CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

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

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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

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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]

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%

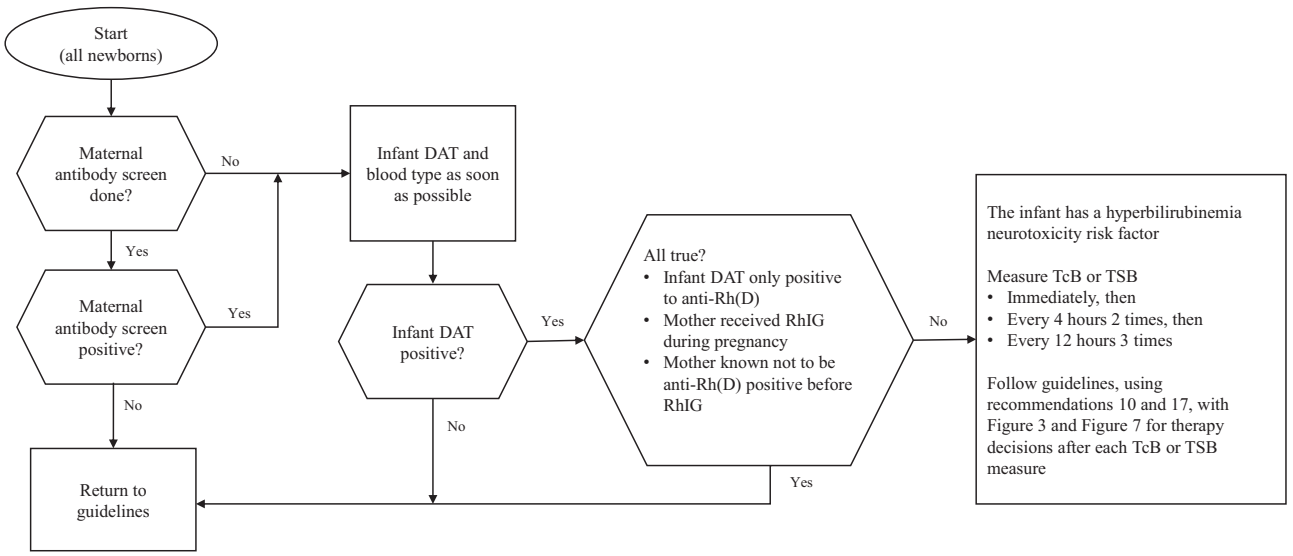


FIGURE 1
Approach to identify newborns with maternal anti-erythrocyte antibodies and to guide early management.[15]

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.

(Aggregate Evidence Quality Grade B, Strong Recommendation)

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.

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 G6PD deficiency.

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

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

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.

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 attributable to significant hemolysis justify TSB or TcB measurement. This recommendation for visual assessment does not replace the need to obtain at least 1 screening TSB or TcB as described below.

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).

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 recommended to have an outpatient follow-up 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 other expert 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 μW/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.

The committee determined that new evidence that bilirubin 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

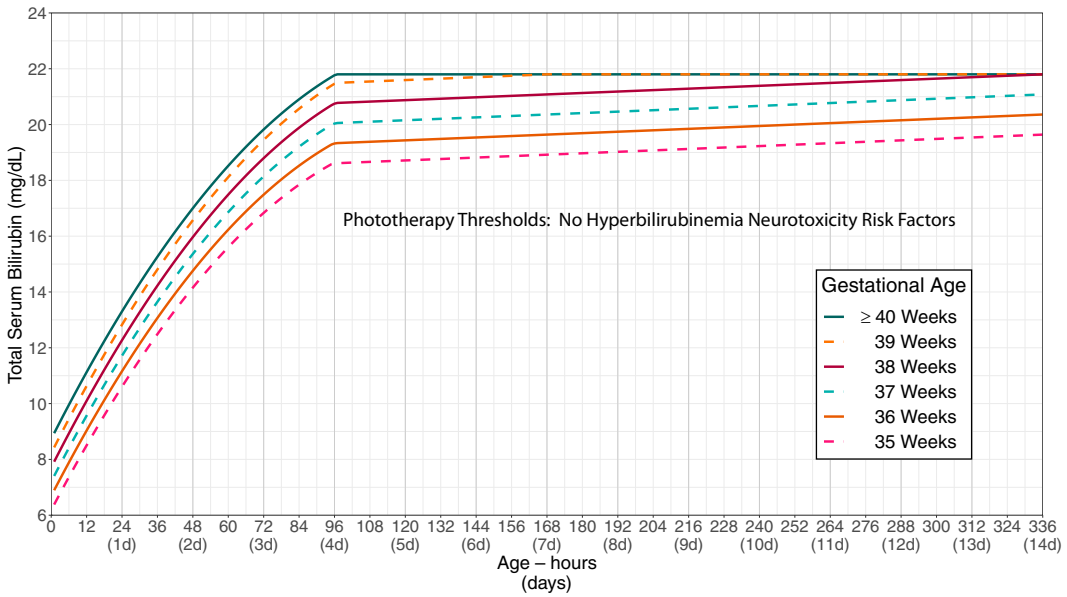


FIGURE 2

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.

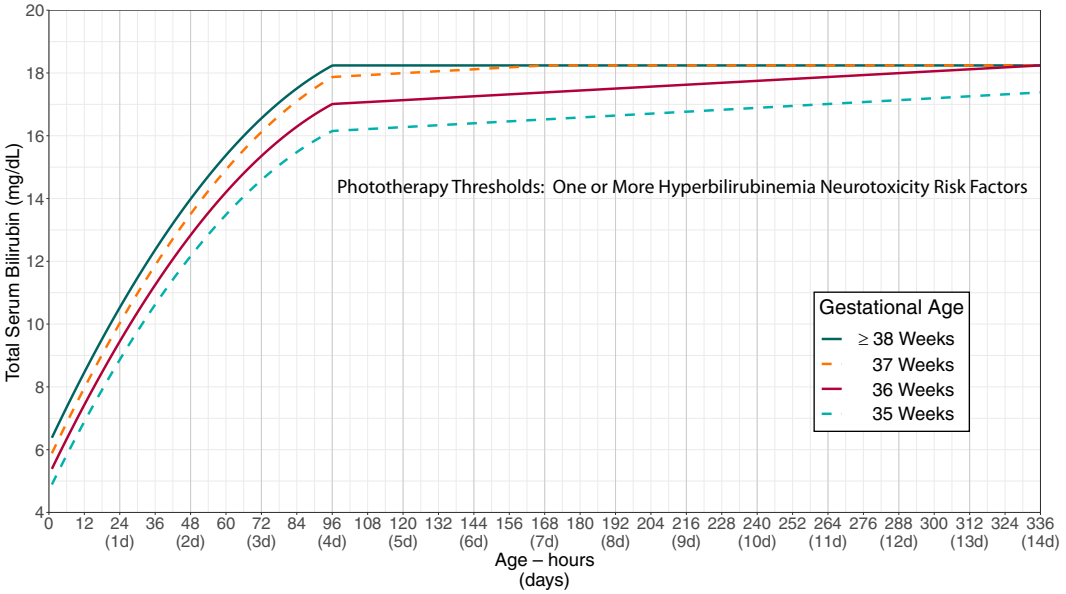


FIGURE 3

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 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 intended irradiance, following the recommendations of the 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.[22] 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 studies have not found this association.[111] Because most infants 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 $\geq$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.

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)

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

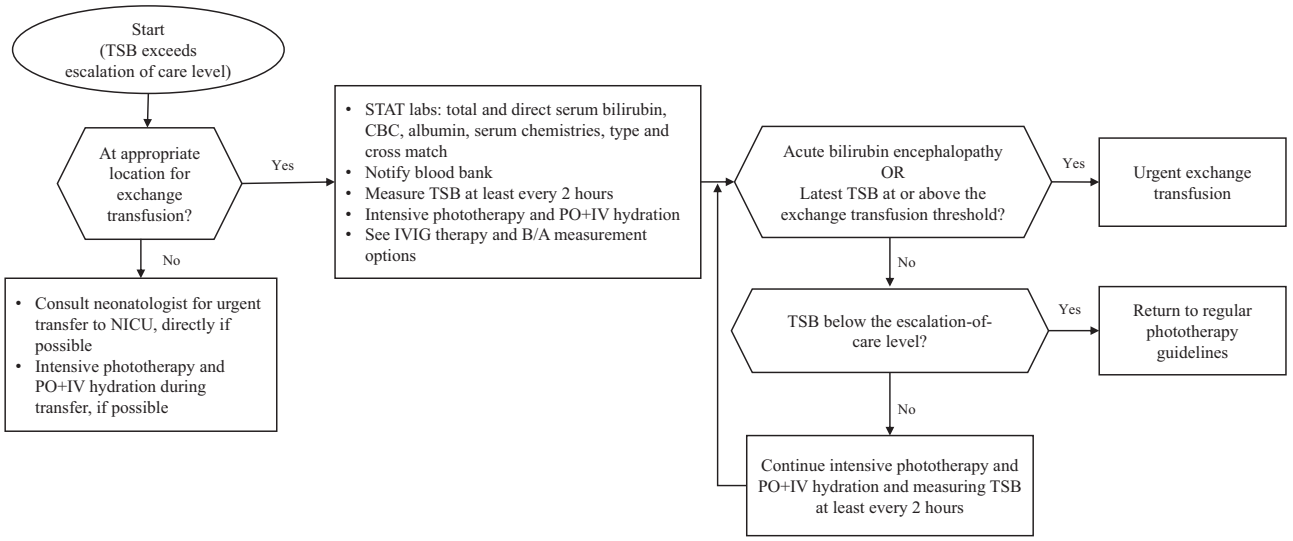


FIGURE 4

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.

