Managing neonatal hyperbilirubinemia: An updated guideline

Andrew P. Chastain, MSPAS, PA-C; Anne L. Geary, MPAS, PA-C; Kevin M. Bogenschutz, DMS, PA-C

ABSTRACT

More than 80% of newborn infants experience jaundice as a result of elevated bilirubin during the first few weeks after birth. In most cases, hyperbilirubinemia is physiologic, but persistent and extreme elevations can lead to serious long-term complications, such as kernicterus. To avoid these complications and help clinicians in the successful assessment, evaluation, and treatment of hyperbilirubinemia, the American Academy of Pediatrics updated its clinical practice guideline for neonatal hyperbilirubinemia. This article reviews the guideline and highlights significant updates, such as an elevation in the threshold for phototherapy and exchange transfusion, inclusion of gestational age, and removal of racially based norms.

Keywords: hyperbilirubinemia, neonatal, jaundice, guideline, pediatrics, phototherapy

Learning objectives

- Identify the risks of high serum bilirubin concentrations in a neonate.
- Differentiate physiologic jaundice from pathologic jaundice.
- Apply a management plan based on thresholds of TSB.
- Understand how the updated AAP guideline changes the standard of care in evaluating and treating newborns and infants with jaundice.
- Discuss how genetic ancestry, not race alone, plays a role in identifying risk factors for hyperbilirubinemia neurotoxicity.

More than 80% of all newborns exhibit some degree of jaundice during the first few weeks of life.[1,2] For most, this jaundice is self-limiting and not related to a pathologic cause but rather linked to physiologic reduction in bilirubin conjugation and excretion or increased production. For some, however, severe hyperbilirubinemia can lead to acute hyperbilirubinemia encephalopathy or kernicterus.[3] Jaundice within the first 24 hours after birth is one of several major risk factors for severe hyperbilirubinemia. To aid clinicians in evaluating and treating neonatal hyperbilirubinemia and preventing kernicterus and lifelong neurologic complications, the American Academy of Pediatrics (AAP) has provided clinical practice guidelines since 1994.[3,4] In late 2022, the AAP updated its guideline on managing newborn hyperbilirubinemia in infants born at 35 weeks gestation or later, and published an accompanying technical report, building on previous recommendations and framed by an additional 14 years of new data.[5,6]

© ANASTASIIA YLITKO/SHUTTERSTOCK.COM

Key updates from the guideline include:

- Increased thresholds for initiating phototherapy or exchange transfusion.
- Guidance on when follow-up or repeated measurement of bilirubin should occur.
- Determination of when escalation of care is warranted.
- Risk assignment revision for developing significant hyperbilirubinemia (eliminating race and ethnicity as independent variables).[5,7]

PHYSIOLOGY OF NEONATAL JAUNDICE

Jaundice results from elevated levels of bilirubin, a waste product of senescent red blood cell (RBC) breakdown. Neonatal jaundice generally is divided into two types: physiologic and pathophysiologic jaundice. At the end of their 60 to 90 days of life, fetal hemoglobin (Hb F, which makes up 78% of all hemoglobin at birth) is broken down

At Butler University in Indianapolis, Ind., **Andrew P. Chastain, Anne L. Geary**, and **Kevin M. Bogenschutz** are assistant professors in the PA program. The authors have disclosed no potential conflicts of interest, financial or otherwise.

DOI:10.1097/01.JAA.0000000000000120

Key points

- The newest AAP guideline on hyperbilirubinemia in neonates increases the thresholds for initiating phototherapy and escalation of care.
- The frequency of bilirubin measurement is guided by neonatal risk factors, gestational age, and the trend in previous measurements.
- The guideline redefines risk factors for developing significant hyperbilirubinemia by eliminating race and ethnicity as independent variables.

by macrophages in the spleen.[8] The heme component is further broken down into unconjugated bilirubin. Unconjugated bilirubin requires albumin transport to the liver, where hepatocytes conjugate the bilirubin through the uridine 5'-diphospho-glucuronosyltransferase (UGT) enzyme, making it water-soluble. The bilirubin then travels through the bile ducts and gallbladder to eventually be excreted into the small intestine. Microbes in the small intestine transform conjugated bilirubin into urobilinogen, which is then excreted through the stool and urine or reabsorbed by the liver.

