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Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation FREE

Alex R. Kemper, MD, MPH, MS, FAAP ✉; Thomas B. Newman, MD, MPH, FAAP; Jonathan L. Slaughter, MD, MPH, FAAP; M. Jeffrey Maisels, MB BCh, DSc, FAAP; Jon F. Watchko, MD, FAAP; Stephen M. Downs, MD, MS; Randall W. Grout, MD, MS, FAAP; David G. Bundy, MD, MPH, FAAP; Ann R. Stark, MD, FAAP; Debra L. Bogen, MD, FAAP; Alison Volpe Holmes, MD, MPH, FAAP; Lori B. Feldman-Winter, MD, MPH, FAAP; Vinod K. Bhutani, MD; Steven R. Brown, MD, FAAFP; Gabriela M. Maradiaga Panayotti, MD, FAAP; Kymika Okechukwu, MPA; Peter D. Rappo, MD, FAAP; Terri L. Russell, DNP, APN, NNP-BC

Address correspondence to Alex R. Kemper, MD. Email: alex.kemper@nationwidechildrens.org

FINANCIAL/CONFLICT OF INTEREST DISCLOSURES: Dr Newman reported providing expert witness consultation in medical malpractice litigation. Dr Maisels reported providing expert witness review and testimony in kernicterus medical malpractice litigation. Dr Watchko disclosed a financial relationship with McGraw Hill. Dr Grout reported receiving grant funding from Pfizer for a non-pediatric study. Dr Bogen disclosed a Board of Directors relationship with Mid-Atlantic Mothers' Milk Bank. No other disclosures were reported.

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Video Abstract

Subjects: Evidence-Based Medicine, Hyperbilirubinemia

Topics: hyperbilirubinemia, phototherapy, bilirubin, exchange transfusion, whole blood

More than 80% of newborn infants will have some degree of jaundice.[1,2] Careful monitoring of all newborn infants and the application of appropriate treatments are essential, because high bilirubin concentrations can cause acute bilirubin encephalopathy and kernicterus.[3] Kernicterus is a permanent disabling neurologic condition characterized by some or all of the following: choreoathetoid cerebral palsy, upward gaze paresis, enamel dysplasia of deciduous teeth, sensorineural hearing loss or auditory neuropathy or dyssynchrony spectrum disorder, and characteristic findings on brain MRI.[4] A description of kernicterus nomenclature is provided in Appendix A. Central to this guideline is having systems in place including policies in hospitals and other types of birthing locations to provide the care necessary to minimize the risk of kernicterus.

This article updates and replaces the 2004 American Academy of Pediatrics (AAP) clinical practice guideline for the management and prevention of hyperbilirubinemia in the newborn infant ≥35 weeks' gestation.[3] This clinical practice guideline, like the previous one, addresses issues of prevention, risk assessment, monitoring, and treatment.

Guideline Development Process

The AAP convened a clinical practice guideline committee with membership that included neonatologists, hospitalists, primary care pediatricians, a nurse, and breastfeeding experts. Some members also had special expertise in neonatal hyperbilirubinemia. This committee worked from 2014 to 2022 to review new evidence and to identify opportunities to clarify and improve the 2004 guideline. This report underwent extensive peer review by a wide array of clinicians and experts in neonatal hyperbilirubinemia and by parents of children with kernicterus.

The committee recognizes that in the United States and other high-resource countries, the recommended management of hyperbilirubinemia and the risk of kernicterus can differ significantly from countries with more limited resources. The management of hyperbilirubinemia can also vary among high-resource countries where early discharge from the mother-baby unit is less common. The committee recommends caution and incorporation of local expertise in adapting these guidelines for use outside the United States.

This clinical practice guideline provides specific recommendations where evidence or significant clinical experience suggests the benefit of the clinical action. In some cases, options for clinical care delivery are provided when the evidence or clinical experience is less certain. For selected recommendations that are central to this guideline, the subcommittee reports the aggregate quality evidence and the strength of the recommendation according to the AAP policy statement "Classifying Recommendations for Clinical Practice Guidelines."[5] These recommendations are formatted as Key Action Statements (KAS) for easy identification, and the evidence tables supporting them appear in Appendix B. Note

that throughout the guideline, the term “parent” is used to represent the caregiver(s) responsible for the infant and “mother” is used to represent the birthing and/or breastfeeding parent.

Previous Guidelines

The 2004 guideline focused on infants ≥35 weeks’ gestation. This gestational age range includes most newborn infants cared for, and subsequently followed by, general pediatricians and other primary care clinicians on well newborn services or mother-baby care units. The 2004 guideline made recommendations for primary prevention (eg, maternal Rh typing and treatment) and secondary prevention (eg, risk-factor assessment and close monitoring for the development of hyperbilirubinemia, and, when necessary, treatment).

In 2009, a commentary describing several clarifications and modifications[6] to the 2004 clinical practice guideline was published. These included clarifying the distinction between “hyperbilirubinemia risk factors,” which increase the risk of subsequent hyperbilirubinemia, and “hyperbilirubinemia neurotoxicity risk factors,” which increase the risk of bilirubin neurotoxicity. A new recommendation was for universal predischarge bilirubin screening with measures of total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) linked to specific recommendations for follow-up. Although it is difficult to determine the direct impact of these recommendations, the incidence of hazardous hyperbilirubinemia, defined as TSB ≥30 mg/dL,[7] decreased in at least 3 large US health systems after the adoption of universal predischarge bilirubin screening with closer postdischarge follow-up.[8–10]

Evidence Leading to Changes

Since the publication of the previous guideline, the evidence base regarding the monitoring and treatment of hyperbilirubinemia has expanded. Key new research findings appear in the evidence tables included in Appendix B and in the accompanying technical report.[11] In addition, the committee reviewed guidelines from the Northern California Neonatal Consortium[12] and the Academy of Breastfeeding Medicine.[13] Because the new evidence is insufficient to derive specific treatment thresholds by quantitatively estimating the risks and benefits of different approaches to care, the committee began with the previous AAP guidelines. On the basis of an evaluation of evidence published since 2004, the committee raised the phototherapy thresholds by a narrow range that the committee considered to be safe. The committee also used new research findings to revise the risk-assessment approach based on the hour-specific bilirubin concentration and the approach to rapidly address elevated bilirubin concentrations, defined as "escalation of care."

I. Prevention of Hyperbilirubinemia

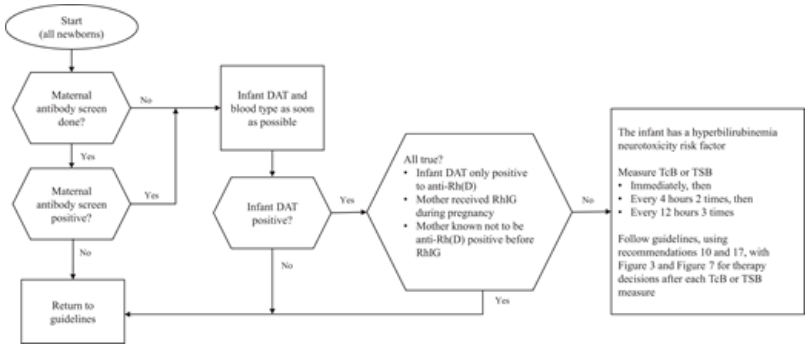
A. Preventing Hyperbilirubinemia Associated With Isoimmune Hemolytic Disease

Prevention of hyperbilirubinemia begins in pregnancy by recognizing and treating women who are at risk for developing antibodies to red cell antigens, which can lead to hemolytic disease of the newborn (ie, isoimmune hemolytic disease). If the mother was not screened for anti-erythrocyte antibodies during pregnancy, evaluation and treatment should occur shortly after delivery. The American College of Obstetricians and Gynecologists recommends that pregnant women be tested to determine their ABO blood group and Rh(D) type and receive an antibody screen to determine the

need for Rh(D) immunoglobulin (RhIG) and to assess the potential for isoimmune hemolytic disease of the fetus or newborn.[14]

The approach to identify newborns with maternal anti-erythrocyte antibodies and guide early management is outlined in Fig 1.[15]

FIGURE 1



Approach to identify newborns with maternal anti-erythrocyte antibodies and to guide early management.[15]

KAS 1: If the maternal antibody screen is positive or unknown because the mother did not have prenatal antibody screening, the infant should have a direct antiglobulin test (DAT) and the infant's blood type should be determined as soon as possible using either cord or peripheral blood. (Aggregate Evidence Quality Grade B, Recommendation)

The DAT helps to identify infants at risk for hyperbilirubinemia attributable to hemolysis. DAT-negative infants may be managed with usual care. Mothers who received RhIG can have a positive antibody screen for anti-Rh(D), and RhIG can cause a positive DAT (anti-Rh[D]) in the infant but generally no hemolysis.[16] If an infant's DAT is known to be positive only to

anti-Rh(D) because the mother received RhIG during pregnancy and the mother was known not to have Rh(D) antibodies before receiving RhIG, the infant can be treated as if the infant is DAT negative. However, any infant with a positive DAT attributable to an antibody other than anti-Rh(D) following maternal receipt of RhIG should be considered to be DAT positive.[15]

If the maternal blood type is Rh(D)−, the Rh type of the infant should be determined to assess the need for administration of RhIG to the mother. If the maternal blood is O+ and the maternal antibody screen is negative, it is an option to test the cord blood for the infant's blood type and/or DAT. Determining the infant's blood type or DAT is not necessary if bilirubin surveillance and risk assessment follows this clinical practice guideline and appropriate follow-up after discharge is arranged. Otherwise, this testing should be done.