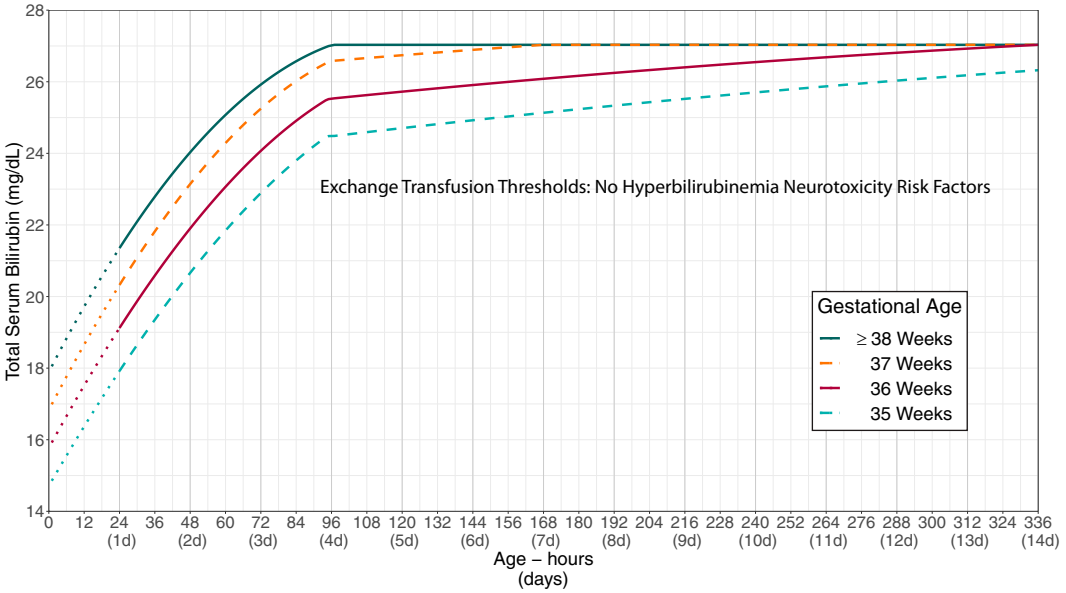


FIGURE 5

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.

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

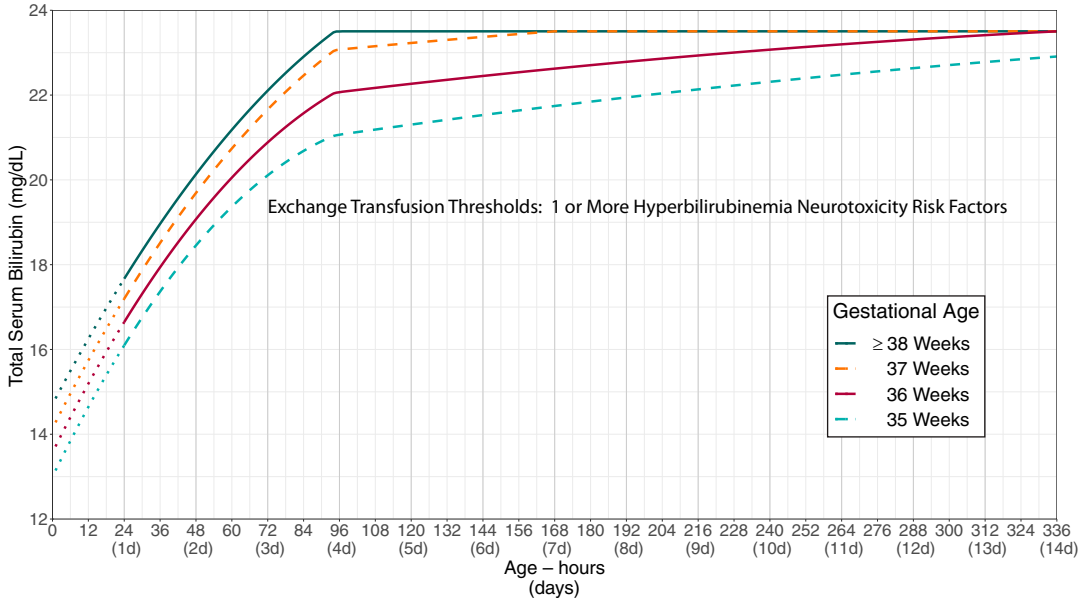


FIGURE 6

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.

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

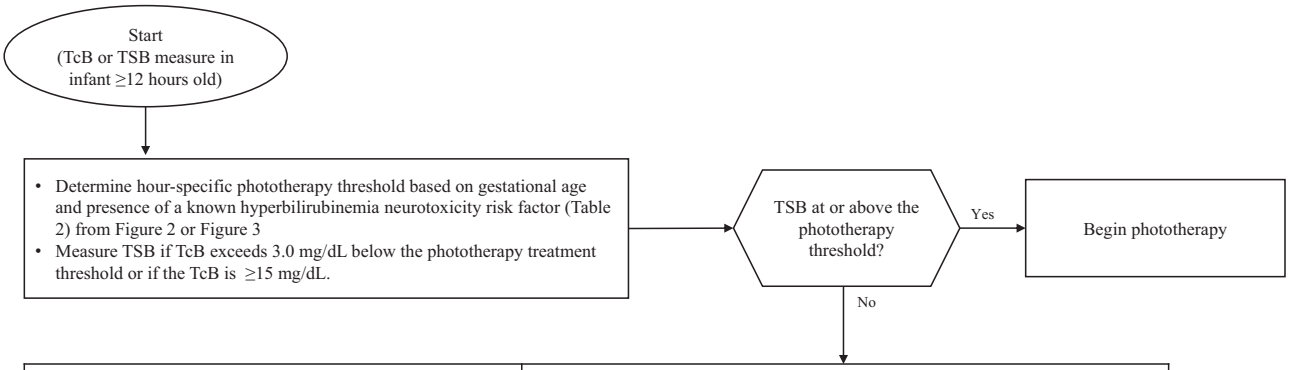
A. Timing of Follow-Up After Discharge

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).

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.

KAS 24: Beginning at least 12 hours after birth, if discharge



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]

FIGURE 7
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.

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.

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ABBREVIATIONS

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

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Supplemental Information

Appendix A. Kernicterus Nomenclature

The term kernicterus refers to the 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 magnetic resonance imaging.[1]

The term "kernicterus spectrum disorder" (KSD) has been proposed to provide a broader conceptualization of kernicterus. KSD encompasses all the neurologic sequelae of bilirubin neurotoxicity including classic, motor-predominant, and auditory-predominant subtypes of the continuum.[2,3] This term also suggests a possible association between subtle adverse neurodevelopmental findings and bilirubin concentrations well below those linked to classical kernicterus. However, the literature linking subtle abnormalities with bilirubin is conflicting, and there is no evidence that treating infants at these lower bilirubin concentrations prevents these outcomes.[4–13]

"Bilirubin-induced neurologic dysfunction" is a term that has been variously used to designate both subtle neurodevelopmental findings and all neurologic conditions associated with exposure to hazardous hyperbilirubinemia, as well as a scoring system that quantitatively describes the progression and severity of acute bilirubin encephalopathy (ABE).[5,11] Bilirubin-induced neurologic dysfunction should be used as originally intended as a score to quantify the severity of ABE and risk of an infant with ABE subsequently developing kernicterus or KSD[14,15]; its use for entities for which a causal effect of bilirubin has not been demonstrated should be avoided.

References for Kernicterus Nomenclature

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Appendix B. Key Action Statement Evidence Tables

The following tables summarize the

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)

Aggregate Evidence Quality	B
Benefits	Early DAT testing identifies newborn infants at risk for immune-mediated hemolytic disease and early hyperbilirubinemia born to mothers who carry anti-erythrocyte antibodies.
Risk, harm, and cost	Early DAT testing could involve an extra blood draw from newborn infants. There is a small risk of false-negative and false-positive DAT test results.
Benefit-harm assessment	Isoimmunization is the most common cause of severe hemolysis, and hyperbilirubinemia can progress rapidly. The alternative to early DAT testing is to wait and only test if jaundice develops, which could miss the opportunity for early intervention in some newborn infants with severe hemolysis. The benefit of knowing the risk for severe hemolysis through early DAT testing likely exceeds the harm of a potential extra blood draw and the risk of a false-negative or false-positive DAT in infants born to mothers with positive or unknown antibody screen results.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	1

KAS 2 Oral supplementation with water or dextrose water should not be provided to prevent hyperbilirubinemia or decrease bilirubin concentrations. (Aggregate Evidence Quality Grade B, Strong Recommendation)

Aggregate Evidence Quality	B
Benefits (from not treating)	Avoiding supplementation may help promote breastfeeding because supplementation has been associated with reduced maternal confidence in breastfeeding and breastfeeding duration. One study found no difference in peak serum bilirubin concentrations or the need for phototherapy among term breastfed newborn infants with physiologic jaundice by whether they were fed supplemental water. Another study of breastfed term infants whose weight was appropriate for gestational age found that supplementation with water or dextrose water was associated with higher bilirubin concentrations on day 6 after birth.
Risk, harm, and cost	There are no clear risks, harms, or costs associated with not routinely supplementing infants with water or dextrose water who are not receiving phototherapy.
Benefit-harm assessment	There is no evidence of the benefit of routinely providing water or dextrose water supplementation and there are possible harms, including interference with breastfeeding, hyponatremia, and water intoxication.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Strong Recommendation
Key references	2–6

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

Aggregate Evidence Quality	X
Benefits	Virtually all treatment studies are based on TSB concentrations.
Risk, harm, and cost	There is some laboratory variation.
Benefit-harm assessment	Using TSB can lead to timely treatment and may help reduce overtreatment in infants in whom TcB overestimates TSB. However, there are no direct comparisons between TSB and TcB as a diagnostic test to distinguish between babies in whom the benefits of treatment do and do not exceed the risks and costs and such studies are unlikely to be performed.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	7–11

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)

Aggregate Evidence Quality	X
Benefits	Onset of jaundice within 24 h of birth is more likely to be caused by hemolysis and to need treatment. Early identification of hyperbilirubinemia requiring treatment can lead to earlier initiation of phototherapy and reduce the risk of needing to perform an exchange transfusion. Identification of jaundice with onset after 24 h can inform decisions about measuring TcB or TSB and has the potential benefit of allowing parents to learn to recognize jaundice.
Risk, harm, and cost	Assessing for the onset of jaundice may require turning lights on in a previously dark room, which can interfere with sleep and disturb the infant and other family members. This harm can be minimized if the examination is conducted at the same time as other routine newborn care and by covering the infant's eyes or using focused lighting away from the infant's eyes.
Benefit-harm assessment	The benefits are likely to exceed harms, especially in the first 24 h.
Intentional vagueness	None
Role of patient preferences	Parents may have preferences regarding the frequency or timing of these examinations that can be considered as long as they occur at least every 12 h.
Exclusions	None
Strength	Strong Recommendation
Key references	12