Newborns are inefficient at conjugating bilirubin because their UGT enzyme activity is about 1% of that of adults.[9] In addition, after birth, macrophages destroy a significant number of fetal RBCs. This elevates unconjugated bilirubin for the first 2 to 7 days of life before unconjugated bilirubin gradually decreases.[10] Physiologic jaundice (also called benign neonatal hyperbilirubinemia) is a benign, mild elevation of unconjugated bilirubin that occurs in most newborns. Jaundice becomes pathologic when the total serum bilirubin is significantly elevated. Although unconjugated hyperbilirubinemia may be physiologic, conjugated hyperbilirubinemia of a newborn is more indicative of a pathologic origin and requires prompt evaluation and treatment because of the risk for biliary atresia or cholestasis.[11]

Neonatal jaundice results from increased bilirubin production and/or decreased bilirubin clearance. Complications include hearing loss, visual abnormalities, and poor dentition.[12] Increased production of unconjugated bilirubin may result from ABO or Rh(D) incompatibility, in which case direct antiglobulin testing should be performed to further evaluate an infant whose mother's antibody screen is positive or is unknown. Other causes of increased production of unconjugated bilirubin include cephalohematoma, glucose-6-phosphate dehydrogenase (G6PD) deficiency, spherocytosis, infection, and other causes of RBC breakdown.[13] Decreased clearance of unconjugated bilirubin may result from disruption of the UGT enzyme, such as the genetic disorders Crigler-Najjar and Gilbert syndromes. Patients with Gilbert syndrome, which typically appears in early adolescence, have mildly reduced UGT activity that is overall benign.[14] However, Crigler-Najjar syndrome is caused by absent or defective UGT, and can be fatal. Decreased elimination of stool also impairs bilirubin clearance. Breastfed newborns, as the breast milk supply is established, may have relative volume depletion and caloric deprivation in the first few days of life, resulting in delayed passage of meconium and elevation of unconjugated bilirubin.[13]

Bilirubin toxicity, or kernicterus, results from elevated levels of unbound lipid-soluble unconjugated bilirubin crossing the blood-brain barrier. Bilirubin inhibits DNA and protein synthesis, particularly in the brainstem nuclei and basal ganglia, which may result in permanent molecular and cytologic injury to brain cells.[15] The duration of exposure and amount of bilirubin in the brain determines the severity of brain damage; however, total serum bilirubin (TSB) level alone does not always correlate well with bilirubin toxicity.[12] Kernicterus may cause significant and irreversible bilirubin-induced neurologic dysfunction, such as cerebral palsy, sensorineural impairment, or encephalopathy.[12] Preterm infants are at even higher risk of toxic effects because of their lower serum albumin levels.[12]

SCREENING AND DIAGNOSIS

Screening for neonatal hyperbilirubinemia begins with a careful investigation of the maternal record or family history. Risk factors that increase a patient's likelihood of developing bilirubin neurotoxicity are not always obvious. Common risk factors include lower gestational age at birth, jaundice in the first 24 hours, exclusive breastfeeding (with suboptimal intake), family history of inherited RBC disorders, and risk for hemolytic disease.[5] Infants with risk factors for significant hyperbilirubinemia require close monitoring. In its 2022 revision of its clinical practice guideline, the AAP recommends screening of all infants born at 35 weeks gestation or later for hyperbilirubinemia; many hospital systems require this documentation.[1] This often starts with transcutaneous monitoring, but includes TSB. The goal of this universal screening for neonatal hyperbilirubinemia is to reduce the incidence of bilirubin toxicity while minimizing harm to the patient and parental anxiety.[13] Neonatal jaundice is a common cause of readmission to the hospital after birth, and screening before discharge can identify patients who may need earlier and more frequent follow-up. However, the cost also must be considered. Suresh and Clark estimated that 128,000 newborns would need to be screened to prevent a single case of kernicterus, at a cost of $5.7 to $9.2 million.[16] Although the cost of screening must be considered, kernicterus can leave a patient with severe neurologic disability requiring long-term highly skilled care.