B. Providing Feeding Support

Exclusive breastfeeding and hyperbilirubinemia are strongly associated.[13] Jaundice in breastfed infants falls into 2 main categories, depending on its timing of onset. These types of jaundice must be differentiated to guide appropriate management. Suboptimal intake can lead to hyperbilirubinemia, the so-called "breastfeeding jaundice," which typically peaks on days 3 to 5 after birth and is frequently associated with excess weight loss. Because this type of jaundice, especially when excessive, is almost always associated with inadequate milk intake rather than breastfeeding per se, it is more correctly described as "suboptimal intake hyperbilirubinemia."[13] Breastfeeding fewer than 8 times per day has been associated with higher TSB concentrations.[17] Low milk and low caloric intake contribute to decreased stool frequency and increased enterohepatic

circulation of bilirubin.[13] In contrast to suboptimal intake, hyperbilirubinemia that persists with adequate human milk intake and weight gain is referred to as “breast milk jaundice” or the “breast milk jaundice syndrome.” This cause of prolonged unconjugated hyperbilirubinemia, which can last up to 3 months, is almost always nonpathologic and not associated with direct or conjugated hyperbilirubinemia.[13] One study found that 28 days after birth, 34% of predominantly breastfed infants had TcB concentrations ≥5 mg/dL, 9% had concentrations ≥10 mg/dL, and 1% had concentrations ≥12.9 mg/dL.[18]

Although this clinical practice guideline cannot fully address early infant feeding, adequate feeding is an important component of preventing hyperbilirubinemia.[19] The AAP recommends implementation of maternity care practices that promote comprehensive, evidence-based, family-centered breastfeeding support.[19,20] Clinicians should promote breastfeeding support for all mothers and breast milk feeding within the first hour after birth with frequent feeding on demand (ie, at least 8 times in 24 hours).[19] Signs of suckling adequacy include appropriate urine output and transitional stooling, normal weight loss by hour of age and delivery method, absence of maternal discomfort, and audible swallowing as the mother’s milk volumes increase.[20,21] Breastfed infants who are adequately hydrated should not routinely receive supplementation with commercially available infant formula.[19]

KAS 2: Oral supplementation with water or dextrose water should not be provided to prevent hyperbilirubinemia or decrease bilirubin concentrations.

(Strong recommendation based on high-quality evidence)

Decisions about temporary supplementation with either donor breast milk or infant formula should be made jointly with the infant's parents, when possible, after discussion of risks and benefits.[22–25]

II. Assessment and Monitoring for Hyperbilirubinemia

A. Identifying Risk Factors for Hyperbilirubinemia

Infants with risk factors for hyperbilirubinemia (Table 1) require closer monitoring than infants without risk factors. Determining the presence of these risk factors requires examining the infant, assessing laboratory data, and obtaining a family history of blood disorders or neonatal jaundice.

TABLE 1 Risk Factors for Developing Significant Hyperbilirubinemia

Risk Factors
• Lower gestational age (ie, risk increases with each additional week less than 40 wk)
• Jaundice in the first 24 h after birth
• Predischarge transcutaneous bilirubin (TcB) or total serum bilirubin (TSB) concentration close to the phototherapy threshold
• Hemolysis from any cause, if known or suspected based on a rapid rate of increase in the TSB or TcB of >0.3 mg/dL per hour in the first 24 h or >0.2 mg/dL per hour thereafter.
• Phototherapy before discharge
• Parent or sibling requiring phototherapy or exchange transfusion
• Family history or genetic ancestry suggestive of inherited red blood cell disorders, including glucose-6-phosphate dehydrogenase (G6PD) deficiency
• Exclusive breastfeeding with suboptimal intake

• Scalp hematoma or significant bruising
• Down syndrome
• Macrosomic infant of a diabetic mother

Glucose-6-phosphate dehydrogenase (G6PD) deficiency, an X-linked recessive enzymopathy that decreases protection against oxidative stress, is now recognized as one of the most important causes of hazardous hyperbilirubinemia leading to kernicterus in the United States and across the globe.[9,26–28] Identifying neonates with G6PD deficiency is a challenge. Most affected infants will not have a positive family history. Genetic ancestry from a population in which this condition is prevalent (eg, Sub-Saharan Africa, Middle East, Mediterranean, Arabian Peninsula, and Southeast Asia) can be helpful in predicting risk. This is an example of how the delivery of race-conscious medicine can lead to improved health outcomes.[29] Knowing information about genetic ancestry can help inform the assessment of G6PD risk. Overall, 13% of African American males and about 4% of African American females have G6PD deficiency.[30–34]

There are clinical events that should raise suspicion about the presence of G6PD deficiency. Newborn infants with G6PD deficiency are more likely to receive phototherapy before hospital discharge,[31] probably because of both increased bilirubin production and decreased conjugation,[35] and have a greater risk of readmission and retreatment.[36] Severe hyperbilirubinemia or atypical development of hyperbilirubinemia, such as elevated TSB in a formula-fed infant or late-onset jaundice, should raise the possibility of

An infant with G6PD deficiency can develop a sudden and extreme increase in TSB that may be hard to anticipate or prevent.[26,27,34,37–40] Even after what appears to be an acute hemolytic event, there may be little or no laboratory evidence of hemolysis.[40] It is important for clinicians to recognize that measuring the G6PD activity during or soon after the hemolytic event or after an exchange transfusion can lead to a falsely normal result. If G6PD deficiency is strongly suspected but the measurement of G6PD activity is normal or close to normal, the G6PD activity should be measured at least 3 months later.

B. Identifying the Need for Treatment

Although there is considerable laboratory variability in TSB measurements,[41–43] virtually all treatment studies are based on TSB levels measured in hospital clinical laboratories.

KAS 3: Use TSB as the definitive test to guide phototherapy and escalation-of-care decisions, including exchange transfusion. (Aggregate Evidence Quality Grade X, Recommendation)

Decisions to initiate phototherapy or escalate care are guided by the gestational age, the hour-specific TSB, and the presence of risk factors for bilirubin neurotoxicity (**Table 2**). The presence of hyperbilirubinemia neurotoxicity risk factors lowers the threshold for treatment with phototherapy and the level at which care should be escalated. It is important that clinicians use their judgment in determining the presence of neurotoxicity risk factors, including clinical instability or sepsis. Although acidemia can indicate clinical instability, insufficient evidence is available to provide a specific pH threshold for increased neurotoxicity risk.

TABLE 2 Hyperbilirubinemia Neurotoxicity Risk Factors

Risk Factors
• Gestational age <38 wk and this risk increases with the degree of prematurity[a]
• Albumin <3.0 g/dL
• Isoimmune hemolytic disease (ie, positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions
• Sepsis
• Significant clinical instability in the previous 24 h

a Gestational age is required to identify the phototherapy thresholds (Figs 2 and 3; Supplemental Tables 1 and 2, and Supplemental Figs 1 and 2) and the exchange transfusion thresholds (Figs 5 and 6; Supplemental Tables 3 and 4, and Supplemental Figs 3 and 4).

Lower gestational age and isoimmune hemolytic disease are risk factors both for developing significant hyperbilirubinemia and for bilirubin neurotoxicity. Although it is not clear if hemolysis attributable to causes other than isoimmunization also increases the risk of bilirubin neurotoxicity, it is prudent to assume that it does. Other important neurotoxicity risk factors are related to serious illness in the newborn infant (eg, sepsis). Low serum albumin can increase the risk of neurotoxicity because of the greater availability of unbound bilirubin (ie, bilirubin not bound to albumin).[44,45] Most clinical laboratories cannot directly measure unbound bilirubin concentrations, and even if this information were available, there are insufficient data to guide clinical care using specific unbound bilirubin concentrations. To address those gaps, these guidelines consider an albumin concentration <3.0 g/dL to be a hyperbilirubinemia neurotoxicity risk factor (Table 2). Although there were insufficient data for the committee to recommend measuring the albumin concentration of all

newborn infants, measuring albumin is recommended as part of escalation of care.

C. Visual Estimation of TSB Concentrations

Several studies have examined the accuracy of visual estimation of TSB concentrations, correlating either the cephalocaudal progression of jaundice[46] or the visually estimated TSB concentration with measured TSB. Although correlations are generally highly statistically significant, differences as great as 13 to 15 mg/dL between the actual TSB or TcB and bilirubin values estimated by the jaundice level have been observed.[1,18,47,48] A more consistent finding is that if the infant is not jaundiced at all[18,47,48] or the clinician's visual bilirubin estimate is <4 mg/dL,[48,49] a TSB ≥12 mg/dL is highly unlikely. Visual estimation is routinely used to guide decisions about obtaining TcB or TSB measures in term-born outpatients 3 or more days old, for whom treatment thresholds are high enough that distinguishing between milder degrees of jaundice is not important. However, all infants should have at least 1 TcB or TSB measured, as described below (KAS 5).

KAS 4: All infants should be visually assessed for jaundice at least every 12 hours following delivery until discharge. TSB or TcB should be measured as soon as possible for infants noted to be jaundiced <24 hours after birth. (Aggregate Evidence Quality Grade X, Strong Recommendation)

Although jaundice before 24 hours of age may not have an identifiable cause,[50] when a cause is identified, it is most likely to be a hemolytic process. The consequences of missing early jaundice are treatable but significant. Hence, we justify TcB or TSB measurement. This recommendation for visual assessment does not replace the need to obtain at least 1

screening TSB or TcB as described below. Visual assessment is supplementary to measuring TSB or TcB.

D. Transcutaneous Bilirubin Levels

The TSB level can be estimated based on measurements of the TcB. TcB instruments from 2 manufacturers (Draeger, Inc. [JM instruments]; Philips, Inc [BiliChek instruments]) have been extensively studied.[51–53] These devices measure the yellowness of reflected light transmitted from the skin and use an algorithm to predict the TSB level from the objective measurement of skin color. Although TcB measurements do not directly assess bilirubin levels, they are valid and reliable when used as a screening test to identify infants who require a TSB measurement.[54] Using TcB measures in this way may result in a reduction in blood draws.[55] Implementing universal TcB screening during the nursery stay and at subsequent public health nurse visits has been associated with a reduction in both blood draws and the likelihood of having a TSB level ≥20 mg/dL.[56]

There is a good correlation between TcB measures and TSB concentrations, with the TSB generally within 3 mg/dL of the TcB among newborn infants with TSB concentrations <15 mg/dL.[57–61] The magnitude and direction of the average difference between TcB measures and TSB concentrations may depend on skin melanin concentration and the instrument used to measure TcB. For example, BiliChek instruments may underestimate TSB at higher levels (eg, above about 15 mg/dL) in infants with greater skin melanin concentration by an average of about 1 to 2 mg/dL.[62–64] In contrast, JM instruments may overestimate the TSB infants with greater skin melanin concentration by an average of about 0.7 to 2.5 mg/dL.[64–68] The recommendations for the use

of TcB measures takes into account the degree of uncertainty related to skin melanin concentration.

KAS 5: The TcB or TSB should be measured between 24 and 48 hours after birth or before discharge if that occurs earlier. (Aggregate Evidence Quality Grade C, Recommendation)

Blood for TSB can be obtained at the time it is collected for newborn screening tests to avoid an additional heel stick.