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

Aggregate Evidence Quality	C
Benefits	Routine TcB or TSB screening can identify significant but undetected hyperbilirubinemia. This benefit will be greater among infants whose jaundice is harder to recognize. The TcB or TSB value can be used to plan for postdischarge follow-up and the need for subsequent measures of TcB or TSB. This planning can help increase the timely identification of subsequent hyperbilirubinemia and also avoid unnecessary follow-up care or treatment.
Risk, harm, and cost	TSB measurements can cause discomfort, which could be minimized by using TcB measures or obtaining additional blood at the same time as the collection of the dried blood spot for newborn screening. In some newborn infants, TcB measurements might lead to TSB measurements that would otherwise not have been performed and are not high enough to affect management. This may be more likely in infants with greater skin melanin concentration when JM TcB instruments are used.[8,13] There is a risk that hyperbilirubinemia could be detected that would have resolved without treatment had it not been identified. It is possible that the follow-up based on the TcB or TSB measure could be more or less than what the infant needs. There is the possibility of a false sense of security based on having a low TcB or TSB in infants with hyperbilirubinemia that presents later, such as from G6PD deficiency. There are additional costs related to measuring TcB or TSB.
Benefit-harm assessment	Evidence from large health care systems that implemented universal bilirubin screening suggest a decrease in the already low incidence of infants who reach a TSB ≥25 mg/dL, with a number needed to screen in the range of 1000 to 6000. The number needed to screen to prevent one infant from reaching a TSB ≥30 mg/dL is approximately 15 000. The screening test alone does not directly lead to the benefit, but instead relies on follow-up care including subsequent TSB measurements and treatment with phototherapy. The effect on health disparities is uncertain but probably small: an increase in sensitivity at identifying significantly jaundiced babies, which may disproportionately benefit babies with greater skin melanin concentration, but possible increase in unnecessary TSB testing in this group. There are no randomized trials of bilirubin screening.
Intentional vagueness	None
Role of patient preferences	Parents may prefer strategies to minimize the number of heel pricks or venipunctures and, therefore, prefer TcB compared with TSB.
Exclusions	None
Strength	Recommendation
Key references	13–22

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)

Aggregate Evidence Quality	C
Benefits	The TcB is a good screening test but is not accurate enough to determine treatment decisions. TSB provides a better guide for treatment decisions than the TcB because studies of hyperbilirubinemia risk prediction and studies of treatment have been based on the TSB. As the TcB approaches the phototherapy treatment thresholds, the likelihood that the TSB will change management increases.
Risk, harm, and cost	There is a risk of an unnecessary blood test when the TSB might not change management. Infants whose skin has greater melanin concentration tend to have higher TcB measurements with JM instruments,[8,13,22] increasing the risk of unnecessary blood tests, whereas infants with greater skin melanin concentration and higher TSB levels may have slightly lower TcB with Spectrix instruments. However, these differences are relatively small.
Benefit-harm assessment	The benefit of having a more accurate measure to guide treatment decisions outweighs the discomfort associated with measuring the TSB.
Intentional vagueness	None
Role of patient preferences	In borderline cases, especially if one or more TcB measurements has been greater than a contemporaneous TSB level, parents may prefer to rely on the TcB.
Exclusions	None
Strength	Recommendation
Key references	8, 23, 24

KAS 7 If more than 1 TcB or TSB measure is available, the rate of increase may be used to identify higher risk of subsequent hyperbilirubinemia. 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 and suggests hemolysis. In this case, obtain a DAT if not previously done. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Identification of a rapid rate of increase could lead to the identification of unrecognized hemolysis.
Risk, harm, and cost	Insufficient evidence is available to assess the test accuracy of different thresholds for the rate of rise or to recommend routinely obtaining more than 1 TcB or TSB measure.
Benefit-harm assessment	Although the balance of benefit and harm cannot be determined, evaluating the rate of rise could help detect unrecognized hemolysis.
Intentional vagueness	None
Role of patient preferences	Because this is an option, a parental preference to avoid monitoring might lead to having only 1 TcB or TSB measure available. In that case, the rate of rise cannot be calculated. However, once a rapid rate of rise is identified, a DAT should be obtained if not previously even if parents prefer to avoid additional testing because of the importance of DAT in making treatment decisions.
Exclusions	None
Strength	Option
Key references	25, 26

KAS 8 If appropriate follow-up cannot be arranged for an infant recommended to have an outpatient follow-up bilirubin measure, discharge may be delayed. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Follow-up after discharge for some families can be challenging and potentially contribute to missing the opportunity for timely treatment of hyperbilirubinemia.
Risk, harm, and cost	Delay in discharge can be difficult for families and increase nursery-related expenses.
Benefit-harm assessment	The balance of benefit and harm depend on the risk of hyperbilirubinemia and the challenge of follow-up. Extending access for newborn follow-up can reduce the need to delay discharge.
Intentional vagueness	None
Role of patient preferences	Shared decision making can help inform the benefit-harm assessment.
Exclusions	None
Strength	Option
Key references	27

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)

Aggregate Evidence Quality	X
Benefits	Although cholestasis is uncommon, early detection of pathologic causes of cholestasis, such as biliary atresia or certain metabolic diseases, can lead to improved health outcomes.
Risk, harm, and cost	The harm is an additional blood test and the pain associated with any additional evaluation based on the laboratory findings. The additional costs are those associated with the blood test and additional evaluation.
Benefit-harm assessment	The benefit of early identification and treatment of pathologic causes of cholestasis outweighs the harm of the testing and subsequent evaluation among infants who are still jaundiced at 2 wk of age.
Intentional vagueness	None
Role of patient preferences	Parents may prefer to measure TSB at the 2-wk visit rather than returning for a TSB level at 4 wk.
Exclusions	None
Strength	Exceptional situation
Key references	28–30

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 Figure 2) on the basis of gestational age, hyperbilirubinemia neurotoxicity risk factors, and age of the infant in hours. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Intensive phototherapy can reduce TSB levels and decrease the need for escalation of care, including the need for exchange transfusion, to prevent kernicterus. The phototherapy treatment thresholds are higher than those in the 2004 guideline but still leave a wide margin of safety. Compared with the 2004 guideline, overtreatment will be decreased.
Risk, harm, and cost	Phototherapy may lead to separation of mother and baby, maternal anxiety, and reduce breastfeeding. Phototherapy can lead to oxidative stress and DNA damage, although these risks appear to be lower with LED-based phototherapy. Two observational studies found a small increased risk of epilepsy in males treated with phototherapy. If the findings are causal, for approximately each 100 to 250 males treated with phototherapy, 1 will be diagnosed with epilepsy by 10 years of age. Hospitalization for phototherapy can increase costs because of a prolonged initial hospital stay or the need for readmission. See the technical report appendix for a review of other risks of phototherapy.
Benefit-harm assessment	Benefits are believed to exceed potential harms at the phototherapy treatment thresholds in this guideline. A weakness of the evidence linking specific TSB levels to adverse neurologic outcomes is that studies are typically based on maximum TSB levels, which are not known when decisions to initiate phototherapy are made. Even at the treatment thresholds in this guideline, the number needed to treat to prevent 1 infant from receiving an exchange transfusion may be in the hundreds or thousands, and the number needed to treat to prevent 1 case of kernicterus is considerably higher. The more the TSB exceeds the phototherapy threshold, the lower the number that will be needed to treat to prevent the need for an exchange transfusion or prevent kernicterus.
Intentional vagueness	None
Role of patient preferences	The phototherapy treatment thresholds are based on expert opinion. Some families might choose to accept a higher probability of unnecessary treatment and begin phototherapy below recommended thresholds to reduce the risk of a rehospitalization and its accompanying costs and inconvenience. Other families, with infants with TSB levels at or <2 mg/dL above thresholds, may prefer only blanket phototherapy (in the hospital or at home) or withholding phototherapy and very close follow-up of TSB concentrations.
Exclusions	None
Strength	The evidence is strong that phototherapy reduces TSB concentrations and the need for exchange transfusion. The evidence is weak regarding the specific phototherapy treatment threshold at which benefits exceeds harms. This is a recommendation because the guideline thresholds were set to reduce overtreatment while not missing the potential benefit for reducing the risk of exchange transfusion or kernicterus.
Key references	31–38

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: 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, Supplemental Fig 1), an LED-based phototherapy device will be available in the home without delay, and TSB can be measured daily. (Aggregate Evidence Quality Grade D, Option)

Aggregate Evidence Quality	D
Benefits	Home phototherapy for infants already discharged can help avoid readmission.
Risk, harm, and cost	Home phototherapy might not prevent significant hyperbilirubinemia if it is not used correctly and there is not close clinical follow-up. Infants with any risk factor are more likely to develop worsening hyperbilirubinemia even with appropriate home therapy use.
Benefit-harm assessment	The balance of benefit and harm depend on the risk of worsening hyperbilirubinemia.
Intentional vagueness	None
Role of patient preferences	Shared decision making can help inform the benefit-harm assessment. As with inpatient phototherapy, beginning home phototherapy at a somewhat lower threshold could reduce the readmission risk. Some families may prefer inpatient treatment, especially if lactation support is more available for inpatients than outpatients.
Exclusions	None
Strength	Option
Key references	39, 40

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)

Aggregate Evidence Quality	X
Benefits	Early identification of infants without adequate response to phototherapy can lead to earlier escalation of care, potentially averting the need for an exchange transfusion and possibly preventing kernicterus. Early identification of infants whose TSB has decreased will facilitate timely discontinuation of phototherapy.
Risk, harm, and cost	There is a small risk that some infants would receive escalation of care who would have responded to phototherapy without additional interventions. There are costs associated with the additional testing.
Benefit-harm assessment	Although most infants treated with phototherapy will not require escalation of care, missing an infant could lead to significant harm. More frequent TSB measurements might allow earlier discontinuation of phototherapy, which might reduce the risk of adverse effects associated with phototherapy and would reduce costs.
Intentional vagueness	None
Role of patient preferences	For some families, the benefit of finding out sooner that phototherapy can be discontinued might lead to a preference for more frequent blood tests.
Exclusions	None
Strength	Exceptional situation
Key references	41–43

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 ≥ 1mg/dL above the phototherapy threshold. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	TSB measurement is the only way to document whether there has been a response to phototherapy and to determine when phototherapy can be discontinued.
Risk, harm, and cost	TSB measurement is associated with discomfort and for those infants who have been discharged, there will often be the need to travel to a clinic or laboratory. For some families, travel can be difficult, and some infants might require an emergency department visit for TSB testing. TSB measurement increases cost.
Benefit-harm assessment	The overall benefit of assessing response to phototherapy outweighs the harms and additional expense of daily TSB testing for infants receiving home phototherapy.
Intentional vagueness	None
Role of patient preferences	Families might prefer a slightly higher or lower frequency of TSB monitoring. Factors that could influence this include the values of the previous TSB concentrations.
Exclusions	None
Strength	Recommendation
Key references	39, 44, 45

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)