Assessment of bilirubin is achieved by considering either TSB or transcutaneous bilirubin (TcB) measured at age 24 to 60 hours, in combination with clinical risk factors.[1] Transcutaneous measurement devices reduce the frequency

of blood testing, which often is an anxiety-provoking experience for new parents. However, infants with darker skin phenotypes may have less reliable transcutaneous measurements.[17]

Evidence suggests that combining the predischarge TcB or TSB measurement with clinical risk factors improves the prediction model of those at risk for developing hyperbilirubinemia.[4]

The AAP recommends universal screening using a TcB or TSB at 24 to 28 hours of life or before hospital discharge, whichever occurred sooner.[3-5] The AAP warns against using visual inspection as the sole screening tool, indicating differences as great as 13 to 15 mg/dL between the measured bilirubin and the clinician-assessed visual dermal zones.[5,18] The updated AAP guideline notes the importance of the physical examination in evaluating for hyperbilirubinemia, indicating that all infants should be visually assessed for jaundice at least every 12 hours following delivery until discharge.[5] If visual inspection is concerning for jaundice, a TcB or TSB should be promptly measured.[5]

In the clinical setting, neonatal hyperbilirubinemia is diagnosed by plotting the patient's TSB compared with chronologic age, while considering their gestational age. The likelihood of developing severe hyperbilirubinemia in conjunction with patient-specific risk factors drives clinical decision-making.

CHANGES IN THE 2022 GUIDELINE

The guideline outlines a comprehensive approach to screening and treating hyperbilirubinemia, with practice changes based on evidence or significant clinical experience.[5] It focuses on five essential components: prevention, assessment and monitoring, treatment, postdischarge follow-up, and hospital policies and procedures.[5] The first four components contain the most clinically relevant changes. Within each of these essential components are 25 key action statements.[5,7] These action statements were framed as recommendations in previous versions of the guideline. Each action statement is appended with an aggregate evidence statement and grade of recommendation.

PREVENTION

Prevention of hyperbilirubinemia starts with identifying the risk for isoimmune hemolytic disease of the fetus or newborn; this begins during pregnancy with maternal screening for ABO blood group, Rh(D) type, and antibodies. Early testing can identify mothers for whom Rh(D) immunoglobulin (RhIG) would be indicated, as well as newborns who would be at risk for hemolytic disease of the newborn. The guideline also includes a focus on prevention by providing feeding support while promoting a comprehensive, evidence-based approach to aiding breastfeeding mothers. This includes encouraging breastfeeding mothers to feed on demand 8 to 12 times in 24 hours. In addition, it continues to warn against supplementing oral intake with water or dextrose water but does recognize the role of temporary supplementation with formula or donor breast milk to improve hydration status and promote defecation.[5]

ASSESSMENT AND MONITORING

Assessment for hyperbilirubinemia begins with risk factor evaluation. The updated guideline includes two tiers of risk stratification.

The first tier considers risk factors for developing significant hyperbilirubinemia. Lower gestational age is directly proportional to an increased risk for significant hyperbilirubinemia (increasing for every additional week below 40 weeks). Other updated risk factors include the need for phototherapy before discharge, Down syndrome, macrosomia in an infant whose mother has diabetes, perinatal jaundice in a parent or sibling requiring treatment, predischarge screening that approaches the threshold for treatment, and a rapid rate of increase in TcB or TSB. New language in the updated AAP guideline shapes the approach to exploring family history and genetic ancestry for inherited RBC disorders. Gone is the language in the 2009 and earlier updates that cited East Asian race as a specific race-based risk factor. Using race alone to identify risk for hyperbilirubinemia has been shown to be scientifically erroneous. Genetic ancestry contributes to the increased risk of hyperbilirubinemia, and this is not always phenotypically obvious.[19,20] Clinicians and healthcare systems use these risk factors to create monitoring plans for neonatal bilirubin.

> Frequently monitor patients who have multiple measures of bilirubin showing a rapid rate of rise.

The second tier of the risk stratification includes consideration of risk factors for developing kernicterus and gives clinicians increased clinical justification for starting treatment or escalating care. Additionally, this list includes the increased risk among premature infants, whose risk of developing neurotoxic hyperbilirubinemia increases with decreasing gestational age (**Table 1**).