Infants born at home should also have bilirubin testing between 24 and 48 hours after birth.[69]

KAS 6: TSB should be measured if the TcB exceeds or is within 3 mg/dL of the phototherapy treatment threshold or if the TcB is ≥15 mg/dL. (Aggregate Evidence Quality Grade C, Recommendation)

KAS 7: If more than 1 TcB or TSB measure is available, the rate of increase may be used to identify infants at higher risk of subsequent hyperbilirubinemia.[70–72] A rapid rate of increase (≥0.3 mg/dL per hour in the first 24 hours or ≥0.2 mg/dL per hour thereafter) is exceptional[73] and suggests hemolysis. In this case, perform a DAT if not previously done. (Aggregate Evidence Quality Grade D, Option)

If available, measurement of end-tidal carbon monoxide production, corrected for ambient carbon monoxide (ETCOc), is a potentially useful method for quantifying hemolysis.[74] Carbon monoxide is produced in equimolar amounts with bilirubin when heme is catabolized to bilirubin.

KAS 8: If appropriate follow-up cannot be arranged for an infant with a second bilirubin measurement before the next bilirubin measure, discharge may be delayed. (Aggregate Evidence Quality Grade D, Option)

Among infants with TSB concentrations below the phototherapy threshold, the potential need for future phototherapy or escalation of care increases the closer the TSB is to the phototherapy threshold. However, once a spontaneous decline in TcB or TSB (ie, not associated with phototherapy) over at least 6 hours has been documented, the risk of subsequent hyperbilirubinemia is low and it is not necessary to obtain additional bilirubin measurements unless there are other worrisome signs, such as worsening jaundice or acute illness.

E. Evaluating Elevated Direct-Reacting or Conjugated Bilirubin Concentrations

In some laboratories, either a direct or conjugated bilirubin concentration is measured whenever a TSB is measured. It is helpful to understand that direct and conjugated bilirubin are different. Bilirubin is made water soluble by conjugation with glucuronic acid in the liver, which facilitates excretion. Conjugated bilirubin and a small amount of unconjugated bilirubin react directly (ie, without the addition of an accelerating agent) in the chemical reactions used to measure bilirubin concentrations, which is how “direct-reacting” or “direct” bilirubin is measured. After the direct-reacting bilirubin is measured, the accelerating agent is added and the bilirubin is measured again to obtain the total bilirubin. Direct bilirubin concentrations are higher and more variable than conjugated bilirubin[75,76] and tend to increase with the TSB.[41] Reference ranges for direct bilirubin measurements vary by clinical laboratory.[77]

A joint recommendation from the North American and European Societies for Pediatric Gastroenterology, Hepatology, and Nutrition defines a direct serum bilirubin concentration >1.0 mg/dL as abnormal,[78] whereas a cutoff of

≥0.3 mg/dL has been used for conjugated bilirubin.[76] Because the prevalence of biliary atresia is low (~1 in 14 000[79]) and this cut-off value is only about the 95th percentile,[75,80] nearly all (> 99%) infants who have a single elevation of the direct or conjugated bilirubin concentration do not have biliary atresia. The positive predictive value for biliary atresia and other causes of pathologic cholestasis can be greatly improved with a repeat measurement within a few days to 2 weeks.[76] An increase in the direct or conjugated bilirubin concentration suggests the possibility of pathologic cholestasis that requires further evaluation.[76,81,82] A direct bilirubin concentration of >20% of the total is no longer regarded as necessary for the diagnosis of cholestasis.[78] It is important to also consider causes of neonatal direct hyperbilirubinemia other than biliary atresia that require early treatment. These include urinary tract infection, isoimmune hemolytic disease, sepsis, and some inborn errors of metabolism.

KAS 9: For breastfed infants who are still jaundiced at 3 to 4 weeks of age, and for formula-fed infants who are still jaundiced at 2 weeks of age, the total and direct-reacting (or conjugated) bilirubin concentrations should be measured to identify possible pathologic cholestasis. (Aggregate Evidence Quality Grade X, Recommendation)

When prolonged jaundice occurs, clinicians should also review the newborn screening results, because some conditions detected through newborn screening (eg, galactosemia, hypothyroidism, tyrosinemia) can lead to persistent jaundice. In formula-fed infants with any prolonged jaundice, or in breastfed infants with direct or conjugated hyperbilirubinemia, consultation with a gastroenterologist or [illegible] is recommended.

III. Treatment of Hyperbilirubinemia

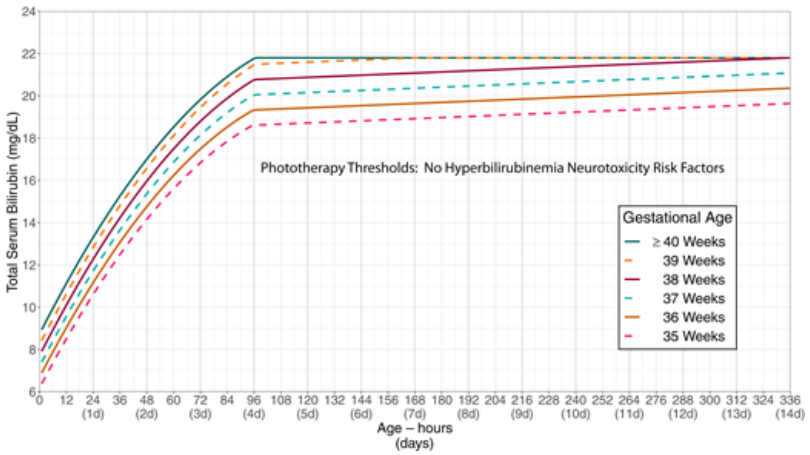
A. Providing Phototherapy

Phototherapy decreases bilirubin concentrations through a variety of photochemical reactions that allow the bilirubin to be more easily excreted. The effectiveness of phototherapy is dependent on the intensity of phototherapy administered and the surface area of the infant exposed to phototherapy (ie, double-sided). Unfortunately, no standard method for delivering phototherapy exists and there is substantial variation in phototherapy equipment. Comprehensive information about phototherapy, including its mechanism of action and strategies for its use, can be found in the Appendix to the 2004 guideline,[3] a technical report of the AAP Committee on Fetus and Newborn,[83] and comprehensive recent reviews.[84,85] The general approach is to provide intensive phototherapy to as much of the infant's surface area as possible. Intensive phototherapy requires a narrow-spectrum LED blue light with an irradiance of at least 30 $\mu W/cm^2$ per nm at a wavelength around 475 nm. Light outside the 460 to 490 nm range provides unnecessary heat and potentially harmful wavelengths.[84,86] The advantage of intensive phototherapy is that it can quickly lower the TSB and should shorten the duration of treatment.[84]

The primary goal of phototherapy is to decrease the likelihood of further increases in the TSB concentration that would lead to a need for escalation of care, including exchange transfusion. The recommended phototherapy thresholds (**Figs 2** and **3**; Supplemental Tables 1 and 2; Supplemental Figs 1 and 2) are far below those at which overt acute bilirubin neurotoxicity or kernicterus occurs.[9,26,87–95] Phototherapy should not be used solely with a goal of preventing subtle adverse neurodevelopmental findings, because the literature

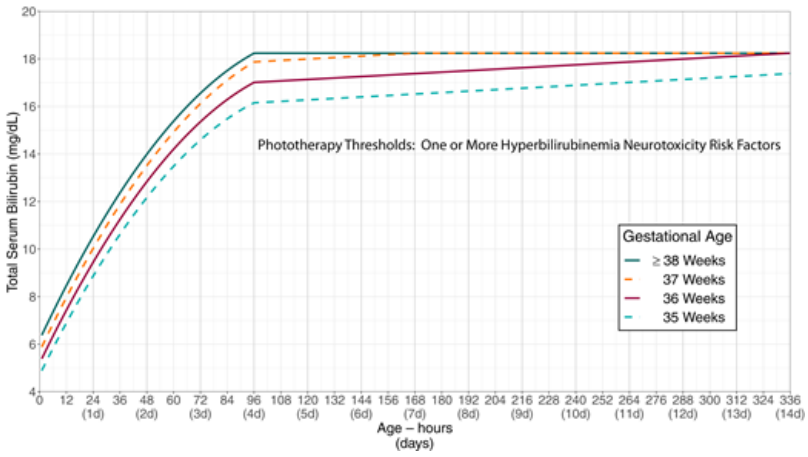
linking subtle abnormalities with bilirubin is conflicting; there is no evidence that phototherapy improves or prevents any of these outcomes,[96] and there is some evidence that phototherapy may lead to a small increase in the risk of subsequent childhood epilepsy (see accompanying technical report).[97,98] The committee believes that the benefit of phototherapy exceeds the small potential risk of epilepsy when the TSB is at or above the phototherapy threshold.

FIGURE 2



Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Note that infants <24 hours old with a TSB at or above the phototherapy threshold are likely to have a hemolytic process and should be evaluated for hemolytic disease as described in recommendation 14. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 1.

FIGURE 3



Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use total serum bilirubin concentrations; do not subtract the direct-reacting or conjugated bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include gestational age <38 weeks; albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 2.

The study also found that severe hyperbilirubin neurotoxicity does not occur until concentrations well above the 2004 exchange transfusion thresholds justified raising the

phototherapy treatment thresholds by a narrow range (Appendix C, Phototherapy and exchange transfusion levels).[9,91–95,99] With the increased phototherapy thresholds, appropriately following the current guidelines, including bilirubin screening during the birth hospitalization and timely postdischarge follow-up is important.

Although direct exposure to sunlight has been shown to decrease TSB concentrations,[100] the practical difficulties involved in safely exposing infants to the sun, either inside or outside, while also avoiding sunburn preclude the use of sunlight as a reliable therapeutic tool, and therefore, it is not recommended. Although filtered sunlight has been safely used in resource-constrained settings where phototherapy is not readily available, these guidelines were not developed for use in such settings.[101] Note that these guidelines, including the phototherapy and exchange transfusion thresholds, were not developed for use in low- and middle-income countries where the resources described for screening, follow-up, and treatment might not be available.

KAS 10: Intensive phototherapy is recommended at the total serum bilirubin thresholds in Fig 2 (Supplemental Table 1 and Supplemental Fig 1) or Fig 3 (Supplemental Table 2 and Supplemental Fig 2) on the basis of gestational age, hyperbilirubinemia neurotoxicity risk factors, and age of the infant in hours. (Aggregate Evidence Quality Grade X, Recommendation)

The phototherapy treatment thresholds take both gestational age and the presence of other neurotoxicity risk factors into account. **Figure 2** provides suggested phototherapy thresholds if there are no known hyperbilirubinemia neurotoxicity risk factors in addition to gestational age. Figure 3 should be used if there are any hyperbilirubinemia

neurotoxicity risk factors other than gestational age. Infants born at ≥38 weeks' gestation are grouped together in **Fig 3**, because although infants born at ≥39 weeks' gestation are at lower risk of subsequent hyperbilirubinemia than infants born at 38 weeks' gestation, there is no evidence that they are at lower risk of neurotoxicity. The direct-reacting or conjugated bilirubin concentration should not be subtracted from the total serum bilirubin concentration when using **Figs 2** or **3**. If the direct-reacting or conjugated fraction of the TSB exceeds 50% of the TSB, consultation with a knowledgeable specialist (eg, pediatric gastroenterologist or neonatologist) is recommended.

