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Ronald J. Sokol

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Biliary Atresia Screening: Why, When, and How?

Ronald J. Sokol, MD

Section of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of Colorado Denver School of Medicine and The Children's Hospital, Aurora Colorado

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BILIARY ATRESIA IS one of the most important liver diseases in childhood. At an incidence of 1 in 13 000 live births in the United States, it is considered a rare disease; however, it is the indication for 40% to 50% of all liver transplants performed in children.¹ It uniquely presents only during the first few months of life and seems to be a phenotype caused by at least several etiologies, including a proposed perinatal insult that initiates an immune-mediated obliteration of the extrahepatic bile duct lumen and a proposed embryonic or fetal defect in the normal morphogenesis of the biliary tree.² Outcome is uniformly poor unless a hepatic portoenterostomy (HPE) (the Kasai operation) reestablishes bile drainage from the liver into the jejunum and leads to resolution of jaundice. If HPE is not successful or not performed, liver transplantation is the only life-saving alternative. Even with successful HPE, the majority of these children's conditions will progress to cirrhosis, leaving survival rates without liver transplantation at only 20% by 20 years of age.¹ Thus, there is a great need to improve outcomes.

One proposed approach has been to screen infants for biliary atresia at an early age, with the goal of instituting HPE earlier in life. Why this approach? The report by Serinet et al³ in this issue of *Pediatrics* extends previous reports and shows that HPE in the first month of life (versus at an older age) provides the best surgical outcomes and chance of avoiding, or significantly delaying, a liver transplant. On the basis of this new analysis of data from France, efforts should now be directed toward making the diagnosis of biliary atresia before 30 to 45 days of life. However, this would not be achieved easily in the United States, because most infants are not routinely seen by health care providers between 2 weeks and 2 months of age. HPE results are progressively worse if performed after 60 to 90 days of age. Moreover, the jaundice of biliary atresia is frequently overlooked in favor of a probable, but incorrect, diagnosis of breast milk-associated jaundice, despite recommendations to check for conjugated (direct) hyperbilirubinemia in infants with jaundice beyond 2 weeks of age.¹ Unfortunately, the average age at diagnosis of biliary atresia and HPE in the United States has not changed over the last 15 years.⁴ Thus, some form of screening for biliary atresia may be the most effective means of identifying infants with the disease earlier than the current US average of 60 to 70 days of life.⁵ This screening clearly would need to be performed before 30 to 40 days of life so that infants could be further evaluated and undergo HPE by 45 days of life to achieve best results.

The most promising screening method for biliary atresia has been the use of stool color cards to identify the lack of stool pigmentation (acholic stools) that typically is present by the age of 30 days in biliary atresia. In Taiwan, in which a screening program infrastructure is now in place, this has been effective in reducing the average age at diagnosis and age at HPE and increasing the rate of postoperative resolution of jaundice,⁶ setting the stage for better long-term outcomes. It is important to note that infants in Taiwan have a routine visit to a caregiver at 1 month of age, at which time the stool color card is examined; this process leaves sufficient time to initiate the evaluation and HPE for biliary atresia. In the United States, use of stool color cards at the typical 2-month visit may not significantly bring about earlier diagnosis; however, late diagnosis (beyond 90 days of age) could potentially be avoided. Thus, it would be important to determine the cost/benefit and effectiveness of a stool color card screening program in the United States in a pilot study in several states. In addition, continued emphasis needs to be placed on obtaining a fractionated bilirubin level from all infants who are jaundiced at 2 weeks of age. By following the current recommendation of the American Academy of Pediatrics⁷ to evaluate for conjugated hyperbilirubinemia if an infant remains jaundiced at 3 weeks or beyond, the opportunity for early diagnosis of biliary atresia in most cases will, unfortunately, be missed, because this falls between the routine caregiver visit schedule. Finally, using modern biotechnology to analyze neonatal samples may lead to identification of new diagnostic biomarkers for biliary atresia, with the potential to develop novel newborn blood spot screening methodologies. Other strategies for improving outcomes should be explored simultaneously. For example, a randomized, controlled trial of postoperative corticosteroids is currently underway in the National Institutes of Health-supported Biliary Atresia Research Consortium.⁸ Confining and concentrating biliary

Abbreviation: HPE, hepatic portoenterostomy

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Address correspondence to Ronald J. Sokol, MD, Children's Hospital, Box B290, 13123 E 16th Ave, Aurora, CO 80045. E-mail: sokol.ronald@tchden.org
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atresia surgery to the most experienced centers may also improve outcomes, as demonstrated in the United Kingdom.⁹

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