Risk factors are combined with a set of nomograms that display TSB plotted against the patient's age in hours (up to 14 days) while also considering the patient's gestational age (from term to 35 weeks). The new guideline uses four nomograms, compared with the previous two, to guide the thresholds for treatment of the newborn with hyperbilirubinemia.[3-5] The guideline no longer uses risk zones to forecast risk for the progression of significant hyperbilirubinemia.[3] The latest guideline has two nomo-

grams that guide phototherapy treatment thresholds (**Figures 1** and **2**). The first incorporates neonates with no hyperbilirubinemia risk factors, and the second guides treatment of those with one or more hyperbilirubinemia neurotoxicity risk factor. Each graph also presents threshold curves that vary based on the newborn's gestational age at birth (from 35 weeks through and beyond 40 weeks). The second set of nomograms defines thresholds for more severe hyperbilirubinemia where exchange transfusion is indicated. Both consider the TSB, chronologic age (in hours, up to 336), gestational age, and assessed risk factors. This information guides how frequently to obtain additional monitoring for bilirubin and determinations about when treatment and escalation of care should be initiated. Escalation of care includes hospital admission, intensive phototherapy, IV fluid administration, and exchange transfusion.[5] TcB should be measured in the first 24 to 48 hours. TSB should be performed in infants whose TcB is 15 mg/dL or greater or in those whose measured TcB is within 3 mg/dL of the treatment threshold. Additionally, more frequent monitoring should occur in patients who have multiple measures of bilirubin showing a rapid rate of rise (defined as 0.3 mg/dL per hour or greater in patients age 24 hours and younger or 0.2 mg/dL per hour or greater in patients older than age 24 hours).[5]

Infants who have a high TSB because of a high direct bilirubin concentration (defined as greater than 1 mg/dL)

TABLE 1. Risk factors for developing significant or neurotoxic hyperbilirubinemia: Comparison of the updated 2022 AAP guideline with the 2009 guideline[4,5]

Items marked with an asterisk indicate changes in the 2022 guideline.

Risk factors for developing significant hyperbilirubinemia		Risk factors for developing neurotoxic hyperbilirubinemia	
2022	**2009**	**2022**	**2009**
Predischarge TSB or TcB concentration close to phototherapy threshold	Predischarge TSB or TcB measurement in the high-risk or high-intermediate-risk zone	*Isoimmune hemolytic disease (i.e., positive direct antiglobulin test), G6PD deficiency, or other hemolytic conditions	Isoimmune hemolytic disease
			G6PD deficiency
Lower gestational age (risk increases with each additional week less than 40 weeks)	Lower gestational age	*Significant clinical instability in the previous 24 hours	Asphyxia
			Acidosis
Jaundice in the first 24 hours after birth	Jaundice observed in the first 24 hours	Sepsis	Sepsis
*Parent or sibling with history of requiring perinatal phototherapy or exchange transfusion	Sibling with history of perinatal jaundice	Albumin less than 3 mg/dL	Albumin less than 3 mg/dL
*Hemolysis from any cause, if known or suspected based on rapid rate of increase in TSB or TcB of 0.3 mg/dL per hour or greater in the first 24 hours OR greater than 0.2 mg/dL per hour thereafter	Isoimmune or other hemolytic disease (for example, G6PD deficiency)	*Gestational age less than 38 weeks (which increases with the degree of prematurity)	
Exclusive breastfeeding with suboptimal intake	Exclusive breastfeeding, particularly if nursing is not going well and weight loss is excessive		
Scalp hematoma or significant bruising	Cephalohematoma or significant bruising		
*Family history or genetic ancestry suggestive of inherited RBC disorders, including G6PD deficiency	East Asian race		
*Macrosomic infant of a diabetic mother			
*Down syndrome			
*Phototherapy before discharge			