These thresholds, like those in the 2004 guidelines, are based on expert opinion rather than strong evidence that they distinguish between infants in whom the benefits of phototherapy do or do not exceed its risks. Clinicians and families may choose to treat at lower levels, based on individual circumstances and preferences. For example, it is an option to begin phototherapy at subthreshold level during a birth hospitalization to reduce the risk of readmission if the absolute level or rate of rise in relation to the slope of the phototherapy threshold suggests that there is a high likelihood of exceeding the threshold after discharge.[22] Those making the decision to begin phototherapy below the treatment threshold should consider the risk of overtreatment on the infant and family. Whenever possible, phototherapy should be provided in the mother's room or in a room in which the mother can remain with the infant.

To optimize the effectiveness of inpatient phototherapy, hospitals should verify that phototherapy systems provide the [illegible] manufacturer. Although the routine measurement of irradiance in infants receiving phototherapy is encouraged,

studies of this issue in the United States are lacking. However, studies in the Netherlands have found that suboptimal phototherapy dosages are common.[102] Different irradiance measurement devices can lead to varying results,[83] so it is reasonable to follow the manufacturer recommendations regarding how and when to measure irradiance. It is also important to recognize that the amount of irradiance received by infants is higher directly below the light source than at the periphery.[103] The irradiance levels recommended in these guidelines refer to those measured below the center of the light source.

KAS 11: For newborn infants who have already been discharged and then develop a TSB above the phototherapy threshold, treatment with a home LED-based phototherapy device rather than readmission to the hospital is an option for infants who meet the following criteria.[104,105] (Aggregate Evidence Quality Grade D, Option)

- Gestational age ≥38 weeks
- ≥48 hours old
- Clinically well with adequate feeding
- No known hyperbilirubinemia neurotoxicity risk factors (**Table 2**)
- No previous phototherapy
- TSB concentration no more than 1 mg/dL above the phototherapy treatment threshold (**Fig 2**; Supplemental Table 1 and Supplemental Fig 1)
- An LED-based phototherapy device will be available in the home without delay

- TSB can be measured daily

Home phototherapy can be less costly and disruptive to family routines and breastfeeding and may help improve bonding and reduce stress compared with readmission for phototherapy.[106] However, its effectiveness depends on the quality of the home phototherapy device as well as the ability of the family to appropriately use it. Therefore, caution is needed when considering home phototherapy. Furthermore, home phototherapy is not recommended for infants with any hyperbilirubinemia neurotoxicity risk factor.

Home phototherapy should not be used if there is any question about the quality of the home phototherapy device, the ability to have the device delivered to the home rapidly, concerns about the family's ability to use the device, or concerns about the ability to measure bilirubin concentrations daily. As with inpatient phototherapy, it is an option to start home phototherapy at a lower threshold (eg, 2 mg/dL below the phototherapy threshold) to reduce the readmission risk.

Feeding should be maintained during inpatient or home phototherapy to promote bilirubin clearance and avoid dehydration. Interrupting phototherapy for breastfeeding does not impact the overall effectiveness of phototherapy if it is otherwise appropriately used.[107,108] These interruptions should be minimized if the bilirubin concentration is approaching the need to escalate care.

Although breastfeeding and human milk have many benefits, brief use of formula might lead to a more rapid decline in TSB concentrations and reduce the risk of readmission for phototherapy.[109] Although insufficient data are available, supplementation using the mother's expressed milk may have similar benefits to infant formula supplementation without

the potential concerns associated with formula. The risks to the establishment of breastfeeding and milk supply, including potential health consequences to the infant and mother unrelated to jaundice, must be weighed against any benefit of introducing infant formula supplementation for bilirubin reduction. Use of intravenous fluids is not recommended unless there is evidence of dehydration that cannot be corrected enterally or if the TSB exceeds the escalation of care threshold. The potential use of supplemental formula, mother's expressed milk, or donor human milk may be considered as an alternative to readmission for phototherapy in the breastfed infant who has been discharged and presents with excess weight loss, a maternal history consistent with a diagnosis of suboptimal intake hyperbilirubinemia, and a bilirubin concentration approaching or at the phototherapy threshold.

B. Prolonged Indirect Hyperbilirubinemia

Infants 7 days or older with a persistently elevated TSB within 2 mg/dL of the phototherapy threshold may have prolonged indirect hyperbilirubinemia, which can be confirmed by measuring serum direct-reacting or conjugated bilirubin (ie, a fractionated bilirubin measure) in addition to total bilirubin. The indirect bilirubin concentration is the difference between the total and the direct-reacting or conjugated bilirubin. Most of these infants have breast milk jaundice,[13] but other causes include hemolytic disease, hypothyroidism, extravascular blood, pyloric stenosis with Gilbert syndrome,[109] and Crigler-Najjar syndrome. Limited studies suggest that prolonged exposure to indirect hyperbilirubinemia might be associated with an increased risk of neurotoxicity,[110] although other

nts with prolonged indirect hyperbilirubinemia have been discharged from the hospital, it is an option to treat

prolonged indirect hyperbilirubinemia within 2 mg/dL of the phototherapy threshold with home phototherapy.

C. Monitoring Infants Receiving Phototherapy

KAS 12: For hospitalized infants, TSB should be measured within 12 hours after starting phototherapy. The timing of the initial TSB measure after starting phototherapy and the frequency of TSB monitoring during phototherapy should be guided by the age of the child, the presence of hyperbilirubinemia neurotoxicity risk factors, the TSB concentration, and the TSB trajectory. (Aggregate Evidence Quality Grade X, Recommendation)

TcB measurements on skin exposed to phototherapy tend to underestimate TSB concentrations. Studies of TcB measurements on skin that has been covered by opaque patches during phototherapy have yielded mixed results regarding accuracy.[112–115] If these patches are used, it is prudent to check the correlation between TcB on patched skin and the TSB on each infant receiving phototherapy before relying on the TcB.

KAS 13: For infants receiving home phototherapy, the TSB should be measured daily. Infants should be admitted for inpatient phototherapy if the TSB increases and the difference between the TSB and the phototherapy threshold narrows or the TSB is ≥1 mg/dL above the phototherapy threshold. (Aggregate Evidence Quality Grade X, Recommendation)

KAS 14: For infants requiring phototherapy, measure the hemoglobin concentration, hematocrit, or complete blood count to assess for the presence of anemia and to provide a baseline in case subsequent anemia develops. Evaluate the underlying cause or causes of

hyperbilirubinemia in infants who require phototherapy by obtaining a DAT in infants whose mother had a positive antibody screen or whose mother is blood group O regardless of Rh(D) status or whose mother is Rh(D)−. G6PD activity should be measured in any infant with jaundice of unknown cause whose TSB increases despite intensive phototherapy, whose TSB increases suddenly or increases after an initial decline, or who requires escalation of care. (Aggregate Evidence Quality Grade X, Recommendation)

An infant <24 hours old with a TSB concentration above the phototherapy threshold likely has hemolytic disease. Measurement of ETCOc, if available, may help identify hemolysis. Identifying whether there is G6PD deficiency or hereditary spherocytosis or other red cell membrane defects can help identify infants at risk for recurrent hemolysis and also provide information for families about increased risk in future pregnancies.[27,30–32,35,116] However, in many cases the underlying cause of hyperbilirubinemia is not identified.[117] In challenging clinical circumstances, such as an increasing TSB despite intensive phototherapy, which is suggestive of hemolysis, a neonatologist or hematologist can be consulted for guidance. Genomic sequencing may be helpful when the cause of hemolysis cannot otherwise be identified in neonates who receive escalation of care.[116]

D. Discontinuing Phototherapy

The decision to discontinue phototherapy is based on balancing the desire to minimize exposure to phototherapy and separation of mothers and infants against the desire to avoid a rebound in TSB following phototherapy. Rebound hyperbilirubinemia is defined as a TSB concentration that reaches the phototherapy threshold for the infant's age within

72 to 96 hours of discontinuing phototherapy. Infants who receive phototherapy during their birth hospitalization are much more likely to experience rebound hyperbilirubinemia than those whose first treatment with phototherapy occurs on readmission.[90,118,119] The risk factors for rebound hyperbilirubinemia include younger postnatal age (ie, <48 hours) at the start of phototherapy, hemolytic disease, gestational age <38 weeks, and higher TSB at the time of phototherapy discontinuation in relationship to the phototherapy threshold.[120] Although most studies have found these same predictors of rebound,[118,119,120–123] the overall risk of rebound has varied fivefold across studies, from 4.6%[118,120,124] to approximately 24%.[121,122] Although most of this variation may be related to differences in the prevalence of risk factors, this and the fact that stakeholders may vary in the relative value they place on a shorter course of phototherapy compared with a lower risk of rebound preclude strong recommendations about when phototherapy should be discontinued.

KAS 15: Discontinuing phototherapy is an option when the TSB has decreased by at least 2 mg/dL below the hour-specific threshold at the initiation of phototherapy. A longer period of phototherapy is an option if there are risk factors for rebound hyperbilirubinemia (eg, gestational age <38 weeks, age <48 hours at the start of phototherapy, hemolytic disease). (Aggregate Evidence Quality Grade C, Option)

E. Follow-up After Phototherapy

The timing of follow-up bilirubin testing after discontinuing phototherapy should be based on the risk of rebound hyperbilirubinemia. Except in specific circumstances as described in recommendation 16, at least 12 hours, and

preferably 24 hours, should elapse to allow sufficient time for the bilirubin concentration to demonstrate whether there is rebound hyperbilirubinemia.[119] Rebound hyperbilirubinemia should be treated according to the previous recommendations regarding the initiation of phototherapy (see Recommendation 10).

KAS 16: Repeat bilirubin measurement after phototherapy is based on the risk of rebound hyperbilirubinemia.