Aggregate Evidence Quality	X
Benefits	Identifying the cause of hyperbilirubinemia might identify a previously unrecognized diagnosis that leads to the need for additional care.
Risk, harm, and cost	Additional laboratory tests and related costs.
Benefit-harm assessment	The estimated overall benefit of providing potentially useful information is expected to outweigh the potential harms.
Intentional vagueness	None
Role of patient preferences	Some families might place added value in knowing the cause of the hyperbilirubinemia, especially if it could inform the care of future pregnancies.
Exclusions	None
Strength	Recommendation
Key references	46–54

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)

Aggregate Evidence Quality	C
Benefits	Discontinuing phototherapy as soon as it is safe reduces unnecessary exposure to phototherapy while minimizing the risk of rebound hyperbilirubinemia.
Risk, harm, and cost	Stopping phototherapy too soon increases the risk that it will need to be restarted again. The cost and inconvenience of restarting phototherapy is greater when it would require readmission to the hospital. Continuing phototherapy longer than necessary increases costs and might increase the risk of adverse effects.
Benefit-harm assessment	Suggested levels for discontinuing phototherapy reflect an attempt to minimize both the duration of phototherapy and need to initiate it again. Different families and clinicians may have different values for these conflicting goals; estimation of the risk of significant rebound hyperbilirubinemia can facilitate joint decision making.
Intentional vagueness	None
Role of patient preferences	Parents wanting to end phototherapy sooner may be willing to accept a higher risk of rebound; those who want to reduce even a small risk of readmission may wish to continue the phototherapy until the TSB is lower.
Exclusions	None
Strength	Recommendation
Key references	55, 56

KAS 16 Follow-up 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 in 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 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. (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Following up closely with infants discharged early or with hyperbilirubinemia risk factors can lead to more timely identification of those who need treatment. Infants who required phototherapy should be followed closely because of the risk of rebound hyperbilirubinemia. TcB is reliable after 24 h of phototherapy and can, therefore, be used instead of TSB.
Risk, harm, and cost	Some infants might receive additional TSB or TcB testing or have clinic follow-up that might not be necessary.
Benefit-harm assessment	The benefits of identifying infants with hyperbilirubinemia that develops after discharge or infants with rebound hyperbilirubinemia exceeds the associated follow-up risks.
Intentional vagueness	None
Role of patient preferences	Parents wanting to avoid additional testing or clinic follow-up might accept a higher risk of delayed detection of hyperbilirubinemia. However, other parents might want closer follow-up to avoid this risk.
Exclusions	None
Strength	Recommendation
Key references	55–58

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 and or infants with at least one recognized hyperbilirubinemia neurotoxicity risk factor; Supplemental Table 4 and Supplemental Fig 4). (Aggregate Evidence Quality Grade X, Recommendation)

Aggregate Evidence Quality	X
Benefits	Escalation of care below the exchange transfusion threshold may prevent the need for an exchange transfusion or allow for a timelier exchange transfusion if it is necessary, which could help prevent kernicterus.
Risk, harm, and cost	Some infants for whom care is escalated may have experienced a leveling off or decrease in TSB without this additional care. Escalation of care can lead to separation of mother and baby and greater costs if transfer to another hospital is required.
Benefit-harm assessment	The overall benefit of escalation of care to potentially avoid the need for an exchange transfusion and to be prepared to provide an exchange transfusion in as safe a manner as possible is believed to outweigh the potential harms at about the TSB concentrations at which escalation of care is recommended. The TSB concentration or trajectory at which the benefits of escalation of care exceed the risks and costs is not known, and will vary with individual circumstances, such as the proximity of a NICU.
Intentional vagueness	None
Role of patient preferences	Decisions regarding NICU transfer can be difficult, especially if this would require transfer to another hospital or separation from the mother. Parent preferences should be considered in in borderline cases.
Exclusions	None
Strength	Recommendation
Key references	37, 59

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)

Aggregate Evidence Quality	X
Benefits	Avoiding delays for infants who require exchange transfusion can improve outcomes. Knowledge of the albumin level and complete blood count results can inform exchange transfusion decisions and the differential diagnosis of the hyperbilirubinemia.
Risk, harm, and cost	Some infants might receive additional testing that might not be necessary.
Benefit-harm assessment	The benefits of being prepared for an exchange transfusion outweigh the harm of additional testing.
Intentional vagueness	None
Role of patient preferences	None
Exclusions	None
Strength	Recommendation
Key references	Expert opinion

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

Aggregate Evidence Quality	C
Benefits	Emergent intensive phototherapy and intravenous (IV) hydration can increase the rate of decline in TSB and may prevent the need for an exchange transfusion.
Risk, harm, and cost	The risks and costs of short-term intensive phototherapy and IV hydration are small and minimal compared with the possibility of an exchange transfusion.
Benefit-harm assessment	The possible benefit of preventing an exchange transfusion outweighs the potential harm.
Intentional vagueness	None
Role of patient preferences	Parents might choose to defer IV hydration if obtaining vascular access is difficult and the TSB is stabilizing.
Exclusions	None
Strength	Recommendation
Key references	60–65

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)

Aggregate Evidence Quality	X
Benefits	Frequent measurement of TSB provides timely guidance regarding the efficacy of phototherapy and the possible need for an exchange transfusion.
Risk, harm, and cost	Frequent TSB monitoring requires repeated blood sampling and laboratory testing.
Benefit-harm assessment	Infants who require escalation of care benefit from frequent monitoring to identify if or when they qualify for an exchange transfusion. The benefit of identifying those who exceed exchange thresholds as soon as possible outweighs the possible harms from the risks and costs of frequent blood sampling and laboratory testing.
Intentional vagueness	None
Role of patient preferences	Minimal to none
Exclusions	None
Strength	Recommendation
Key references	Expert opinion

KAS 21 Intravenous immune globulin (IVIG; 0.5–1 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)

Aggregate Evidence Quality	C
Benefits	Use of IVIG during escalation of care may reduce homolysis and thereby stabilize or reduce TSB concentrations, preventing the need for exchange transfusion.
Risk, harm, and cost	The effect of IVIG for immune-mediated hemolytic disease has been understudied with conflicting evidence supporting a reduction in exchange transfusions. Recent investigations using routine single early dose prophylactic IVIG do not demonstrate benefit in reducing the need for exchange transfusion and the routine use of prophylactic IVIG in DAT+ neonates should be discouraged. However, targeted dosing may be more effective. Although observational studies suggest that IVIG may be associated with necrotizing enterocolitis, the risk of necrotizing enterocolitis with exchange transfusion is well documented so the benefits of IVIG may outweigh this potential harm when exchange thresholds are approached.
Benefit-harm assessment	The benefits of IVIG are not clear, and there is a small risk of harm. Treatment with IVIG may be more strongly considered if there is a poor response to phototherapy and there is difficulty in obtaining an exchange transfusion.
Intentional vagueness	None
Role of patient preferences	Some families may want to avoid IVIG treatment given limited evidence for its effectiveness, especially for Rh+ infants and the potential risk of necrotizing enterocolitis.
Exclusions	None
Strength	Option
Key references	Technical report and 66–75

KAS 22 An urgent exchange transfusion should be performed for infants with signs of intermediate or advanced stages 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)

Aggregate Evidence Quality	C
Benefits	There are some case reports and case series that suggest an immediate exchange transfusion may prevent kernicterus in some infants already showing signs of intermediate to advanced stages of bilirubin encephalopathy, and reduction of the time the brain is exposed to high TSB concentration may also reduce the severity of chronic bilirubin encephalopathy if it develops.
Risk, harm, and cost	The risks of exchange transfusion include death, necrotizing enterocolitis, apnea, hypocalcemia and other electrolyte abnormalities, and thrombocytopenia. The infectious risks from donor blood products are low. The costs of an exchange transfusion are incompletely described but at least thousands of dollars.
Benefit-harm assessment	The benefit of avoiding kernicterus or reducing its severity among newborns already showing signs of intermediate or advanced acute bilirubin encephalopathy probably exceed the risks and costs of exchange transfusion.
Intentional vagueness	None
Role of patient preferences	Some parents have a strong preference to avoid blood products.
Exclusions	None
Strength	Recommendation
Key references	59, 64, 65, 76–82

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)

Aggregate Evidence Quality	C
Benefits	Treatment at these levels may prevent kernicterus.
Risk, harm, and cost	The risks of exchange transfusion include death, necrotizing enterocolitis, apnea, hypocalcemia and other electrolyte abnormalities, and thrombocytopenia. The infectious risks from donor blood products are low. The costs of an exchange transfusion are incompletely described but at least thousands of dollars.
Benefit-harm assessment	Studies are not sufficient to set a definite TSB concentration or duration of time with TSB above exchange thresholds at which the kernicterus-preventing benefits of exchange transfusion exceed the risks and costs. These thresholds may differ in low- and middle-income countries, where the risk of kernicterus may be substantially higher. The potential benefits of exchange transfusions are unlikely to exceed risks at the exchange thresholds in the AAP 2004 guideline. Whether benefits exceed risk at these levels is not known. The exchange transfusion thresholds were raised in this guideline to decrease the likelihood of harm while still recommending treatment of infants most likely to benefit.
Intentional vagueness	None
Role of patient preferences	Given uncertainty about what the exchange transfusion thresholds should be, parent preferences may be considered.
Exclusions	None
Strength	Recommendation
Key references	35, 59, 83–86

KAS 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)

Aggregate Evidence Quality	C
Benefits	These recommendations for timing of follow-up after discharge seek to improve follow-up of those at highest risk of developing jaundice that will benefit from treatment while minimizing unnecessary visits and laboratory testing.
Risk, harm, and cost	These guidelines for follow-up may lead to some infants with significant hyperbilirubinemia being detected late or missed and others receiving more visits or earlier visits than were needed to detect and manage their hyperbilirubinemia.
Benefit-harm assessment	These thresholds for bilirubin testing and follow-up seek to balance benefit and harm, but necessarily depend on value judgements. Depending on the level of concern about jaundice and the difficulty of outpatient follow-up and bilirubin testing, clinicians and families can jointly decide on more or less aggressive follow-up, especially with TSB concentrations close to the cutoffs suggested here.
Intentional vagueness	None
Role of patient preferences	Parent preferences around the specific timing of TcB or TSB monitoring can be considered given the gaps in evidence.
Exclusions	None
Strength	Recommendation
Key references	20, 87–91

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)

Aggregate Evidence Quality	X
Benefits	Educating families and providing explicit instructions for follow-up can decrease the risk of missed cases of hyperbilirubinemia or other problems requiring treatment.
Risk, harm, and cost	There is a small risk of causing anxiety. The costs of providing the information and appropriate education are minimal.
Benefit-harm assessment	The benefits far exceed the potential harms.
Intentional vagueness	None
Role of patient preferences	Parents value complete information about their newborn infants.
Exclusions	None
Strength	Strong recommendation
Key references	92

evidence for each key statement according to the AAP evidence review process.