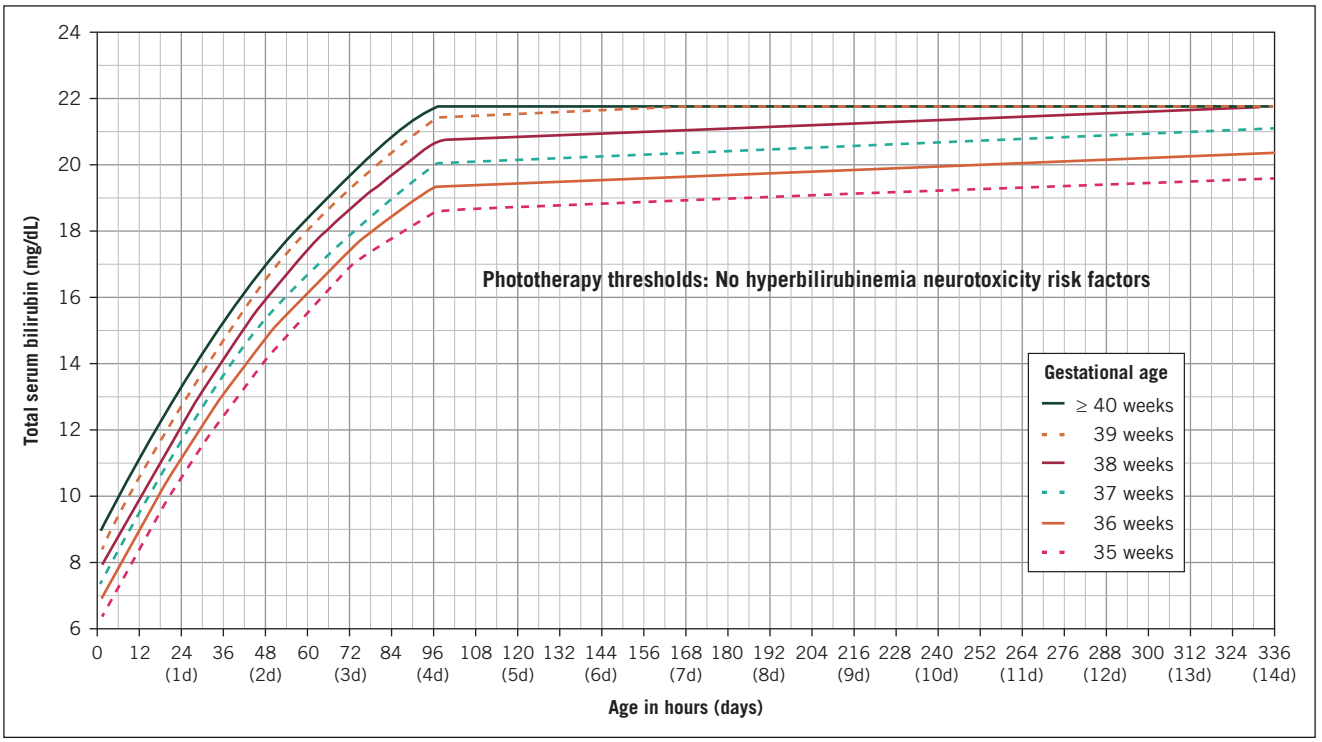

FIGURE 1. Phototherapy thresholds by gestational age and age in hours for infants with no recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age.

