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Long-Awaited AAP Hyperbilirubinemia Guidelines Have Arrived

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The highly anticipated update to the American Academy of Pediatrics (AAP) Clinical Practice Guideline for management of hyperbilirubinemia in newborns ≥35 weeks gestation was published in August 2022.[1] The revised guideline and accompanying technical report[2] build on the prior recommendations with a decade and a half of new research.

Several key changes in the AAP's revised guideline are important to highlight. In homage to Dr. Oski and Watchko's conversation (*Vigintiphobia*, 1982),[3] the new guidance brings us closer to avoiding treatment of hyperbilirubinemia in term newborns without hemolysis. The treatment thresholds for phototherapy and exchange transfusion have been increased, and the new nomograms incorporate gestational age more smoothly along a continuum. The hour-specific nomogram that guided us for decades to assign risk is replaced by more individualized guidance that incorporates both gestational age and neurotoxicity risk. Specifically, more standardized follow up assessments are recommended according to distance from treatment thresholds.[4] Newly added is escalation of care guidance, steps to take when the serum bilirubin approaches the exchange transfusion level. In alignment with the AAP's Eliminating Race-Based Medicine policy statement,[5] race and ethnicity have been removed as independent variables to be used when assessing risk of developing severe hyperbilirubinemia, compelling individualized care with surveillance and careful assessment of family history of hyperbilirubinemia requiring treatment. In the 2004 guideline,[6] infants assigned as Black race were classified as being at decreased risk of severe hyperbilirubinemia while those assigned East Asian race were classified at elevated risk. Despite the perceived lower risk, Black infants are overrepresented in cases of kernicterus,[7] likely reflecting decreased vigilance, delayed treatment, and failed recognition of glucose-6-phosphate dehydrogenase (G6PD) deficiency.[8] Newborns of Asian race were potentially

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at risk of overtreatment and additional healthcare utilization from care based on higher perceived risk rather than genetic risk identified via family history.[9]

The AAP provides welcome news for jaundiced term newborns without hemolysis while emphasizing the vulnerability of early term and late preterm newborns and those with hemolysis. Higher treatment thresholds and standardization of practice provides a smooth transition for those clinicians who strictly followed the 2004 AAP guidelines. For those who practice with more variability or who had transitioned to the Northern California Neonatal Consortium (NCNC) guidelines,[10] the updated AAP guidance endorses higher treatment thresholds similar to NCNC guidelines but raises concerns of healthcare overutilization. Some of the recommendations with lower quality evidence may differ from long-standing clinical practice and may result in unnecessary testing and treatment. For example, we question the utility of obtaining laboratories (e.g. albumin, hemoglobin) in well term infants who meet phototherapy treatment criteria rather than reserving expanded laboratory evaluation for those approaching exchange or following an unexpected trajectory. Likewise, the recommendations for follow-up testing once phototherapy is initiated are overly prescriptive. Experienced clinicians know that an infant without hemolysis who has a feeding problem and hyperbilirubinemia will respond well to addressing the feeding problem in combination with phototherapy; sampling of bilirubin at specific time points is not always required.

The specificity provided in the new guidance is appreciated but will pose challenges for less resourced healthcare settings. Escalation of care, particularly in settings without proximate access to NICU care has the potential to prioritize transfer over treatment. A trial of intensive phototherapy, with or without intravenous fluids, should be an option for some infants who are within points of exchange transfusion prior to arranging transport. Home phototherapy is featured more prominently in this guidance but remains difficult to procure in many health systems and communities, as is even routine follow-up. More flexibility in criteria for those who may benefit from home phototherapy would be useful. Late preterm infants with serial bilirubin measurements who are predicted to reach a treatment threshold in ensuing days might be excellent candidates for home phototherapy. The emphasis on safe discharge bilirubin management compels hospital systems to invest in case management to assist busy clinicians facing increasing amounts of information to digest and process during shorter birth hospitalizations.

Implementation of the new recommendations requires a multidisciplinary and patient-centered approach. The new guideline all but necessitates that hospital units and clinics caring for newborns purchase a transcutaneous bilimeter. For example, for infants who are found to be direct antiglobulin test (DAT) positive, the recommended bilirubin checks every 4 hours x2 then every 12 hours x3, even in the absence of identified bilirubin elevation, would necessitate a significant number of blood draws for an otherwise well newborn in the absence of a transcutaneous bilimeter. Surveillance of breastfed infants for direct hyperbilirubinemia is suggested at a time when there is no standard touch point. It is more practical to obtain a fractionated bilirubin at the two-week visit when some states standardly obtain a blood sample for the newborn screen. The guideline authors provided helpful supplemental tables with hour-specific phototherapy and exchange transfusion thresholds.

While use of these tables allows for better precision than comparing an infant's value at a given hour to a nomogram, it does not seamlessly update electronic health record data. As of three weeks following publication of the updated guidelines, clinical decision tools built into the electronic health record have not yet incorporated updated nomograms. While third-party, open access sites have created tools, such as peditools.org,[10] that facilitate graphing, lack of real-time updates of the curves embedded in the electronic health record can leave members of the care team, including nurses, confused about a patient's clinical status and plan of care. A future state where electronic health records are provided with the permissions necessary to facilitate timely incorporation of major clinical decision tool updates like this has the potential to minimize risk to patients and ease the implementation process for providers.