- Infants who exceeded the phototherapy threshold during the birth hospitalization and (1) received phototherapy before 48 hours of age; (2) had a positive DAT; or (3) had known or suspected hemolytic disease, should have TSB measured 6 to 12 hours after phototherapy discontinuation and a repeat bilirubin measured on the day after phototherapy discontinuation.
- All other infants who exceeded the phototherapy threshold during the birth hospitalization should have bilirubin measured the day after phototherapy discontinuation.
- Infants who received phototherapy during the birth hospitalization and who were later readmitted for exceeding the phototherapy threshold should have bilirubin measured the day after phototherapy discontinuation.
- Infants readmitted because they exceeded the phototherapy threshold following discharge but who did not receive phototherapy during the birth hospitalization and infants treated with home phototherapy who exceeded the phototherapy threshold should have bilirubin measured 1 to 2 days after phototherapy

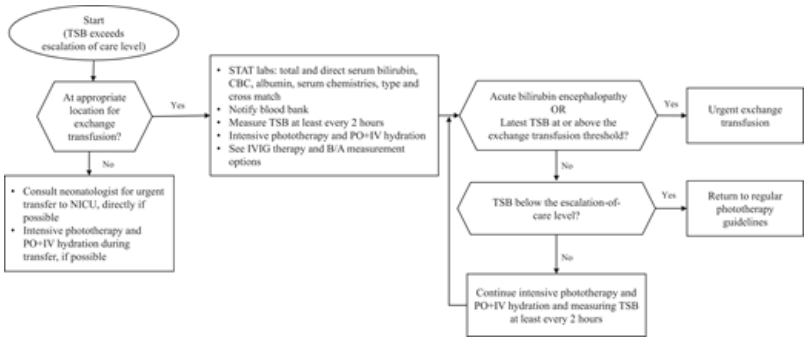
discontinuation or clinical follow-up 1 to 2 days after phototherapy to determine whether to obtain a bilirubin measurement. Risk factors for rebound hyperbilirubinemia to consider in this determination include the TSB at the time of phototherapy discontinuation in relationship to the phototherapy threshold, gestational age <38 weeks, the adequacy of feeding and weight gain, and the other hyperbilirubinemia and hyperbilirubinemia neurotoxicity risk factors.

It is an option to measure TcB instead of TSB if it has been at least 24 hours since phototherapy was stopped.[125,126] **(Aggregate Evidence Quality Grade X, Recommendation)**

F. Escalation of Care and Providing an Exchange Transfusion

Escalation of care refers to the intensive care that some infants with elevated or rapidly increasing bilirubin concentrations need to prevent the need for an exchange transfusion and possibly prevent kernicterus. The algorithm presented in **Fig 4** outlines the approach to escalation of care. This algorithm requires knowledge of the infant's exchange transfusion threshold.

FIGURE 4



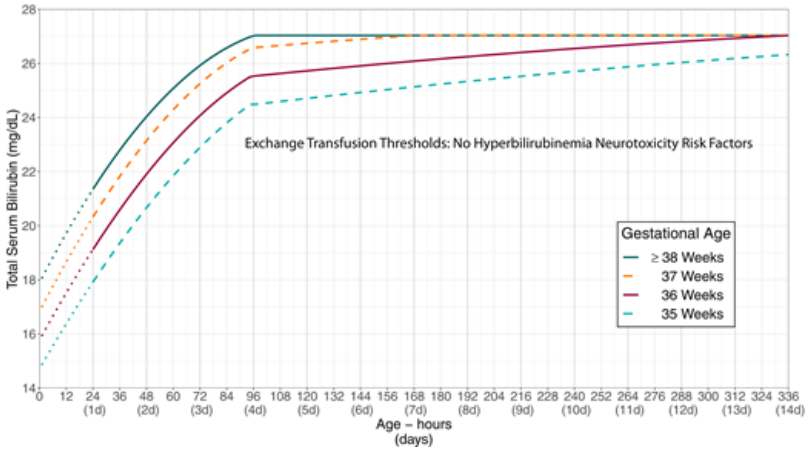
Approach to escalation of care. The escalation-of-care threshold is 2 mg/dL below the exchange transfusion threshold. IVIG, intravenous immune globulin; B/A, bilirubin to albumin ratio.

The escalation-of-care threshold is 2 mg/dL below the exchange transfusion threshold.

The direct-reacting or conjugated bilirubin value should not be subtracted from the total bilirubin value when determining management.

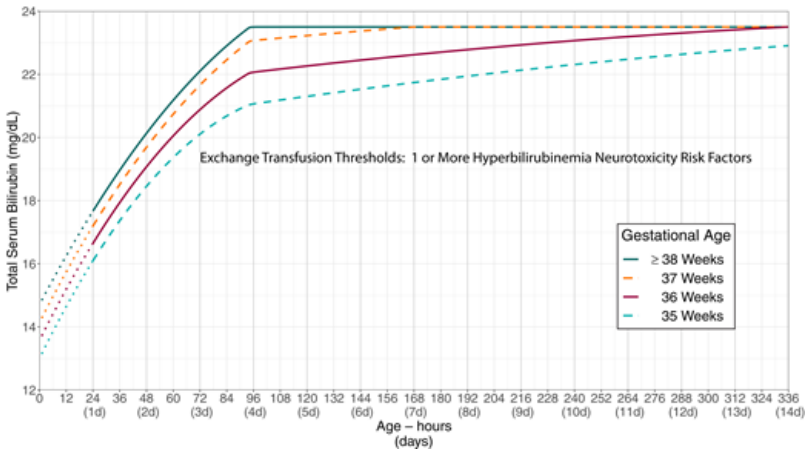
KAS 17: Care should be escalated when an infant's TSB reaches or exceeds the escalation-of-care threshold, defined as 2 mg/dL below the exchange transfusion threshold, as detailed in Fig 5 (infants with no known hyperbilirubinemia neurotoxicity risk factors; Supplemental Table 3 and Supplemental Fig 3) or Fig 6 (infants whose TSB is increasing despite phototherapy or infants with at least 1 recognized hyperbilirubinemia neurotoxicity risk factor; Supplemental Table 4 and Supplemental Fig 4). (Aggregate Evidence Quality Grade X, Recommendation)

FIGURE 5



Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 4.

FIGURE 6



Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. See Fig 4, which describes escalation of care. These thresholds are based on expert opinion rather than strong evidence on when the potential benefits of escalation of care exceed its potential harms. The stippled lines for the first 24 hours indicate uncertainty because of the wide range of clinical circumstances and responses to intensive phototherapy. Use total serum bilirubin concentrations; do not subtract direct bilirubin from the total serum bilirubin. In rare cases of severe hyperbilirubinemia in which the direct-reacting or conjugated bilirubin exceeds 50% of the TSB, consult an expert. Hyperbilirubinemia neurotoxicity risk factors include albumin <3.0 g/dL; isoimmune hemolytic disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, or other hemolytic conditions; sepsis; or any significant clinical instability in the previous 24 hours. See Supplemental Fig 5.

Initiating escalation of care is a medical emergency. The escalation-of-care period starts from the time the infant's TSB result first mandates starting escalation of care and ends when the TSB is below the escalation of care threshold. These infants are optimally managed in a neonatal intensive care unit (NICU). If the infant is in an institution that lacks facilities for an emergent exchange transfusion, a neonatologist should be consulted about urgent transfer to a NICU that can perform an exchange transfusion. If possible, intensive phototherapy and intravenous hydration should be initiated and continued during hospital transfer. Whenever possible, the infant should be admitted directly to the NICU rather than through the emergency department to avoid delaying care.

KAS 18: For infants requiring escalation of care, blood should be sent STAT for total and direct-reacting serum bilirubin, a complete blood count, serum albumin, serum chemistries, and type and crossmatch. (Aggregate Evidence Quality Grade X, Recommendation)

KAS 19: Infants requiring escalation of care should receive intravenous hydration and emergent intensive phototherapy. A neonatologist should be consulted about urgent transfer to a NICU that can perform an exchange transfusion. (Aggregate Evidence Quality Grade C, Recommendation)

KAS 20: TSB should be measured at least every 2 hours from the start of the escalation-of-care period until the escalation-of-care period ends. Once the TSB is lower than the escalation-of-care threshold, management should proceed according to the section "C. Monitoring Infants Receiving Phototherapy." (Aggregate Evidence Quality Grade X, Recommendation)

KAS 21: Intravenous immune globulin (IVIG; 0.5 to 1 g/kg) over 2 hours may be provided to infants with isoimmune hemolytic disease (ie, positive DAT) whose TSB reaches or exceeds escalation of care threshold. The dose can be repeated in 12 hours. (Aggregate Evidence Quality Grade C, Option)

The effectiveness of IVIG to prevent the need for an exchange transfusion is unclear. Observational studies suggest an association between IVIG and necrotizing enterocolitis. A detailed review of the potential benefits and harms is provided in the technical report. Factors that should be considered include response to phototherapy, TSB rate of increase, and the challenge of providing a timely exchange transfusion. All aspects of the escalation-of-care guidelines should continue to be followed if IVIG is used.

KAS 22: An urgent exchange transfusion should be performed for infants with signs of intermediate or advanced stages of acute bilirubin encephalopathy (eg, hypertonia, arching, retrocollis, opisthotonos, high-pitched cry, or recurrent apnea). (Aggregate Evidence Quality Grade C, Recommendation)

KAS 23: An urgent exchange transfusion should be performed for infants if the TSB is at or above the exchange transfusion threshold. If, while preparing for the exchange transfusion but before starting the exchange transfusion, a TSB concentration is below the exchange transfusion threshold and the infant does not show signs of intermediate or advanced stages of acute bilirubin encephalopathy, then the exchange transfusion may be deferred while continuing intensive phototherapy and following the TSB every 2 hours until the TSB is below

the escalation of care threshold. (Aggregate Evidence Quality Grade C, Recommendation)

Cross-matched washed packed red blood cells mixed with thawed adult fresh-frozen plasma to a hematocrit approximating 40% is preferred for exchange transfusions.[127–129] The additional albumin-containing fresh-frozen plasma that infants receive by keeping the hematocrit close to 40% will augment bilirubin removal.[127–129]

The bilirubin to albumin ratio can be used in conjunction with the TSB level in determining the need for exchange transfusion. The bilirubin to albumin ratio treatment threshold for exchange transfusion, measured as TSB (measured in mg/dL) divided by serum albumin (measured in g/dL), varies by gestational age and risk. In addition to the criteria described above, an exchange transfusion may be considered if the bilirubin to albumin ratio is:

- ≥8.0 if the gestational age is ≥38 weeks' gestation and there are no hyperbilirubinemia neurotoxicity risk factors, or
- ≥7.2 if the gestational age is ≥38 weeks' gestation and there is at least 1 hyperbilirubinemia neurotoxicity risk factor, or
- ≥7.2 if the gestational age is 35 through 37 weeks' gestation with no hyperbilirubinemia neurotoxicity risk factor, or
- ≥6.8 if the gestational age is 35 through 37 weeks' gestation and at least 1 hyperbilirubinemia neurotoxicity risk factor.[130]