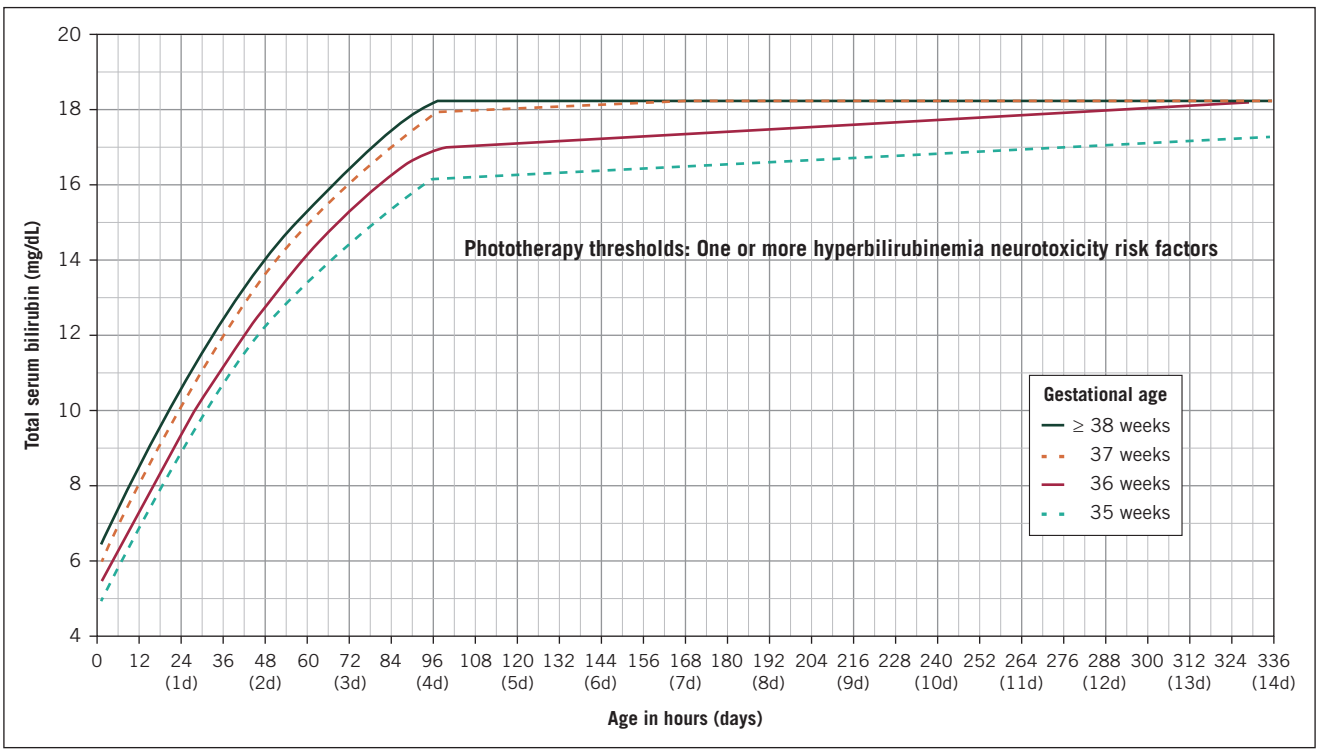

FIGURE 2. Phototherapy thresholds by gestational age and age in hours for infants with any recognized hyperbilirubinemia neurotoxicity risk factors other than gestational age.

or conjugated bilirubin (defined as 0.3 mg/dL or greater) should be monitored for other signs that might indicate biliary atresia or cholestasis. Consider that in addition to the more common causes of direct hyperbilirubinemia mentioned above, other conditions in the differential diagnosis for these newborns include urinary tract infections, inborn errors of metabolism, neonatal sepsis, and hemolytic disease.

The guideline calls for continued assessment and monitoring of TSB at a frequency that considers patient risk factors, measured TSB values, and trajectory of TSB rise over time. Measured values should continue to help guide treatment or escalation (or de-escalation) of care until a decreasing trend in bilirubin is noted or the patient has reached the physiologic nadir.

TREATMENT

Since 1958, the mainstay of treatment for hyperbilirubinemia in infants is phototherapy, which reduces bilirubin levels by converting unconjugated bilirubin via photoisomerization.[21] The goal of treatment with phototherapy is to reduce the risk for kernicterus and the probability that escalation of care (hospitalization, exchange transfusion) would be needed.[5] Treatment with phototherapy is initiated once a patient has reached the threshold based on the hour-specific nomogram that fits the patient's risk profile. Regardless of risk, the thresholds now are appreciably higher than those seen in previous guidelines. This is due in part to an appreciation that kernicterus does not occur until bilirubin levels far exceed previously published recommendations.[5,22-25] These threshold changes also are informed by research into the risks of exposure to photons (particularly in wavelengths above those that are indicated as therapeutic), including oxidative stress and increased risks for epilepsy.[26,27] Included in the guideline are the specifics for optimizing the effectiveness of phototherapy by maximizing the exposed body surface area to phototherapy and using devices that emit blue light-emitting diode light with a specific irradiance (at least 30 mcW/cm^2 per nm) and a wavelength of about 475 nm.[28,29] In patients whose bilirubin remains elevated or continues to increase despite treatment, measure the irradiance and distance to the patient's skin from the light source to ensure effectiveness. Adding sources of phototherapy can increase the body surface area exposed. Efforts should be made to provide treatment in the presence of the patient's mother to encourage bonding and support the establishment of breast milk supply and feeding consistency. Optimal phototherapy shortens duration of treatment and allows for resumption of mother-baby bonding and earlier discharge. Hospital discharge should not necessarily be delayed based on the need for treatment with phototherapy as long as there is a follow-up plan, the necessary equipment can be made available without delay, and the patient has no risk factors for hyperbilirubinemia neurotoxicity.[5]

Ongoing treatment should be guided by continued assessment of bilirubin by transcutaneous or serum measures. Infants exposed to phototherapy will no longer be easily assessed with TcB and will require serum measurements to evaluate their bilirubin levels accurately. TcB meters use optical spectroscopy to read the bilirubin in the cutaneous space (which includes the intra- and extravascular space) at the site of measurement. If this site has been exposed to phototherapy, the quotient of bilirubin in the extravascular space is reduced and total bilirubin will be underestimated.[30]

