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EDITORIAL

# The African-American neonate at risk for extreme hyperbilirubinemia: a better management strategy is needed

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In 2010, Watchko[1] summarized the clinical concerns of managing jaundiced African-American neonates. Though acknowledging the data[1–4] identifying Black/African-American infants (defined based on maternal race) as having a lower risk for significant hyperbilirubinemia, he argued that glucose-6-phosphate dehydrogenase (G6PD) deficiency, coupled with polymorphisms in genes involved in bilirubin metabolism and other factors (ABO isoimmunization, late preterm gestation and limited clinical visualization), may predispose these newborns to developing pathologic bilirubin levels. Additional studies in the United States[5] and in Europe[6] have verified elevated risks of extreme hyperbilirubinemia and bilirubin encephalopathy, respectively, in newborns of African descent.

In their article in this issue of the *Journal*, Schutzman *et al.*[7] highlight the difficulties of genetic screening for hyperbilirubinemia in a prospective study of healthy African-American newborns. Multiple variants in the *UGT1A1* and *SLCO1B1* genes (which result in decreased bilirubin metabolism) were identified in their cohort; however, these variants did not correlate with the degree of hyperbilirubinemia in their patients. Furthermore, the authors acknowledge that their findings fail to provide resolution to a persistent problem faced by clinicians: identifying and caring for a small yet important fraction of African-American newborns who will have severely elevated bilirubin levels, putting them at an increased risk of developing short-term and long-term neurodevelopmental sequelae. Given that hyperbilirubinemia is a multigenetic process[8,9] that remains incompletely understood, clinicians and scientists must address several gaps in our knowledge and management of hyperbilirubinemia in this unique population.

First, consideration should be given to identification of an infant's race and/or ethnicity based on more than the mother's self-report, as has been previously discussed regarding hyperbilirubinemia.[10] In the United States currently, many parents and newborns are born of multiracial or multiethnic unions or relationships, rendering the singular classifications of 'Black/African-American' or 'White/Caucasian' imperfect and somewhat obsolete. Additionally, a mother who self-identifies by one race may fail to acknowledge other key components of her ancestry, hindering full comprehension of her genetic composition. As previously noted,[10,11] identification of children at risk for hyperbilirubinemia can be underestimated by incomplete or inaccurate documentation of a patient's background. Robust recording of ethnicity and race in medical records and health department documents using NIH categories and definitions (instead of traditional categorizations) and allowing for multiple designations (instead of a single check box) likely will identify more babies with African or African-American heritage, aiding in better understanding the heritable patterns of the disease.

Second, the genetics of severe hyperbilirubinemia in African-American neonates must be elucidated fully. Paramount to this task is the introduction of rapid, mandatory neonatal screening for G6PD deficiency across the United States. The absence of significant hyperbilirubinemia in the cohort of infants in this study[7] (all but eight of which were G6PD sufficient) and the association of G6PD deficiency and other polymorphisms in bilirubin metabolism genes with significant or severe jaundice in African-American babies[1,8,12] suggest an important role for early identification of this condition in this population of newborns. G6PD deficiency occurs in roughly 12% of African-American males and 4% of African-American females (based on a study of US military personnel[13]), within or well above the 3–5% male frequency threshold for screening recommended by the World Health Organization over 25 years ago.[14] However, at present, only Pennsylvania (the state in which the current report was based) and the District of Columbia require routine newborn G6PD screening. While a prior article in this *Journal*[11] highlighted the operational challenges of newborn testing for G6PD in the United States, a more recent article (again, in this *Journal*[15]) noted that a combination of routine screening and parental education may be the only way to reduce kernicterus associated with G6PD deficiency. Point-of-care G6PD assays[16–17] have shown promise in small studies and may soon be ready for use on a larger scale in nurseries and mother-baby units. More comprehensive testing for G6PD and other genes involved in bilirubin metabolism may allow for discovery of ancestry-informative markers linked to extreme hyperbilirubinemia.

Finally, hospitals and health-care systems must establish networks to monitor these at-risk newborns closely to prevent unchecked hyperbilirubinemia and resultant bilirubin encephalopathy. Care models in Israel[18] and Brazil[19] utilizing stringent discharge criteria, parental education, dedicated hospital resources for outpatient bilirubin monitoring and community/cultural based interventions have demonstrated decreases in extreme neonatal hyperbilirubinemia in these populations. At present, however, no routine outpatient/community systems exist for such monitoring in the United States, especially in the inner cities. In Baltimore City, for example, many African-American families use federally qualified health centers designed to serve the health-care needs of the underinsured and underserved. However, many of these centers offer reduced hours of service, with no or limited weekend availability. In this scenario, a neonate at risk for severe hyperbilirubinemia followed at one of these clinics might be sent to an emergency department for follow-up, possibly representing improper utilization of resources. As we better understand the inherited factors placing some African-American neonates at risk for potential pathologic jaundice, we must ensure simultaneously that appropriate resources exist for continued care of these babies in the early neonatal period.

The AAP Clinical Practice Guidelines for management of neonatal hyperbilirubinemia[20] and its 2009 update[21] remain mainstays for practitioners, particularly with the clear guidance in the latter document regarding pre-hospital bilirubin measurement and risk assessment. In most cases, African-American infants managed using these guidelines will require only routine newborn care and follow-up. However, the work of Schutzman *et al.*[7] gives us pause to consider steps we can take as practitioners and researchers to find the outliers and minimize the risk of severe hyperbilirubinemia in African-American newborns.

## CONFLICT OF INTEREST

The author declares no conflict of interest.

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