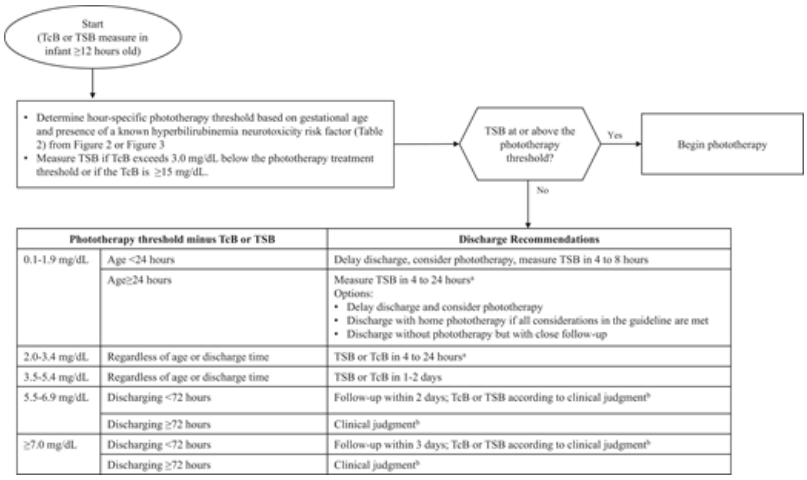
IV. Postdischarge Follow-Up

A. Timing of Follow-Up After Discharge

The 2004 guideline[3] and subsequent 2009 clarification[6] recommended assessing the risk of developing clinically significant hyperbilirubinemia based on a nomogram using postnatal age in hours and the bilirubin concentration coupled with the presence or absence of hyperbilirubinemia risk factors to determine the need for monitoring. Those follow-up recommendations used a previous risk nomogram (**Fig 2** in the 2004 guideline, based on the 1999 study of Bhutani et al[131]) that did not take gestational age and hyperbilirubinemia neurotoxicity risk factors into account and was created from a study population that excluded DAT positive infants.

The current guideline recommends using the difference between the bilirubin concentration and the phototherapy threshold at the time of measurement to determine the interval between discharge and follow-up and the need for additional TSB or TcB measurements (**Fig 7**). This approach incorporates both gestational age and other hyperbilirubinemia neurotoxicity risk factors into the decision-making process. This approach has been studied in newborn infants in the Kaiser Permanente Northern California hospitals.[72] The timing of postdischarge follow-up (**Fig 7**) should also take into consideration the presence of other hyperbilirubinemia risk factors (**Table 1**).

FIGURE 7



Phototherapy threshold minus TcB or TSB		Discharge Recommendations
0.1-1.9 mg/dL	Age <24 hours	Delay discharge, consider phototherapy, measure TSB in 4 to 8 hours
	Age≥24 hours	Measure TSB in 4 to 24 hours[a] Options: • Delay discharge and consider phototherapy • Discharge with home phototherapy if all considerations in the guideline are met • Discharge without phototherapy but with close follow-up
2.0-3.4 mg/dL	Regardless of age or discharge time	TSB or TcB in 4 to 24 hours[a]
3.5-5.4 mg/dL	Regardless of age or discharge time	TSB or TcB in 1-2 days
5.5-6.9 mg/dL	Discharging <72 hours	Follow-up within 2 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]
≥7.0 mg/dL	Discharging <72 hours	Follow-up within 3 days; TcB or TSB according to clinical judgment[b]
	Discharging ≥72 hours	Clinical judgment[b]

Flow diagram for infants during the birth hospitalization to determine postdischarge follow-up for infants who have not received phototherapy. [a]Use clinical judgment and shared decision making to determine when to repeat the bilirubin measure within this 4 to 24 hour time window.

[b]Clinical judgment decisions should include physical examination, the presence of risk factors for the development of hyperbilirubinemia (Table 1) or hyperbilirubinemia neurotoxicity risk factors (Table 2), feeding adequacy, weight trajectory, and family support.

These follow-up guidelines are based only on the management of hyperbilirubinemia. Other considerations that may influence the timing of follow-up include gestational age, postnatal age, assessment of breastfeeding, weight loss from birth weight, and assessment of the well-being of the infant and parents.

KQ 24: Beginning at least 12 hours after birth, if discharge is being considered, the difference between the

bilirubin concentration measured closest to discharge and the phototherapy threshold at the time of the bilirubin measurement should be calculated and used to guide follow-up, as detailed in Fig 7. (Aggregate Evidence Quality Grade C, Recommendation)

Figure 7 is only applicable for infants at least 12 hours after birth and for infants who have not received phototherapy before discharge. Insufficient information is available to provide discharge follow-up guidance based on TcB or TSB measured before 12 hours after birth. Any infant discharged before 12 hours of age should have a follow-up bilirubin measure between 24 and 48 hours of age.

V. Hospital Policies and Procedures

Hospitals and other types of birthing centers should have clearly established policies and procedures to help all infants receive optimal care to prevent kernicterus. Clinicians should document activities specifically related to this clinical practice guideline in the medical record.

Nursing protocols with standing orders should be established for the physical assessment of neonatal jaundice and the circumstances in which the nursing staff can obtain a TcB or TSB measurement. This should include obtaining a TcB or TSB if jaundice is noted within the first 24 hours after birth.

All facilities treating infants should have the necessary equipment to provide intensive phototherapy. Hospitals should have systems to verify that appropriate irradiance is delivered and should follow the recommendations of the phototherapy system manufacturer. Hospitals are encouraged to have a family-centered approach to phototherapy that includes providing phototherapy in the

mother's room, when possible, to allow for bonding and breastfeeding.

All facilities treating infants without the equipment or personnel to escalate care should have written plans for rapid and safe transfer of infants who might require exchange transfusion. These plans should include the ability to provide phototherapy during transfer.

Facilities that provide care for newborn infants should have a mechanism, when needed, for infants to have a follow-up TcB or TSB measured that includes weekends and holidays. A key step to achieving this is to maintain a list of key contacts to support the seamless provision of care. A system should be in place to provide care whenever there is uncertainty regarding the provision of appropriate follow-up. This care includes a mechanism for providing the results of any testing to families and providing care according to these guidelines.

KAS 25: Before discharge, all families should receive written and verbal education about neonatal jaundice. Parents should be provided written information to facilitate postdischarge care, including the date, time, and place of the follow-up appointment and, when necessary, a prescription and appointment for a follow-up TcB or TSB. Birth hospitalization information, including the last TcB or TSB and the age at which it was measured, and DAT results (if any) should be transmitted to the primary care provider who will see the infant at follow-up. If there is uncertainty about who will provide the follow-up care, this information should also be provided to families. (Aggregate Evidence Quality Grade X, Strong Recommendation)

Education should include an explanation of jaundice; the need to monitor infants for jaundice, dehydration, and lethargy;

signs of ineffective feeding, fussiness, and illness; and an assessment of understanding of these issues and the recommended follow-up. The AAP has a parent handout addressing these issues.

Summary

Although kernicterus is rare, the impact on affected individuals and their families can be devastating. Clinicians who provide care for newborn infants should understand the importance of the strategies to prevent kernicterus outlined in this guideline. Implementation of systems to provide consistent application of these recommendations for all infants 35 or more weeks of gestation within mother-baby units, hospitals, and primary care clinics is critical to the success of these recommendations.

This clinical practice guideline emphasizes the opportunities for primary prevention (eg, treatment to prevent isoimmune hemolytic disease, adequate breastfeeding support), the need to obtain an accurate history and physical examination to determine the presence of hyperbilirubinemia and hyperbilirubinemia neurotoxicity risk factors, the importance of predicting the risk of future hyperbilirubinemia including a predischarge measurement of TSB or TcB, and the importance of postdischarge follow-up. This clinical practice guideline provides indications and approaches for phototherapy and escalation of care and when treatment and monitoring can be safely discontinued. For all recommendations, the committee recognizes that clinicians should understand the rationale for what is recommended, use their clinical judgment, and, when appropriate, engage in shared decision-making.

Subcommittee Authors

Alex R. Kemper, MD, MPH, MS, FAAP, Chairperson

Thomas B. Newman, MD, MPH, FAAP, Vice-chairperson

Jonathan L. Slaughter, MD, MPH, FAAP, Epidemiologist

M. Jeffrey Maisels, MB BCh, DSc, FAAP

Jon F. Watchko, MD, FAAP

Stephen M. Downs, MD, MS, AAP Partnership for Policy Implementation

Randall W. Grout, MD, MS, FAAP, AAP Partnership for Policy Implementation

David G. Bundy, MD, MPH, FAAP

Ann R. Stark, MD, FAAP, AAP Section on Neonatal-Perinatal Medicine

Debra L. Bogen, MD, FAAP

Alison Volpe Holmes, MD, MPH, FAAP

Lori B. Feldman-Winter, MD, MPH, FAAP

Vinod K. Bhutani, MD, FAAP

Steven Brown, MD, FAAFP, American Academy of Family Physicians Representative

Gabriela M. Maradiaga Panayotti, MD, FAAP

Kymika Okechukwu, MPA, Senior Manager, Evidence-Based Medicine Initiatives

Peter D. Rappo, MD, FAAP

Terri L. Russell, DNP, APN, NNP-BC, National Association of Neonatal Nurses Liaison

STAFF

Kymika Okechukwu, MPA, Senior Manager, Evidence-Based Medicine Initiatives

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medical care. Variations, taking into account individual circumstances, may be appropriate.

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AAP	American Academy of Pediatrics
DAT	direct antiglobulin test
ETCOc	end-tidal carbon monoxide-corrected
G6PD	glucose-6-phosphate dehydrogenase
IVIG	intravenous immune globulin
NICU	neonatal intensive care unit
KAS	Key Action Statement
RhIG	Rh(D) immunoglobulin
TcB	transcutaneous bilirubin
TSB	total serum bilirubin

Competing Interests

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Subjects: Evidence-Based Medicine, Hyperbilirubinemia

Topics: hyperbilirubinemia, phototherapy, bilirubin, exchange transfusion, whole blood

Supplementary data

Supplemental Information- pdf file
Quality Metrics- pdf file
Key Driver Diagram- pdf file
Additional Support for Follow-up Recommendations- pdf file
Jaundice and Your Newborn PDF – Parent Handout (English)- pdf file
Jaundice and Your Newborn PDF – Parent Handout (Spanish) - pdf file

Comments

12 Comments

Check the Serum Albumin Level Earlier

January 13 2024 | Timothy Brannon, MD, MS
UT SOUTHWESTERN MEDICAL CENTER, DALLAS

While developing decision support tools to implement these Guidelines, we discovered inconsistencies regarding serum albumin levels.