Discontinuation of phototherapy can be considered if the patient's TSB is less than at least 2 mg/dL below the treatment threshold based on the hour-specific threshold at the initiation of phototherapy. Consider a longer period of treatment with phototherapy if the infant has risk factors for rebound hyperbilirubinemia, such as gestational age less than 38 weeks, age less than 48 hours at the start of phototherapy, or hemolytic disease.[5]

In newborns who reach (or rebound back to) the phototherapy threshold as an outpatient, home phototherapy can be used. The guideline suggests that this be used only in infants who were born at more than 38 weeks of gestation, have no neurotoxicity risk factors, are feeding and otherwise clinically well, have access to home phototherapy without significant delay, and are not more than 1 mg/dL above the phototherapy threshold at the time of measurement. These infants must have daily bilirubin measurements. Exclusion of any of these criteria would support the decision for readmission for continued care.

Newborns who continue to have increasing levels of bilirubin despite treatment, or those whose rate of rise is alarmingly high, need to be evaluated for escalation of care using the exchange transfusion graphs. If a patient is within 2 mg/dL of the exchange transfusion curve, provisions should be made to ensure the patient is in, admitted to, or transferred to a center capable of providing advanced care, such as a level III or IV neonatal ICU. If all efforts fail to control the rise in the measured bilirubin, exchange transfusion(s) are indicated to avoid acute kernicterus.

POSTDISCHARGE FOLLOW-UP

Follow-up after discharge is a complex algorithm and is informed by how likely the patient is to develop hyperbilirubinemia. The updated guideline suggests that the interval between discharge and outpatient follow-up is based on the calculated difference between the most recent measurement and the phototherapy threshold. The proximity to a patient's phototherapy threshold, based on their postnatal age, guides the recommended interval to follow-up. Other continued considerations, such as neurotoxicity risk factors, gestational age, feeding quality, and weight, should be considered when determining the interval between discharge and follow-up with the primary

care provider. The PCP also should consider these factors when determining when the patient should next be examined and when additional measures of TSB or TcB should be collected.

Engaging parents in discourse about the importance of keeping outpatient appointments should center on avoiding the deleterious effects of kernicterus.

CONCLUSION

Because the vast majority of newborns will experience some degree of jaundice, screening, close monitoring, and appropriate treatment (when indicated) are important. Elevated bilirubin concentrations can lead to acute bilirubin encephalopathy and to kernicterus, a permanent disabling neurologic condition, reinforcing the importance of screening and prevention measures. Risk assessment, in combination with measured TcB or TSB and gestational age at birth, guides further evaluation and management strategy. The updated AAP guideline makes significant revisions to previous publications, such as an elevated threshold for phototherapy and exchange thresholds, inclusion of gestational age, and removal of racially based norms. Successful implementation of the guideline gives clinicians the data-driven knowledge to ensure that infants will not develop kernicterus. **JAAPA**

Earn AAPA Category 1 CME credit by reading both CME articles in this issue, reviewing the post-test, then taking the online test at http://cme.aapa.org. Successful completion is defined as a cumulative score of at least 70% correct. This material has been reviewed and is approved for 1 AAPA Category 1 CME credit. The term of approval is for 1 year from the publication date of October 2024.

