitative study. *Breastfeed Med* 2015;10:102–106.
 83. Hill PD. Insufficient milk supply syndrome. *NAACOGS Clin Issu Perinat Womens Health Nurs* 1992;3:605–612.
 84. Hill PD. The enigma of insufficient milk supply. *MCN Am J Matern Child Nurs* 1991;16:312–316.
 85. Lauer BJ, Spector ND. Hyperbilirubinemia in the newborn. *Pediatr Rev* 2011;32:341–349.
 86. Maisels MJ. Screening and early postnatal management strategies to prevent hazardous hyperbilirubinemia in newborns of 35 or more weeks of gestation. *Semin Fetal Neonatal Med* 2010;15:129–135.
 87. Schwartz HP, Haberman BE, Ruddy RM. Hyperbilirubinemia: Current guidelines and emerging therapies. *Pediatr Emerg Care* 2011;27:884–889.
 88. Watchko JF. Identification of neonates at risk for hazardous hyperbilirubinemia: Emerging clinical insights. *Pediatr Clin North Am* 2009;56:671–687.
 89. Gulcan H, Tiker F, Kilicdag H. Effect of feeding type on the efficacy of phototherapy. *Indian Pediatr* 2007;44:32–36.
 90. Maisels MJ, Newman TB, Watchko J, et al. Phototherapy and other treatments. In: *Care of the Jaundiced Neonate*, Stevenson DK, Maisels MJ, Watchko JF, eds. New York: McGraw Hill, 2012, pp. 195–227.
 91. Lau SP, Fung KP. Serum bilirubin kinetics in intermittent phototherapy of physiological jaundice. *Arch Dis Child* 1984;59:892–894.
 92. Vogl TP, Hegyi T, Hiatt IM, et al. Intermediate phototherapy in the treatment of jaundice in the premature infant. *J Pediatr* 1978;92:627–630.
 93. Sachdeva M, Murki S, Oleti TP, et al. Intermittent versus continuous phototherapy for the treatment of neonatal non-hemolytic moderate hyperbilirubinemia in infants more than 34 weeks of gestational age: A randomized controlled trial. *Eur J Pediatr* 2015;174:177–181.
 94. de Carvalho M, Hall M, Harvey D. Effects of water supplementation on physiological jaundice in breast-fed babies. *Arch Dis Child* 1981;56:568–569.
 95. Nicoll A, Ginsburg R, Tripp JH. Supplementary feeding and jaundice in newborns. *Acta Paediatr Scand* 1982;71:759–761.
 96. Howard CR, Howard FM, Lanphear B, et al. Randomized clinical trial of pacifier use and bottle-feeding or cupfeeding and their effect on breastfeeding. *Pediatrics* 2003;111:511–518.
 97. Gartner LM, Lee KS, Moscioni AD. Effect of milk feeding on intestinal bilirubin absorption in the rat. *J Pediatr* 1983;103:464–471.
 98. Flaherman VJ, Aby J, Burgos AE, et al. Effect of early limited formula on duration and exclusivity of breastfeeding in at-risk infants: An RCT. *Pediatrics* 2013;131:1059–1065.
 99. Martinez JC, Maisels MJ, Otheguy L, et al. Hyperbilirubinemia in the breast-fed newborn: A controlled trial of four interventions. *Pediatrics* 1993;91:470–473.
 100. Updegrave KH. Donor human milk banking: Growth, challenges, and the role of HMBANA. *Breastfeed Med* 2013;8:435–437.
 101. U.S. Food and Drug Administration. Use of Donor Human Milk. 2014. Available at www.fda.gov/scienceresearch/specialtopics/pediatrictherapeuticsresearch/ucm235203.htm (accessed January 25, 2014).
 102. Kair LR, Colaizy TT, Hubbard D, et al. Donor milk in the newborn nursery at the University of Iowa Children's Hospital. *Breastfeed Med* 2014;9:547–550.
 103. Bulpitt DW, Elmore KE, Catterton LJ. Implementing use of donor breast milk in the well baby population: It's not just for the NICU any more. *J Obstet Gynecol Neonatal Nurs* 2014;43(Suppl 1):S56.
 104. Brownell EA, Lussier MM, Herson VC, et al. Donor human milk bank data collection in North America: An assessment of current status and future needs. *J Hum Lact* 2014;30:47–53.
 105. Gourley GR, Li Z, Kreamer BL, et al. A controlled, randomized, double-blind trial of prophylaxis against jaundice among breastfed newborns. *Pediatrics* 2005;116:385–391.
 106. Samra N, El Taweel A, Cadwell K. The effect of kangaroo mother care on the duration of phototherapy of infants readmitted for neonatal jaundice. *J Matern Fetal Neonatal Med* 2012;25:1354–1357.
 107. Paul IM, Schaefer EW, Miller JR, et al. Weight change nomograms for the first month after birth. *Pediatrics* 2016;138:pii: e20162625.
- ABM protocols expire 5 years from the date of publication. Content of this protocol is up-to-date at the time of publication. Evidence-based revisions are made within 5 years or sooner if there are significant changes in the evidence. The first version of this protocol was authored by Lawrence Gartner.
- The Academy of Breastfeeding Medicine Protocol Committee:
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 Rose St. Fleur, MD
 Michal Young, MD

For correspondence: abm@bfmed.org