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APPENDIX C. PHOTOTHERAPY AND EXCHANGE TRANSFUSION THRESHOLDS

The 2004 AAP guideline did not make specific recommendations for

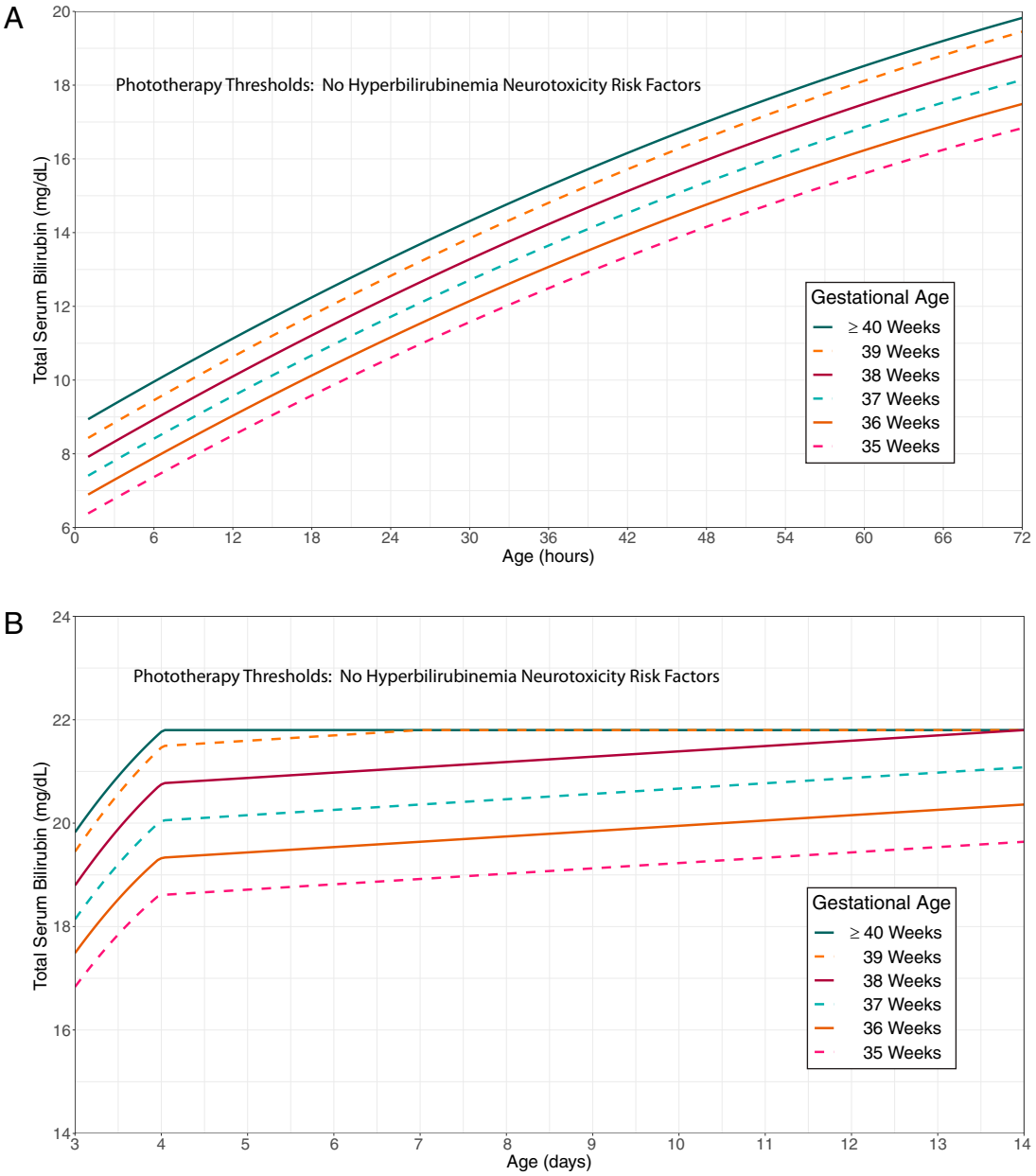
phototherapy or exchange transfusion by week of gestational age.[1] Rather, gestational age dichotomized at 38 weeks was an important, separate hyperbilirubinemia neurotoxicity risk factor that led to more aggressive treatment. In the current guideline, the new phototherapy threshold for infants born at 40 weeks' gestational age and no recognized hyperbilirubinemia neurotoxicity risk factors was set at 2 mg/dL higher than the previous guideline's recommendations for infants at lower risk (≥38 weeks' gestation with no hyperbilirubinemia neurotoxicity risk factors). For infants born at 35 weeks' gestational age with no recognized hyperbilirubinemia neurotoxicity risk factors, the new threshold was set at 1 mg/dL higher than "medium-risk" infants in the 2004 guideline (either gestational age 35 to <38 weeks or presence of hyperbilirubinemia neurotoxicity risk factors but not both). The new thresholds for infants born at 36 to 39 weeks' gestational age with no hyperbilirubinemia neurotoxicity risk factors were evenly spaced between the thresholds for infants with gestational ages of 35 weeks and 40 weeks.

A similar process was used for the phototherapy thresholds for infants with at least 1 hyperbilirubinemia neurotoxicity risk factor. In this case, the new phototherapy threshold for infants with a gestational age of 35 weeks was set to 1 mg/dL above the 2004 threshold for infants at higher risk (both gestational age <38 weeks and hyperbilirubinemia neurotoxicity risk factors), and for infants born at gestational age of ≥38 weeks with at least 1 hyperbilirubinemia neurotoxicity risk factor, the new threshold was set to 1 mg/dL above the threshold for infants at medium risk (defined above), and infants born at gestational age of 36 or 37 weeks were evenly spaced out between these 2 curves.

In addition to the change above, the new guideline takes into account the chronologic (ie, postmenstrual) age of the infant by increasing the phototherapy threshold. For example, by 7 days after birth, the phototherapy threshold for infants born at 39 weeks' gestation far reaches that for infants born at 40 weeks' gestation.

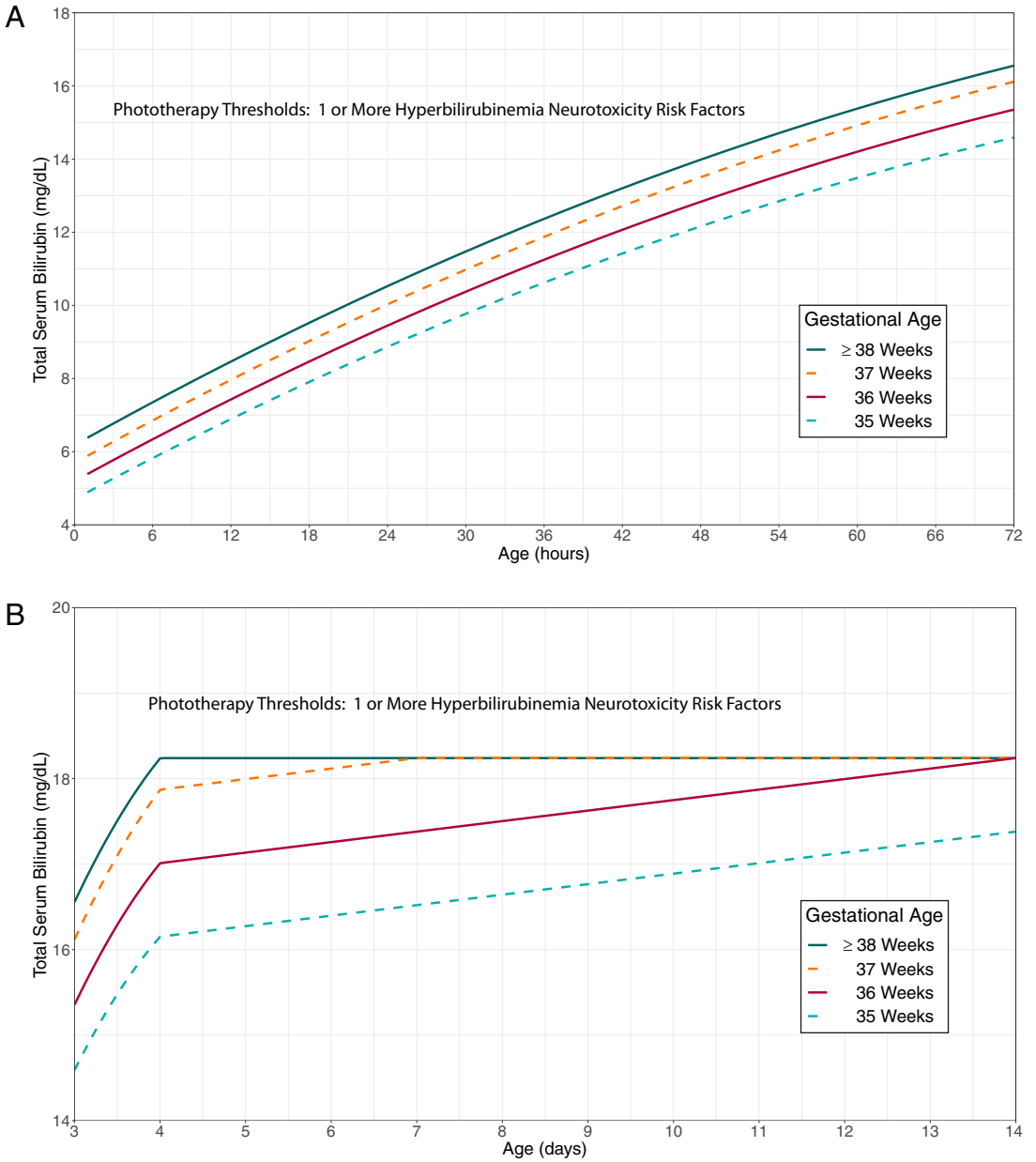
The exchange transfusion thresholds were developed by determining the difference between the exchange transfusion and phototherapy threshold for each group from the 2004 guideline and adding that difference to the new phototherapy thresholds in the current guideline.

The following tables list the specific thresholds for phototherapy and exchange transfusion shown in Figs 2, 3, 6, and 7. Each set of tables is followed by figures that illustrate the thresholds from birth to 72 hours and then from 72 hours (ie, 3 days) to 336 hours (ie, 14 days).