REFERENCES

1. Bhutani VK, Stark AR, Lazzeroni LC, et al. Predischarge screening for severe neonatal hyperbilirubinemia identifies infants who need phototherapy. *J Pediatr*. 2013;162(3):477-482.e1.
2. Keren R, Tremont K, Luan X, Cnaan A. Visual assessment of jaundice in term and late preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 2009;94(5):F317-322.
3. American Academy of Pediatrics. Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2004;114(1):297-316.
4. Maisels MJ, Bhutani VK, Bogen D, et al. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. *Pediatrics*. 2009;124(4):1193-1198.
5. Kemper AR, Newman TB, Slaughter JL, et al. Clinical practice guideline revision: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2022;150(3):e2022058859.
6. Slaughter JL, Kemper AR, Newman TB. Technical report: diagnosis and management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics*. 2022;150(3):e2022058865.
7. Kair LR, Phillipi CA, Wood KE. Long-awaited AAP hyperbilirubinemia guidelines have arrived. *Hosp Pediatr*. 2022;12(12):e443-e445.
8. Wong P, Weerakul J, Sritippayawan S. Hemoglobin analysis in the first year of life. *Mediterr J Hematol Infect Dis*. 2016;8:1-6.
9. Mitra S, Rennie J. Neonatal jaundice: aetiology, diagnosis and treatment. *Br J Hosp Med*. 2017;78(12):699-704.
10. Qian S, Kumar P, Testai FD. Bilirubin encephalopathy. *Curr Neurol Neurosci Rep*. 2022;22(7):343-353.
11. Fawaz R, Baumann U, Ekong U, et al. Guideline for the evaluation of cholestatic jaundice in infants: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*. 2017;64(1):154-168.
12. Shapiro SM. Chronic bilirubin encephalopathy: diagnosis and outcome. *Semin Fetal Neonatal Med*. 2010;15(3):157-163.
13. Par EJ, Hughes CA, DeRico P. Neonatal hyperbilirubinemia: evaluation and treatment. *Am Fam Physician*. 2023;107(5):525-534.
14. Vítek L, Tiribelli C. Gilbert's syndrome revisited. *J Hepatol*. 2023;79(4):1049-1055.
15. Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. *N Engl J Med*. 2001;344(8):581-590.
16. Suresh GK, Clark RE. Cost-effectiveness of strategies that are intended to prevent kernicterus in newborn infants. *Pediatrics*. 2004;114(4):917-924.
17. Casnocha Lucanova L, Matasova K, Zibolen M, Krcho P. Accuracy of transcutaneous bilirubin measurement in newborns after phototherapy. *J Perinatol*. 2016;36(10):858-861.
18. Varughese PM, Krishnan L, Ravichandran. Does color really matter? Reliability of transcutaneous bilirubinometry in different skin-colored babies. *Indian J Paediatr Dermatol*. 2018;19(4):315-320.
19. Wright JL, Trent ME. Applying an equity lens to clinical practice guidelines: getting out of the gate. *Pediatrics*. 2022;150(3):e2022058918.
20. Wright JL, Davis WS, Joseph MM, et al. Eliminating race-based medicine. *Pediatrics*. 2022;150(1):e2022057998.
21. Cremer RJ, Perryman PW, Richards DH. Influence of light on the hyperbilirubinaemia of infants. *Lancet* (*Lond Engl*). 1958;271(7030):1094-1097.
22. Chang PW, Newman TB, Maisels MJ. Update on predicting severe hyperbilirubinemia and bilirubin neurotoxicity risks in neonates. *Curr Pediatr Rev*. 2017;13(3):181-187.
23. Kuzniewicz MW, Wickremasinghe AC, Wu YW, et al. Incidence, etiology, and outcomes of hazardous hyperbilirubinemia in newborns. *Pediatrics*. 2014;134(3):504-509.
24. Vandborg PK, Hansen BM, Greisen G, et al. Follow-up of extreme neonatal hyperbilirubinaemia in 5- to 10-year-old children: a Danish population-based study. *Dev Med Child Neurol*. 2015;57(4):378-384.
25. Wu YW, Kuzniewicz MW, Wickremasinghe AC, et al. Risk for cerebral palsy in infants with total serum bilirubin levels at or above the exchange transfusion threshold: a population-based study. *JAMA Pediatr*. 2015;169(3):239-246.
26. Maimburg RD, Olsen J, Sun Y. Neonatal hyperbilirubinemia and the risk of febrile seizures and childhood epilepsy. *Epilepsy Res*. 2016;124:67-72.
27. Newman TB, Wu YW, Kuzniewicz MW, et al. Childhood seizures after phototherapy. *Pediatrics*. 2018;142(4):e20180648.
28. Lamola AA. A pharmacologic view of phototherapy. *Clin Perinatol*. 2016;43(2):259-276.
29. Tridente A, De Luca D. Efficacy of light-emitting diode versus other light sources for treatment of neonatal hyperbilirubinemia: a systematic review and meta-analysis. *Acta Paediatr*. 2012;101(5):458-465.
30. Bosschaart N, Kok JH, Newsum AM, et al. Limitations and opportunities of transcutaneous bilirubin measurements. *Pediatrics*. 2012;129(4):689-694.