Data reported by Cartlidge and Rutter (1986) and Watchko et al (2017) show that the 50th percentile value for serum albumin in newborns 35-42 weeks gestational age is about 3.0 gm/dL, which is the same as the Neurotoxicity (NT) risk factor level. This implies that about 50% of newborns have an albumin < 3.0 [illegible] factor.

The AAP published online a list of frequently asked questions (FAQ) about the 2022 Guideline which states that “albumin does not need to be measured unless there is a reason to suspect it would be low or the baby reaches the escalation of care threshold.”

We created line graphs from the Guideline TsB data tables for both 35 weeks and 38+ weeks gestation. These included the levels for Phototherapy, Exchange Transfusion, and Escalation of Care, both for No risk factors and +NT risk factors (all 6 curves in juxtaposition). This data visualization revealed that at 35 weeks gestation, in the first 48 hours, the Escalation of Care (No risk factors) curve was approximately the same as the Exchange (+NT risk factors) curve. After 48 hours, the Escalation of Care (No risk factors) curve was above the Exchange (+NT risk factors) curve. For 38+ weeks gestation, the Escalation of Care (No risk factors) curve was always above the Exchange (+NT risk factors) curve. Suppose a newborn is managed using the (No risk factors) curves and reaches the Escalation of Care (No risk factors) threshold, and then albumin is checked as recommended in the FAQ and is found to be < 3.0 gm/dL (an NT risk factor). At that point, the TsB is already at or above the Exchange Transfusion (+NT Risk factors) threshold.

The guidance in the author’s FAQ to check albumin only after reaching the Escalation of Care level may lead to preventable exchange transfusions. Instead, a reasonable approach is to check the albumin one (1) time when the TsB is first checked. This inexpensive blood test can often be done using the same TsB blood sample in the lab. Albumin should not need to be trended or repeated unless it is borderline. Treatment decisions about phototherapy or exchange transfusion can then be made using the appropriate TsB curves from the start. This will promote timely intervention with phototherapy for newborns with NT risk factors, and it will limit needless exposure to phototherapy for

those newborns who truly have no risk factors.

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The Challenges of Phototherapy as a Drug

November 28 2022 | M. Jeffrey Maisels, MB BCh, DSc, FAAP

DEPARTMENT OF PEDIATRICS, OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

Drs Eidelman and Goldenhersh correctly recommend that the dosage of phototherapy be defined and measured as is done with other drugs. Typically, drug dosage is determined based on the desired serum level, the half-life, and the volume of distribution of the drug being administered. Clinicians can measure the serum concentration of many drugs to confirm the delivery of a therapeutic level.

As noted by Drs Eidelman and Goldenhersh, Angelo Lamola, PhD, has beautifully elucidated the scientific data currently available to us about how phototherapy works. But Dr. Lamola also points out that currently " ...

there are no specific standards for phototherapy practice, and a pharmacologic approach to its use remains incomplete. The reasons for this practice gap include (1) the inability to adequately compare studies using different light sources and regimens, (2) the vagaries of spectroradiometrics, (3) the complexities of chemistry of the photo- products of bilirubin and their therapeutic roles, (4) insufficient attention given to the optical properties of neonatal skin, and (5) the limited knowledge of the dynamics of the phototherapy processes."1

In practical terms, there are several reasons why clinicians cannot do what Drs Eidelman and Goldenhersh would like them to do. We lack agreement regarding:

(1) the method of measuring irradiance because we know that different spectroradiometers measure different bandwidths and produce different results.2 We lack "an inexpensive standardized irradiance meter tuned to the 460-nm – 490-nm wavelength range."1

(2) where and how irradiance should be measured and how many measurements should be obtained (e.g., directly under the light above the baby, at the infant's side and periphery, from the LED pad underneath the infant) and synthesized.

(3) a measurement of the total surface area of the infant exposed, which would be necessary to determine the spectral power (i.e., the product of irradiance and surface area exposed).3

(4) a standardized light source emitting narrow-spectrum blue light (475 nm) and perhaps blue-green light.4

Additionally, we also lack what Dr. Lamola describes as "a comprehensive process simulation computer application to guide prescription of infant- specific phototherapy regimens."1

After considering these gaps, it should be clear why this information is not available in existing studies and why, as Dr Kemper notes, it is "unrealistic" to expect

clinicians to routinely collect such data. For the same reasons, it is not currently appropriate for the AAP to recommend a specific light fixture or a standardized distance between the light and the infant.

Certainly, these are areas of research that could be highly productive.

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M. Jeffrey Maisels, MB BCh, DSc, FAAP
Department of Pediatrics
Oakland University William Beaumont School of Medicine
Rochester, Michigan

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Responding to Dr. Eidelman and Dr. Goldenhersh

November 23 2022 | Alex Kemper
NATIONWIDE CHILDREN'S HOSPITAL

The 2022 AAP guideline recommends phototherapy at irradiance of at least 30 µW/cm2 per nm at a wavelength around 475 nm. using narrow-spectrum LED blue lights maintained and calibrated as recommended by the device manufacturer. As Dr. Eidelman and Dr. Goldenhersh suggest, there are important gaps in evidence related to the specific dose

of phototherapy that infants receive and how that is related to outcomes. Recommending that the specific dose received should be recorded might help address gaps in evidence and could lead to improved care. However, asking clinicians to regularly estimate and record the body surface area being exposed to light and the irradiance at multiple sites in the hopes that the data might be used by researchers seems overly burdensome and unrealistic.

We agree that clinicians should minimize unnecessary phototherapy, which led the guideline committee to raise the phototherapy thresholds. Unfortunately, insufficient evidence is available to assess the benefits and risks at each potential threshold by bilirubin level across gestational age, time after birth, and the presence of other hyperbilirubinemia neurotoxicity risk factors. In our assessment of cancer risk with phototherapy, we found that adjusting for bilirubin level moved findings to the null. Unfortunately, most studies of phototherapy did not adjust for bilirubin level. This is an important limitation of published meta-analyses and another important area for future research.

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Phototherapy Guidelines are Based on Incomplete Data as to Actual Phototherapy Use

November 22 2022 | Arthur I Eidelman MD, Michael A Goldenhersh MD

DEPARTMENT PEDIATRICS. SHAARE ZEDEK MEDICAL CENTER, HEBRE UNIVERSITY SCHOOL OF MEDICINE

Phototherapy Guidelines are Based

As long-time clinicians concerned about the proper use

and monitoring of phototherapy for the treatment of neonatal jaundice, we welcome the recently published revised AAP guidelines for the" management of hyperbilirubinemia in the newborn infant"1 The authors of the Guideline and its supporting Technical Report2 noted that the thrust of the revision was to narrowly raise the phototherapy treatment threshold as a result of two factors.

1. New evidence indicating that neurotoxicity from hyperbilirubinemia does not occur until bilirubin concentrations are well above the previously recommended 3 exchange transfusions threshold;
2. Recent reports of phototherapy-associated adverse effects including cancer and epilepsy1,2.

This concern has only been reinforced by a recently published review and meta-analysis that documented a significant association between neonatal phototherapy and "any type of cancer" (OR 1.24), any hematopoietic cancer (OR 1.49), particularly myeloid leukemia (OR 2.85).4

To our dismay, the authors of the Guidelines and its accompanying Technical Report did not note that the calculation of risk/benefit relied solely on retrospective analysis of the use or non-use of phototherapy without any basic pharmacologic data that would be the required for the calculation of dose-related effects and risk/benefit ratios when evaluating any drug therapy. Simply put, there were no data as to the phototherapy doses that were administered and actually received by the infants. Thus, all calculations are suspect and potentially inaccurate.

Lamola his classic article entitled " A Pharmacologic View of Phototherapy 5 emphasized the need to relate to phototherapy as we would with any other drug if we wish to standardize care and improve its efficacy and safety. Surely one would not assess the use of an intravenous drug based solely on the concentration of the drug in the IV bag without knowing the rate and duration of the infusion. Likewise, radiotherapy protocols are based on a specific quantity of radiation

exposure given for a specific number of treatments over a set period to a targeted measured area.
Thus, just recording the use of phototherapy, or at most by measuring irradiance at one specific skin site without estimating the area of exposed surfaces or the actual number of hours of exposure precludes any scientific basis for calculating the relationship of dose to adverse outcome. In addition to this lack of duration data, we know that in reality multiple phototherapy units are not infrequently used at different heights from the infant and to different amounts of the infant's surface (front and/or back), with no recording of such information in the medical charts further precluding any accurate calculation.
It is thus perplexing why the guidelines did not address this basic issue and recommend a standardized level of irradiance at a specified distance from the infant while requiring that accurate monitoring and recording of duration per day and total duration of therapy be a required part of the medical chart. Continuing to solely record the use or non-use of phototherapy without monitoring and recording these basic pharmacologic parameters will preclude the standardization of care and the creation of a proper and valid data set so needed for future analyses. No less so, regulators such as the FDA must define phototherapy as the equivalent of drug administration so that standardized recommended therapy parameters and accurate data sets become part of the legally based medical record.

Arthur I Eidelman MD Michael A Goldenhersh MD

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3. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation Pediatrics 2004 Jul;114(1):297-316.doi: 10.1542/peds.114.1.297.

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Submitted on November 22 2022

Setting Thresholds

September 12 2022 | Alex Kemper
NATIONWIDE CHILDREN'S HOSPITAL

Dr. Al-Abdi compares the revised AAP guideline to the NICE phototherapy thresholds, noting that the new AAP thresholds are higher. The decision to raise the thresholds slightly was based on a review of the evidence, much of which was published after the NICE thresholds were proposed.

Dr. Al-Abdi highlights two perceived advantages of the NICE guideline: the provision of treatment thresholds [illegible] guideline provides phototherapy thresholds for infants from 23-37 weeks' gestation for infants ≥72 hours after

birth (bilirubin in micromol/L = (gestational age 10) – 100). Phototherapy thresholds before age 72 hours are based on a line drawn from 40 micromol/L to the threshold at 72 hours. This formula was based on "informal consensus" and was similar to what was used in neonatal intensive care units in the UK. Neither the revised AAP guideline the previous versions of the guideline have provided recommendations for infants <35 weeks' gestation. This was a purposeful decision to limit the scope of the literature review required and because of concerns about the lack of available data.