Since the 2004 guideline and 2009 clarification,[6,12] the evidence base for hyperbilirubinemia has expanded,[4,13–20] providing the impetus for substantial revisions to the guideline. Specifically, new evidence of potential phototherapy-related harms and reassurance that bilirubin neurotoxicity does not occur until levels well above the 2004 exchange transfusion thresholds was felt to justify raising the phototherapy thresholds. Yet, work remains to be done, as the new thresholds are based on expert opinion as evidence was insufficient to derive specific treatment thresholds. Of the 25 key action statements, only 3 had sufficient evidence to be graded as strong recommendations. Remembering the wisdom of *Vigintiphobia*,[3] clinicians must study the rationale for the original policy as well as the arguments for the proposed changes. Moving forward, ongoing research and surveillance of the impact of the changes on the health of children will be key to drive the next guideline revision.

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Abbreviations:

AAP	American Academy of Pediatrics
DAT	Direct Antiglobulin Test
G6PD	glucose-6-phosphate dehydrogenase
NCNC	Northern California Neonatal Consortium

References:

1. Kemper AR, Newman TB, Slaughter JL, Maisels MJ, Watchko JF, Downs SM, Grout RW, Bundy DG, Stark AR, Bogen DL, Holmes AV, Feldman-Winter LB, Bhutani VK, Brown SR, Maradiaga Panayotti GM, Okechukwu K, Rappo PD, Russell TL. Clinical Practice Guideline Revision: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. Pediatrics. 2022 Aug 5:e2022058859. doi: 10.1542/peds.2022-058859. Epub ahead of print.
2. 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 Aug 5:e2022058865. doi: 10.1542/peds.2022-058865. Epub ahead of print.
3. Watchko JF, Oski FA. Bilirubin 20 mg/dL = Vigintiphobia. Pediatrics. 1983 Apr;71(4):660–3. [PubMed: 6682217]
4. Kuzniewicz MW, Park J, Niki H, Walsh EM, McCulloch CE, Newman TB. Predicting the Need for Phototherapy After Discharge. Pediatrics. 2021 May;147(5):e2020019778. doi: 10.1542/peds.2020-019778. [PubMed: 33903163]
5. Wright JL, Davis WS, Joseph MM, Ellison AM, Heard-Garris NJ, Johnson TL; AAP Board Committee on Equity. Eliminating Race-Based Medicine. Pediatrics. 2022 Jul 1;150(1):e2022057998. doi: 10.1542/peds.2022-057998. [PubMed: 35491483]
6. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004 Jul;114(1):297–316. doi: 10.1542/peds.114.1.297. Erratum in: Pediatrics. 2004 Oct;114(4):1138. [PubMed: 15231951]
7. Okolie F, South-Paul JE, Watchko JF. Combating the hidden health disparity of kernicterus in Black infants: a review. JAMA Pediatr. 2020;174(12):1199–1205 [PubMed: 32628268]
8. Wright JL, Trent ME. Applying an Equity Lens to Clinical Practice Guidelines: Getting Out of the Gate. Pediatrics. 2022 Aug 5:e2022058918. doi: 10.1542/peds.2022-058918. Epub ahead of print.
9. Bentz MG, Carmona N, Bhagwat MM, Thimmig LM, Saleh J, Eke U, Kokroko J, Dadasovich R, Rice B, Cabana MD. Beyond “Asian”: Specific East and Southeast Asian Races or Ethnicities Associated With Jaundice Readmission. Hosp Pediatr. 2018 May;8(5):269–273. doi: 10.1542/hpeds.2017-0234. Epub 2018 Apr 4 [PubMed: 29618489]
10. Northern California Neonatal Consortium. NCNC hyperbilirubinemia treatment guideline. Available at: https://phototherapyguidelines.com. Accessed 8/26/2022.
11. Chou JH, Roumiantsev S, Singh R. PediTools Electronic Growth Chart Calculators: Applications in Clinical Care, Research, and Quality Improvement. J Med Internet Res. 2020 Jan 30;22(1):e16204. doi: 10.2196/16204. [PubMed: 32012066]
12. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks’ gestation: an update with clarifications. Pediatrics. 2009 Oct;124(4):1193–8. doi: 10.1542/peds.2009-0329. Epub 2009 Sep 28. [PubMed: 19786452]
13. Wickremasinghe AC, Kuzniewicz MW, Grimes BA, McCulloch CE, Newman TB. Neonatal Phototherapy and Infantile Cancer. Pediatrics. 2016;137(6).
14. Newman TB, Wu YW, Kuzniewicz MW, Grimes BA, McCulloch CE. Childhood Seizures After Phototherapy. Pediatrics. 2018;142(4).
15. Wickremasinghe AC, Kuzniewicz MW, McCulloch CE, Newman TB. Efficacy of Subthreshold Newborn Phototherapy During the Birth Hospitalization in Preventing Readmission for Phototherapy. JAMA Pediatr. 2018;172(4):378–385. [PubMed: 29482208]
16. Wennberg RP, Watchko JF, Shapiro SM. Maternal empowerment - an underutilized strategy to prevent kernicterus? Curr Pediatr Rev. 2017;13(3):210–219 [PubMed: 28847288]
17. Newman TB, Liljestrand P, Jeremy RJ, et al. ; Jaundice and Infant Feeding Study Team. Outcomes among newborns with total serum bilirubin levels of 25 mg per deciliter or more. N Engl J Med. 2006;354(18):1889–1900 [PubMed: 16672700]
18. Wickremasinghe AC, Risley RJ, Kuzniewicz MW, et al. Risk of sensorineural hearing loss and bilirubin exchange transfusion thresholds. Pediatrics. 2015;136(3):505–512 [PubMed: 26283777]

19. 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 95. [PubMed: 25560920]

20. Vandborg PK, Hansen BM, Greisen G, Mathiasen R, Kasper F, Ebbesen F. 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 [PubMed: 25353277]