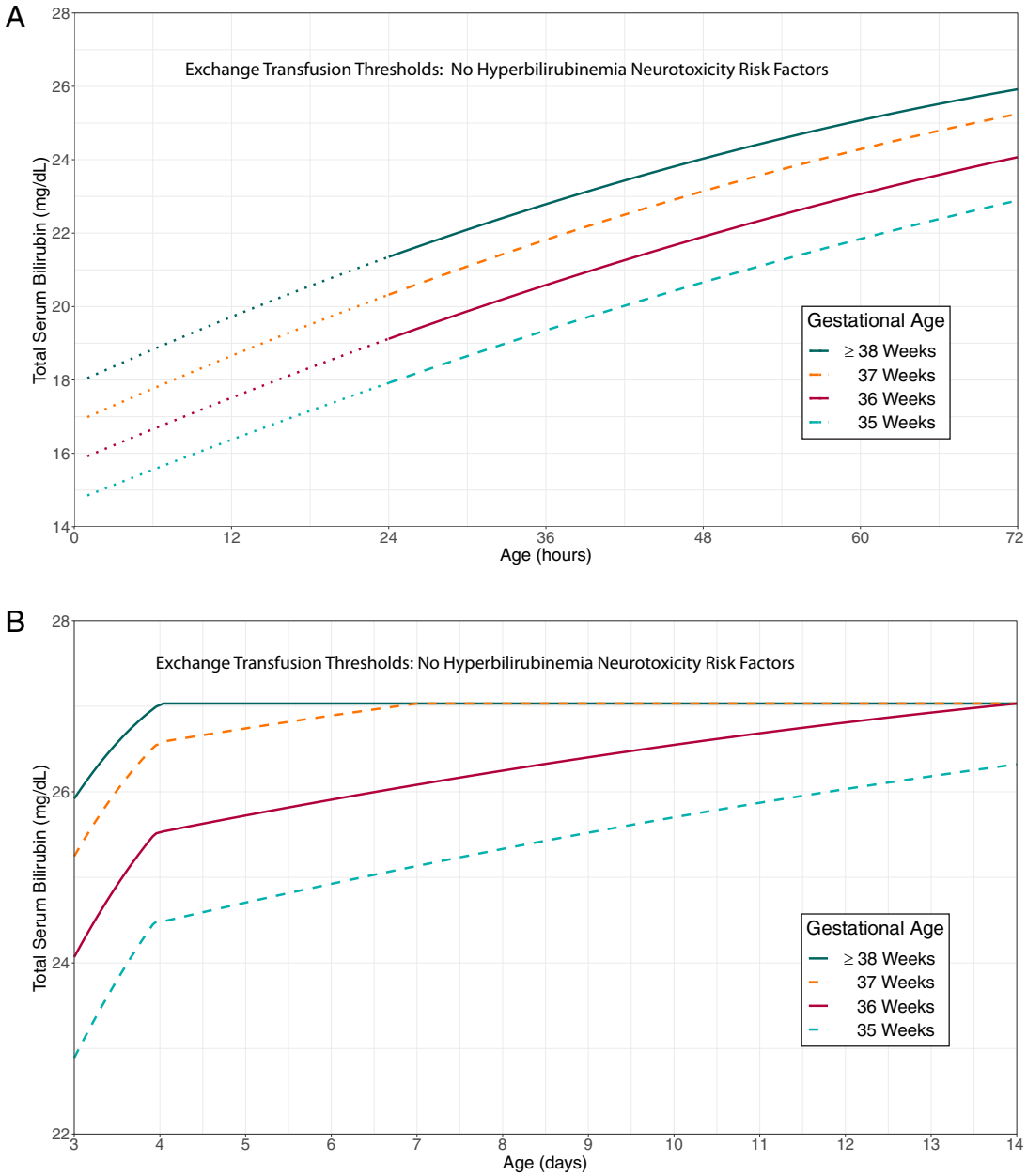
SUPPLEMENTAL FIGURE 1

A, Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 2. 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.



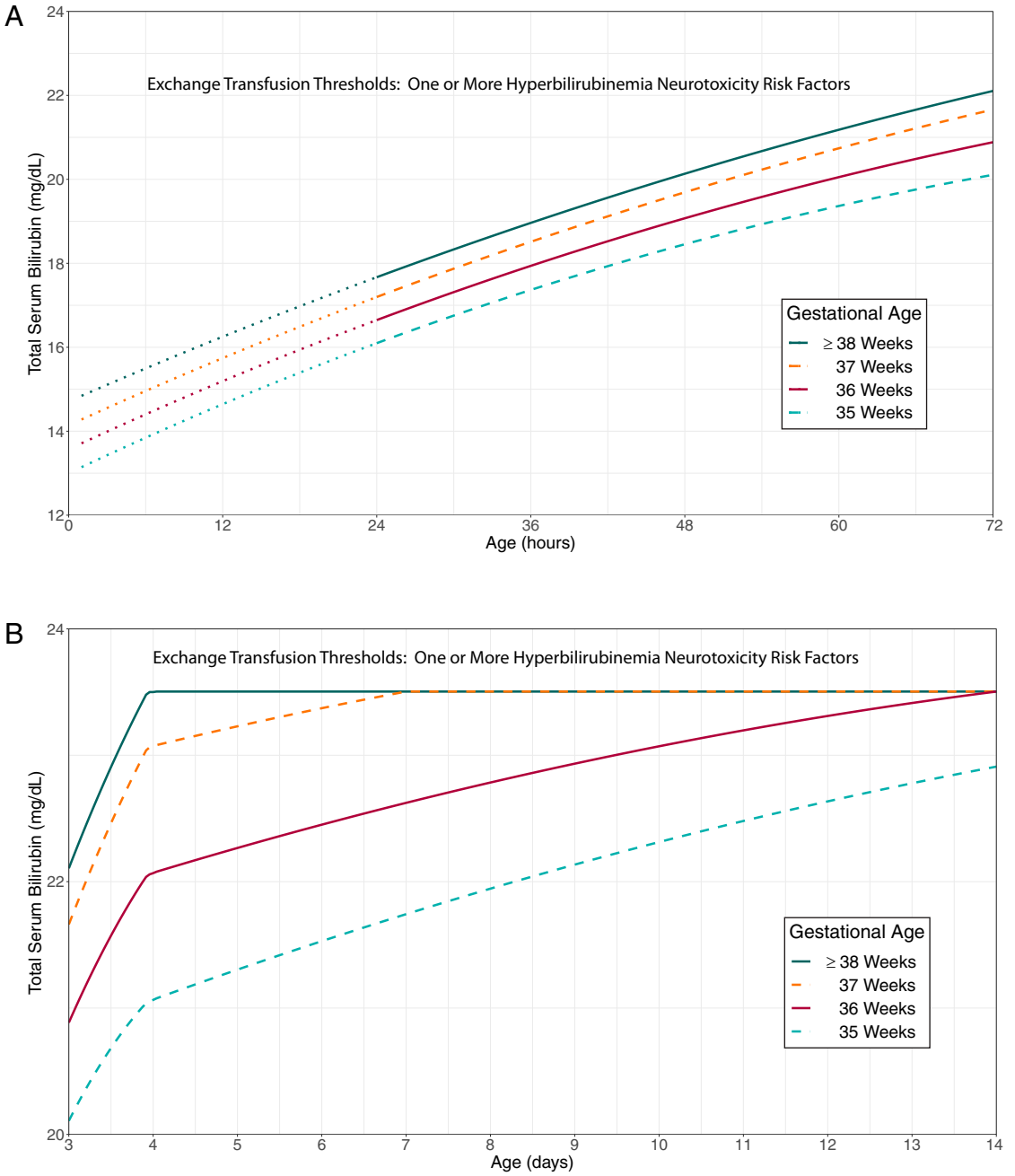
SUPPLEMENTAL FIGURE 2

A, Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 3. 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.



SUPPLEMENTAL FIGURE 3

A, Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from birth to 72 hours (ie, 3 days). B, Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 5. 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 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.



SUPPLEMENTAL FIGURE 4

A, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age, from birth to 72 hours (ie, 3 days). B, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days. This is an enlarged version of Fig 6. 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 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. B, Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age from 3 to 14 days.

SUPPLEMENTAL TABLE 1 Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 2, are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. 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.

Gestational age of 40 weeks or more and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		8.9	9.1	9.3	9.6	9.8	10.0	10.2	10.4	10.5	10.7	10.9	11.1	11.3	11.5	11.7	11.9	12.1	12.2	12.4	12.6	12.8	13.0	13.1
1	13.3	13.5	13.6	13.8	14.0	14.1	14.3	14.5	14.6	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.9	16.0	16.2	16.3	16.4	16.6	16.7	16.9
2	17.0	17.1	17.3	17.4	17.5	17.7	17.8	17.9	18.0	18.2	18.3	18.4	18.5	18.6	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.6	19.7	19.7
3	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.7	20.8	20.9	21.0	21.1	21.1	21.2	21.3	21.4	21.4	21.5	21.6	21.6	21.7
4	21.8[a]	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

[a]The threshold ≥96 h (eg, 4 completed days) after birth is 21.8 mg/dL.

Gestational age of 39 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		8.4	8.6	8.8	9.0	9.3	9.5	9.7	9.9	10.0	10.2	10.4	10.6	10.8	11.0	11.2	11.4	11.6	11.8	11.9	12.1	12.3	12.5	12.7
1	12.8	13.0	13.2	13.3	13.5	13.7	13.8	14.0	14.2	14.3	14.5	14.7	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.9	16.0	16.2	16.3	16.4
2	16.6	16.7	16.8	17.0	17.1	17.2	17.4	17.5	17.6	17.8	17.9	18.0	18.1	18.2	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.1	19.2	19.3
3	19.5	19.6	19.7	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.4	20.5	20.6	20.6	20.7	20.8	20.9	21.0	21.0	21.1	21.2	21.3	21.3	21.4
4	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6
5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7
6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.8[a]	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

[a]The threshold ≥157 h (eg, 6 completed days and 13 h) after birth is 21.8 mg/dL.