Unlike the NICE guideline, the AAP guideline recommends that thresholds be stratified by the presence of hyperbilirubinemia neurotoxicity risk factors. This does increase complexity, but also helps to ensure that treatment is better targeted to those infants who need it. Electronic tools are now becoming available to help with implementation. I agree that it is challenging to determine which infants have G6PD deficiency and how to manage them safely once they are identified. I support Dr. Al-Abdi's efforts to incorporate local expertise in adapting the AAP guidelines to other settings.

I have no doubt that future guideline authors will continue to revise the specific thresholds based on the evidence that emerges. I predict that future iterations will be more complex as we learn how to better assess individual risk. Although in general, I like to believe that "simplicity is the ultimate sophistication," I worry, as H.L. Mencken wrote, "For every complex problem, there is an answer that is clear, simple, and wrong." Regardless, my experience is that the systems put in place to ensure close follow-up based on risk and bilirubin level matter more than the specific treatment thresholds.

Submitted on September 12 2022

“Simplicity is the ultimate sophistication.” – Leonardo da Vinci

August 31 2022 | Sameer Yaseen Al-Abdi
KAH, SAUDI ARABIA

I want to thank Alex Kemper et al. for this update. As working outside the USA, I would like to emphasize their statement, “The committee recommends caution and incorporation of local expertise in adapting these guidelines for use outside the United States.”

I was a proponent of the 2004 AAP phototherapy charts until this update was published. This week I switched to the National Institute for Health and Care Excellence (NICE) phototherapy charts for several reasons. First, I found that the 2022 AAP charts and suggested follow-up plans are a non-friendly user. I think a smartphone application incorporating the guidelines may ease this problem. Second, as a neonatologist and the AAP charts do not cover gestational age (GA) below 35 weeks, I am using the NICE charts for this group. Of course, using a completely different chart system is confusing and increases errors.
Third, dichotomizing phototherapy thresholds based on hyperbilirubinemia neurotoxicity risk factor (HNRF) is not practical and confusing unless the cord blood screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency and direct antiglobulin test is universal. Fourth, increasing the phototherapy threshold may harm more than good in areas such as mine, where the G6PD deficiency is common and the practice is postnatal discharge from birth hospital between 18 to 30 hours of life in addition to not well-established post-discharge follow-up care.

AAP 2022 phototherapy thresholds are higher than the NICE thresholds except for the gestational age (GA) ≥ 38

weeks with one or more HNRF as follows:
GA 35-37 weeks without HNRR: AAP is more than NICE by 4 mg/dL.
GA 35-37 weeks with HNRR: AAP is more than NICE by 2 mg/dL.
GA ≥ 38 weeks without HNRR: AAP is more than NICE by 3 mg/dL.
Ga ≥ 38 weeks with HNRR: AAP is lower than NICE by 2 mg/dL.

The difference between the phototherapy threshold of the 2022 AAP and the NICE implies that phototherapy will be required more by using the NICE charts. Notably, the 2022 AAP endorses, “As with inpatient phototherapy, it is an option to start home phototherapy at a lower threshold (e.g., 2 mg/dL below the phototherapy threshold) to reduce the readmission risk”. Thus, I suggest to the users of the NICE charts to only start the phototherapy if total serum bilirubin is at or above the NICE threshold to offset the possible increased rate of phototherapy requirement using the NICE charts.

Submitted on August 31 2022

Gestational Age and Choosing the Correct Phototherapy and Exchange Transfusion Threshold

August 31 2022 | Alex Kemper
NATIONWIDE CHILDREN'S HOSPITAL

We appreciate the opportunity to clarify how gestational age should be used in determining the phototherapy and exchange transfusion thresholds. Gestational age <38 weeks is an important hyperbilirubinemia neurotoxicity risk factor. Figure 2 in the guideline presents “phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors

other than gestational age." Separate curves are provided for each week of gestational age, 35 through 40, because of the important association between gestational age and risk related to hyperbilirubinemia. Figure 3 presents the phototherapy thresholds if there are additional risk factors beyond gestational age, with separate curves by gestational age, 35 through ≥38 weeks. Figures 5 and 6 present the exchange transfusion thresholds with a similar stratification by risk as in figures 2 and 3. If there are no hyperbilirubinemia risk factors other than gestational age, use figure 5; otherwise, use figure 6. Key action statements 10 and 17 provide additional information about the use of the phototherapy and exchange thresholds provided in figures 2, 3, 5, and 6.

We are working with the American Academy of Pediatrics and other groups to facilitate the adoption of the new guideline using quality-improvement methods and we are also posting additional information to the guideline website to help with implementation. We will use this thoughtful request for clarification to enhance our ongoing activities.

Submitted on August 31 2022

Gestational age < 38 weeks as Hyperbilirubinemia Neurotoxicity Risk Factor

August 30 2022

Estephanie Rivero [1], Faiza Javed [1], Shabih Manzar [2], Ramachandra Bhat [2]

[1] FELLOW [2] ATTENDING NEONATOLOGIST, SCHOOL OF MEDICINE, LSU HEALTH, SHREVEPORT

We read with great interest the newly published and revised American Academy of Pediatrics Clinical [illegible] of neonatal hyperbilirubinemia. Table 2 of the article clearly summarizes the known risk factors of

hyperbilirubinemia-induced neurotoxicity and explicitly states a dose-dependent association between the degree of prematurity and hyperbilirubinemia neurotoxicity in neonates. Consequently, the postnatal hour-specific threshold for phototherapy is determined separately for each gestational age stratum, based on the absence or the presence of hyperbilirubinemia-induced neurotoxicity risk factors using separate graphs (Figures 2 and 3). As the absence of hyperbilirubinemia neurotoxicity risk factors and <38 weeks of gestation are mutually exclusive, it may pose a challenge to the physicians to determine the optimal bilirubin threshold for initiating phototherapy for infants born between 35 to 37 weeks of gestational age. As the degree of prematurity is an important neurotoxicity risk factor, and either graph can be used to determine the phototherapy threshold, the importance of gestational age <38 weeks for the proper selection of phototherapy threshold needs to be explicitly stated, and a clear distinction needs to be made between prematurity and non-prematurity related neurotoxicity risk factors in order to avoid confusion and misinterpretation.

Submitted on August 30 2022

Response to Dr. Cahill

August 21 2022 | Alex R. Kemper, MD, MPH, MS
DIVISION OF PRIMARY CARE PEDIATRICS, NATIONWIDE CHILDREN'S HOSPITAL

We appreciate the kind words from Dr. Cahill about the updated clinical practice guideline. The specific changes in the thresholds are described in the supplement. One of the greatest challenges in revising the guideline was around the new thresholds for phototherapy and for [illegible] these thresholds based on the balance of expected harm. However, additional data are available to suggest

that the thresholds could be slightly increased. As with the previous thresholds, the thresholds were set based on the available evidence and expert consensus. Given these increases, the guideline is also much more specific about the importance of follow-up and strategies to do so.

Sincerely,

Alex R. Kemper, MD, MPH, MS

Submitted on August 21 2022

NCNC v. New AAP phototherapy thresholds

August 19 2022 | Chris Cahill

PEDIATRIC HOSPITALIST, SANTA CLARA VALLEY MEDICAL CENTER

I noticed that the new AAP phototherapy thresholds are very similar to the NCNC guidelines. However, the most notable difference is raising the phototherapy thresholds for 35wk infants with neurotoxicity risk factors by 1mg/dL; NCNC thresholds did not change the phototherapy threshold for 35wk infants with neurotoxocity risk factors. I am curious to know why this change exists. New evidence? Change in expert opinion?

I appreciate the committee's efforts here. Our institution has been using NCNC guidelines for several years and has seen large decreases in the amount of serum bilirubin blood draws and phototherapy usage with good balancing measures. These new guidelines are a welcome change to the AAP's clinical guidance.

Sincerely,

Chris Cahill, MD

Submitted on August 19 2022

Response to Dr. Manzar

August 7 2022 | Alex R. Kemper, MD, MPH, MS
DIVISION OF PRIMARY CARE PEDIATRICS, NATIONWIDE CHILDREN'S HOSPITAL, COLUMBUS, OH

Dear Dr. Manzar,

We appreciate the excellent case study of the revised guideline, which is remarkable given that it has been <72 hours since it was released. One of the great challenges in writing the guideline is that we wanted it to be clear and specific, while also not being too cumbersome. Where possible, we also wanted to allow shared decision making. Some things we were able to simplify. For example, the revised guideline no longer has a separate nomogram to classify risk zone. Instead, as clearly articulated in this case, follow-up is based on the difference between the bilirubin level and the phototherapy level, taking into account gestational age and hyperbilirubinemia neurotoxicity risk factors.

We are committed to helping clinicians implement these new guidelines, including developing electronic tools and partnering with electronic health vendors. The AAP will also be leading a quality-improvement collaborative.

We hope that you and others share your experience with the guideline. Of course, I am really interested to find out about that repeat bilirubin measure six hours from where the story ends!

Submitted on August 07 2022

Hyperbilirubinemia Management in Newborn: It's No More a One-Stop Shop

August 7 2022 | Shabih Manzar
LSU HEALTH, COLLEGE OF MEDICINE, SHREVEPORT, LA

After reviewing the current AAP Clinical Practice Guideline for Management of Hyperbilirubinemia (HB) [1], it is evident that as a pediatrician, the management of HB is no more a one-stop shop. Here is an example of a case: An 18-hour African American male infant is noted to be yellow by the parents. The infant's blood group is B positive (maternal blood group is O positive). The transcutaneous bilirubin (TcB) is obtained at 9 mg/dL. The parents asked if phototherapy was needed or not. The provider looked at the current guidelines. She looked at Table 1 to see if the infant is at risk for developing significant HB (lower gestational age, jaundice in the first 24 hours), then she looked at Table 2 to see if HB neurotoxicity risk factors (NTox RF) were present (gestational age < 38 wk, isoimmune hemolytic disease – ABO and G6PD). Because it was a TcB, she looked at the KAS (Key Action Statements) 6 (TcB exceeds or is within the 3 mg/dL of phototherapy treatment threshold). To get that information, she has to look at Figure 3 (because the infant's clinical information matches NTox RF graph). To answer the parents' question, she ordered a total serum bilirubin (TSB) level, which was 7.5 mg/dL. She plotted that value in Figure 3 using the color-coded line for the specific gestational age, following the time (hours on the x-axis) and TSB value on the y-axis. Involving parents in the decision-making, the phototherapy was deferred, and a follow-up TcB bilirubin was ordered in 6 hours.

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