Gestational age of 38 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		7.9	8.1	8.3	8.5	8.7	8.9	9.1	9.3	9.5	9.7	9.9	10.1	10.3	10.5	10.7	10.8	11.0	11.2	11.4	11.6	11.7	11.9	12.1
1	12.3	12.4	12.6	12.8	12.9	13.1	13.3	13.4	13.6	13.8	13.9	14.1	14.2	14.4	14.5	14.7	14.8	15.0	15.1	15.3	15.4	15.6	15.7	15.8
2	16.0	16.1	16.2	16.4	16.5	16.6	16.8	16.9	17.0	17.1	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.1	18.2	18.3	18.4	18.5	18.6	18.7
3	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.5	19.6	19.7	19.8	19.9	20.0	20.0	20.1	20.2	20.3	20.3	20.4	20.5	20.6	20.6	20.7
4	20.7	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.9	20.9	20.9	20.9	20.9
5	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	21.0	21.0	21.0	21.0	21.0	21.0
6	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.1	21.1	21.1	21.1	21.1	21.1
7	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.2	21.2	21.2	21.2	21.2	21.2	21.2
8	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3
9	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.3	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4
10	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5
11	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6
12	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7
13	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.8[a]	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8

[a]The threshold ≥325 h (eg, 13 completed days and 13 h) after birth is 21.8 mg/dL.

Gestational age of 37 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		7.4	7.6	7.8	8.0	8.2	8.4	8.6	8.8	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.5	10.7	10.8	11.0	11.2	11.4	11.5
1	11.7	11.9	12.1	12.2	12.4	12.5	12.7	12.9	13.0	13.2	13.3	13.5	13.6	13.8	13.9	14.1	14.2	14.4	14.5	14.7	14.8	15.0	15.1	15.2
2	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.3	16.4	16.5	16.6	16.7	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.0
3	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.0	19.1	19.2	19.3	19.4	19.4	19.5	19.6	19.7	19.7	19.8	19.9	19.9	20.0
4	20.0	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1
5	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.3
6	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.4	20.4
7	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.5	20.5	20.5
8	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.5	20.6	20.6	20.6
9	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.6	20.7	20.7	20.7	20.7
10	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.7	20.8	20.8	20.8	20.8	20.8
11	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.8	20.9	20.9	20.9	20.9	20.9
12	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	20.9	21.0	21.0	21.0	21.0	21.0	21.0
13	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.1	21.1	21.1	21.1	21.1	21.1
14	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1

Gestational age of 36 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.9	7.1	7.3	7.5	7.7	7.9	8.1	8.3	8.5	8.7	8.8	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.5	10.6	10.8	11.0
1	11.2	11.3	11.5	11.7	11.8	12.0	12.1	12.3	12.5	12.6	12.8	12.9	13.1	13.2	13.4	13.5	13.7	13.8	13.9	14.1	14.2	14.4	14.5	14.6
2	14.8	14.9	15.0	15.1	15.3	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.2	16.3	16.5	16.6	16.7	16.8	16.9	17.0	17.1	17.2	17.3	17.4
3	17.5	17.6	17.7	17.8	17.9	17.9	18.0	18.1	18.2	18.3	18.4	18.4	18.5	18.6	18.7	18.8	18.8	18.9	19.0	19.0	19.1	19.2	19.2	19.3
4	19.3	19.3	19.3	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4
5	19.4	19.4	19.4	19.4	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5
6	19.5	19.5	19.5	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6
7	19.6	19.6	19.6	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7	19.7
8	19.7	19.7	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8	19.8
9	19.8	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9	19.9
10	19.9	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0	20.0
11	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1	20.1
12	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2	20.2
13	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.3	20.4	20.4
14	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4	20.4

Gestational age of 35 weeks and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.4	6.6	6.8	7.0	7.2	7.4	7.6	7.8	7.9	8.1	8.3	8.5	8.7	8.9	9.0	9.2	9.4	9.6	9.8	9.9	10.1	10.3	10.4
1	10.6	10.8	10.9	11.1	11.3	11.4	11.6	11.7	11.9	12.0	12.2	12.3	12.5	12.6	12.8	12.9	13.1	13.2	13.4	13.5	13.6	13.8	13.9	14.0
2	14.2	14.3	14.4	14.5	14.7	14.8	14.9	15.0	15.1	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5	16.6	16.7
3	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.5	17.6	17.7	17.8	17.8	17.9	18.0	18.1	18.1	18.2	18.3	18.3	18.4	18.5	18.5	18.6
4	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7
5	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.7	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8
6	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.8	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9	18.9
7	18.9	18.9	18.9	18.9	18.9	18.9	18.9	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.0
8	19.0	19.0	19.0	19.0	19.0	19.0	19.0	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1	19.1
9	19.1	19.1	19.1	19.1	19.1	19.1	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2	19.2
10	19.2	19.2	19.2	19.2	19.2	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3	19.3
11	19.3	19.3	19.3	19.3	19.3	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4	19.4
12	19.4	19.4	19.4	19.4	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5	19.5
13	19.5	19.5	19.5	19.5	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6
14	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6	19.6

SUPPLEMENTAL TABLE 2 Phototherapy thresholds by gestational age and age in hours for infants with a recognized hyperbilirubinemia neurotoxicity risk factor. These thresholds, also provided in Fig 3, are based on expert opinion rather than strong evidence on when the potential benefits of phototherapy exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. 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.

Gestational age of 38 weeks or more and a hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		6.4	6.6	6.8	7.0	7.2	7.3	7.5	7.7	7.9	8.1	8.3	8.5	8.6	8.8	9.0	9.2	9.4	9.5	9.7	9.9	10.0	10.2	10.4
1	10.5	10.7	10.8	11.0	11.2	11.3	11.5	11.6	11.8	11.9	12.1	12.2	12.4	12.5	12.7	12.8	12.9	13.1	13.2	13.3	13.5	13.6	13.7	13.9
2	14.0	14.1	14.2	14.4	14.5	14.6	14.7	14.8	14.9	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0	16.1	16.2	16.3	16.4	16.5
3	16.6	16.6	16.7	16.8	16.9	17.0	17.1	17.1	17.2	17.3	17.4	17.4	17.5	17.6	17.6	17.7	17.8	17.8	17.9	18.0	18.0	18.1	18.1	18.2
4	18.2[a]	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

[a]The threshold ≥96 h (eg, 4 completed days) after birth is 18.2 mg/dL.

Gestational age of 37 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		5.9	6.1	6.3	6.5	6.7	6.9	7.0	7.2	7.4	7.6	7.8	8.0	8.1	8.3	8.5	8.7	8.9	9.0	9.2	9.4	9.5	9.7	9.9
1	10.0	10.2	10.4	10.5	10.7	10.8	11.0	11.1	11.3	11.4	11.6	11.7	11.9	12.0	12.2	12.3	12.4	12.6	12.7	12.9	13.0	13.1	13.2	13.4
2	13.5	13.6	13.8	13.9	14.0	14.1	14.2	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3	15.4	15.5	15.6	15.7	15.8	15.9	16.0
3	16.1	16.2	16.3	16.4	16.5	16.6	16.6	16.7	16.8	16.9	17.0	17.0	17.1	17.2	17.2	17.3	17.4	17.4	17.5	17.6	17.6	17.7	17.8	17.8
4	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
5	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1
6	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.2[a]	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

[a]The threshold ≥151 h (eg, 6 completed days and 7 h) after birth is 18.2 mg/dL.

Gestational age of 36 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		5.4	5.6	5.8	6.0	6.2	6.3	6.5	6.7	6.9	7.1	7.3	7.4	7.6	7.8	8.0	8.1	8.3	8.5	8.6	8.8	9.0	9.1	9.3
1	9.4	9.6	9.8	9.9	10.1	10.2	10.4	10.5	10.7	10.8	11.0	11.1	11.2	11.4	11.5	11.7	11.8	11.9	12.1	12.2	12.3	12.5	12.6	12.7
2	12.8	13.0	13.1	13.2	13.3	13.4	13.5	13.7	13.8	13.9	14.0	14.1	14.2	14.3	14.4	14.5	14.6	14.7	14.8	14.9	15.0	15.1	15.2	15.3
3	15.4	15.4	15.5	15.6	15.7	15.8	15.8	15.9	16.0	16.1	16.1	16.2	16.3	16.4	16.4	16.5	16.6	16.6	16.7	16.7	16.8	16.8	16.9	17.0
4	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1
5	17.1	17.1	17.1	17.1	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.3
6	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.4	17.4	17.4	17.4	17.4
7	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5
8	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.5	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6	17.6
9	17.6	17.6	17.6	17.6	17.6	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7	17.7
10	17.7	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.8	17.9	17.9	17.9	17.9
11	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	17.9	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
12	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.1
13	18.1	18.1	18.1	18.1	18.1	18.1	18.1	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2
14	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2	18.2

Gestational age of 35 and an additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		4.9	5.1	5.3	5.5	5.6	5.8	6.0	6.2	6.4	6.5	6.7	6.9	7.1	7.2	7.4	7.6	7.7	7.9	8.1	8.2	8.4	8.6	8.7
1	8.9	9.0	9.2	9.3	9.5	9.6	9.8	9.9	10.1	10.2	10.3	10.5	10.6	10.8	10.9	11.0	11.2	11.3	11.4	11.5	11.7	11.8	11.9	12.0
2	12.2	12.3	12.4	12.5	12.6	12.7	12.8	13.0	13.1	13.2	13.3	13.4	13.5	13.6	13.7	13.8	13.9	14.0	14.1	14.2	14.2	14.3	14.4	14.5
3	14.6	14.7	14.8	14.8	14.9	15.0	15.1	15.1	15.2	15.3	15.3	15.4	15.5	15.5	15.6	15.7	15.7	15.8	15.8	15.9	15.9	16.0	16.1	16.1
4	16.1	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.2	16.3	16.3	16.3	16.3
5	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.3	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4
6	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.4	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5	16.5
7	16.5	16.5	16.5	16.5	16.5	16.5	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6	16.6
8	16.6	16.6	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.7	16.8	16.8	16.8
9	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.8	16.9	16.9	16.9	16.9	16.9	16.9	16.9
10	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	16.9	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
11	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1	17.1
12	17.1	17.1	17.1	17.1	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.2	17.3
13	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.3	17.4	17.4	17.4	17.4	17.4
14	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4	17.4

SUPPLEMENTAL TABLE 3 Exchange transfusion thresholds by gestational age for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 6, are based on expert opinion rather than strong evidence on when the potential benefits of exchange transfusion exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. 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.

Gestational age of 38 weeks or more and no hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		18.0	18.2	18.4	18.5	18.7	18.8	19.0	19.1	19.3	19.4	19.6	19.7	19.9	20.0	20.1	20.3	20.4	20.6	20.7	20.8	21.0	21.1	21.2
1	21.4	21.5	21.6	21.7	21.9	22.0	22.1	22.2	22.3	22.4	22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9
2	24.0	24.1	24.2	24.3	24.4	24.5	24.6	24.7	24.7	24.8	24.9	25.0	25.1	25.2	25.2	25.3	25.4	25.5	25.5	25.6	25.7	25.7	25.8	25.9
3	25.9	26.0	26.0	26.1	26.2	26.2	26.3	26.3	26.4	26.4	26.5	26.5	26.6	26.6	26.7	26.7	26.7	26.8	26.8	26.9	26.9	26.9	27.0	27.0
4	27.0[a]	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

[a]The threshold ≥96 h (eg, 4 completed days) after birth is 27 mg/dL.

Gestational age of 37 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		17.0	17.1	17.3	17.5	17.6	17.8	17.9	18.1	18.2	18.4	18.5	18.7	18.8	18.9	19.1	19.2	19.4	19.5	19.6	19.8	19.9	20.1	20.2
1	20.3	20.5	20.6	20.7	20.8	21.0	21.1	21.2	21.3	21.5	21.6	21.7	21.8	21.9	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8	22.9	23.0
2	23.1	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.9	24.0	24.1	24.2	24.3	24.4	24.5	24.5	24.6	24.7	24.8	24.9	24.9	25.0	25.1	25.2
3	25.2	25.3	25.4	25.5	25.5	25.6	25.7	25.7	25.8	25.8	25.9	26.0	26.0	26.1	26.1	26.2	26.2	26.3	26.3	26.4	26.4	26.5	26.5	26.5
4	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7
5	26.7	26.7	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.9	26.9	26.9	26.9	26.9	26.9
6	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	27.0[a]	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

[a]The threshold ≥151 h (eg, 6 completed days and 10 h) after birth is 27.0 mg/dL.

Gestational age of 36 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		15.9	16.1	16.2	16.4	16.5	16.7	16.8	16.9	17.1	17.2	17.4	17.5	17.7	17.8	17.9	18.1	18.2	18.3	18.5	18.6	18.7	18.9	19.0
1	19.1	19.2	19.4	19.5	19.6	19.7	19.9	20.0	20.1	20.2	20.4	20.5	20.6	20.7	20.8	20.9	21.0	21.2	21.3	21.4	21.5	21.6	21.7	21.8
2	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.7	22.8	22.9	23.0	23.1	23.2	23.2	23.3	23.4	23.5	23.6	23.7	23.8	23.8	23.9	24.0
3	24.1	24.1	24.2	24.3	24.4	24.4	24.5	24.6	24.6	24.7	24.8	24.8	24.9	25.0	25.0	25.1	25.2	25.2	25.3	25.3	25.4	25.4	25.5	25.5
4	25.5	25.5	25.5	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.7
5	25.7	25.7	25.7	25.7	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.9	25.9	25.9	25.9	25.9	25.9	25.9
6	25.9	25.9	25.9	25.9	25.9	25.9	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.1	26.1	26.1	26.1
7	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2
8	26.2	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.4
9	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.4	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5	26.5
10	26.5	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.6	26.7	26.7	26.7	26.7	26.7	26.7
11	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.7	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8
12	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.8	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9	26.9
13	26.9	26.9	26.9	26.9	26.9	26.9	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0
14	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0	27.0

Gestational age of 35 weeks and no hyperbilirubinemia neurotoxicity risk factor other than gestational age. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		14.9	15.0	15.1	15.3	15.4	15.6	15.7	15.8	16.0	16.1	16.2	16.4	16.5	16.6	16.8	16.9	17.0	17.2	17.3	17.4	17.5	17.7	17.8
1	17.9	18.0	18.2	18.3	18.4	18.5	18.7	18.8	18.9	19.0	19.1	19.2	19.4	19.5	19.6	19.7	19.8	19.9	20.0	20.1	20.2	20.3	20.5	20.6
2	20.7	20.8	20.9	21.0	21.1	21.2	21.3	21.4	21.5	21.6	21.7	21.7	21.8	21.9	22.0	22.1	22.2	22.3	22.4	22.5	22.6	22.6	22.7	22.8
3	22.9	23.0	23.1	23.1	23.2	23.3	23.4	23.4	23.5	23.6	23.7	23.7	23.8	23.9	23.9	24.0	24.1	24.1	24.2	24.3	24.3	24.4	24.4	24.5
4	24.5	24.5	24.5	24.5	24.5	24.5	24.5	24.5	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.6	24.7	24.7	24.7	24.7	24.7
5	24.7	24.7	24.7	24.7	24.7	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.8	24.9	24.9	24.9	24.9	24.9	24.9	24.9	24.9
6	24.9	24.9	24.9	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.1	25.1	25.1	25.1	25.1	25.1	25.1	25.1	25.1
7	25.1	25.1	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.2	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3	25.3
8	25.3	25.3	25.3	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.4	25.5	25.5	25.5	25.5	25.5	25.5	25.5	25.5	25.5
9	25.5	25.5	25.5	25.5	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.6	25.7	25.7	25.7	25.7	25.7	25.7	25.7
10	25.7	25.7	25.7	25.7	25.7	25.7	25.7	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.8	25.9	25.9	25.9
11	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.9	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0	26.0
12	26.0	26.0	26.0	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.1	26.2	26.2	26.2	26.2	26.2
13	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.2	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3
14	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3	26.3

SUPPLEMENTAL TABLE 4 Exchange transfusion thresholds by gestational age for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age. These thresholds, also provided in Fig 7, are based on expert opinion rather than strong evidence on when the potential benefits of exchange transfusion exceed its potential harms. Use the total serum bilirubin concentration. Do not subtract direct-reacting or conjugated bilirubin from the total serum bilirubin. 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.

Gestational age of 38 weeks or more and any hyperbilirubinemia neurotoxicity risk factors. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		14.8	15.0	15.1	15.2	15.4	15.5	15.6	15.8	15.9	16.0	16.1	16.3	16.4	16.5	16.6	16.7	16.9	17.0	17.1	17.2	17.3	17.4	17.6
1	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.7	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.6	19.7	19.8	19.9	19.9	20.0
2	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.8	20.8	20.9	21.0	21.1	21.2	21.3	21.3	21.4	21.5	21.6	21.7	21.7	21.8	21.9	22.0	22.0
3	22.1	22.2	22.2	22.3	22.4	22.5	22.5	22.6	22.7	22.7	22.8	22.8	22.9	23.0	23.0	23.1	23.1	23.2	23.3	23.3	23.4	23.4	23.5	23.5
4	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
6	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
7	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
8	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
9	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
10	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
11	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
12	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
13	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
14	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5

Gestational age of 37 weeks and any additional hyperbilirubinemia neurotoxicity risk factors. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		14.3	14.4	14.6	14.7	14.8	15.0	15.1	15.2	15.4	15.5	15.6	15.7	15.9	16.0	16.1	16.2	16.4	16.5	16.6	16.7	16.8	17.0	17.1
1	17.2	17.3	17.4	17.5	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0	19.1	19.2	19.3	19.4	19.5	19.6
2	19.7	19.8	19.9	20.0	20.1	20.1	20.2	20.3	20.4	20.5	20.6	20.7	20.7	20.8	20.9	21.0	21.1	21.1	21.2	21.3	21.4	21.4	21.5	21.6
3	21.7	21.7	21.8	21.9	21.9	22.0	22.1	22.1	22.2	22.3	22.3	22.4	22.5	22.5	22.6	22.6	22.7	22.8	22.8	22.9	22.9	23.0	23.0	23.1
4	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2
5	23.2	23.2	23.2	23.2	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.4	23.4	23.4
6	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
7	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
8	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
9	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
10	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
11	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
12	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
13	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
14	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5

Gestational age of 36 weeks and any additional hyperbilirubinemia neurotoxicity risk factors. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		13.7	13.9	14.0	14.1	14.3	14.4	14.5	14.7	14.8	14.9	15.1	15.2	15.3	15.4	15.6	15.7	15.8	15.9	16.1	16.2	16.3	16.4	16.5
1	16.6	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4	18.5	18.6	18.7	18.8	18.9	19.0
2	19.1	19.2	19.2	19.3	19.4	19.5	19.6	19.7	19.7	19.8	19.9	20.0	20.1	20.1	20.2	20.3	20.3	20.4	20.5	20.6	20.6	20.7	20.8	20.8
3	20.9	20.9	21.0	21.1	21.1	21.2	21.2	21.3	21.4	21.4	21.5	21.5	21.6	21.6	21.7	21.7	21.8	21.8	21.9	21.9	22.0	22.0	22.0	22.1
4	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.3	22.3
5	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4
6	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6
7	22.6	22.6	22.6	22.6	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.8	22.8	22.8	22.8	22.8
8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9
9	22.9	22.9	22.9	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.0	23.1	23.1	23.1
10	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.1	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2
11	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.2	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3
12	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.3	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4
13	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.4	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5
14	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5	23.5

Gestational age of 35 weeks and any additional hyperbilirubinemia neurotoxicity risk factor. The threshold is TSB in mg/dL.

	Hour on Completed Day																							
Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
0		13.1	13.3	13.4	13.6	13.7	13.8	14.0	14.1	14.3	14.4	14.5	14.6	14.8	14.9	15.0	15.1	15.3	15.4	15.5	15.6	15.8	15.9	16.0
1	16.1	16.2	16.3	16.4	16.5	16.6	16.8	16.9	17.0	17.1	17.2	17.3	17.4	17.5	17.6	17.7	17.7	17.8	17.9	18.0	18.1	18.2	18.3	18.4
2	18.5	18.5	18.6	18.7	18.8	18.9	18.9	19.0	19.1	19.2	19.2	19.3	19.4	19.4	19.5	19.6	19.6	19.7	19.8	19.8	19.9	19.9	20.0	20.1
3	20.1	20.2	20.2	20.3	20.3	20.4	20.4	20.5	20.5	20.6	20.6	20.6	20.7	20.7	20.8	20.8	20.8	20.9	20.9	20.9	21.0	21.0	21.0	21.1
4	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.1	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.2	21.3	21.3	21.3	21.3	21.3
5	21.3	21.3	21.3	21.3	21.3	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.4	21.5	21.5	21.5	21.5	21.5	21.5	21.5	21.5
6	21.5	21.5	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7	21.7
7	21.7	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.9	21.9	21.9	21.9	21.9	21.9	21.9	21.9	21.9	21.9	21.9
8	21.9	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.0	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1	22.1
9	22.1	22.1	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.2	22.3	22.3	22.3	22.3	22.3	22.3	22.3	22.3
10	22.3	22.3	22.3	22.3	22.3	22.3	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.4	22.5	22.5	22.5	22.5
11	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.5	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6	22.6
12	22.6	22.6	22.6	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.7	22.8	22.8	22.8	22.8
13	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.8	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9
14	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9	22.9

Reference for Phototherapy and Exchange Transfusion Thresholds

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