Newborn jaundice—an introductory overview

Newborn jaundice is one of the most common conditions encountered in pediatrics. Usually, it is easily overlooked by parents and pediatricians as it is a normal, transitional "right of passage" from fetus to newborn, as passage of unconjugated bilirubin produced by the fetus across the placenta to the mother abruptly ceases with the clamping of the umbilical cord after birth. In addition, bilirubin production in the infant continues at a rate higher than in an adult on a body weight basis and the uptake, conjugation, and excretion of bilirubin by the newborn liver into bile lags because of the delayed induction of a number of metabolic processes. Thus, a transient rise in bilirubin in the blood occurs, typically exceeding 1 mg/dL (17.1 µmol/L). When this level exceeds roughly 4–5 mg/dL (68–86 µmol/L), a yellow coloration of the skin can be observed in most newborns, depending upon skin pigmentation. Jaundice is most easily seen in the normally white sclerae of the eyes, especially when hyperbilirubinemia is in the lower range, or the skin pigment is darker. Because bilirubin is an important antioxidant itself and a signaling molecule that can mediate changes in the immune response of cells and the degree of inflammation, one might speculate teleologically that hyperbilirubinemia is an adaptive response of a mostly hairless primate transitioning rapidly from a relatively low light, low oxygen environment (womb) to an environment rich in light, oxygen, and iron—extremely oxidative stressors (ambient environment). Thus, evolution has ensured the transient rise of a potent antioxidant in the blood and tissues while other antioxidant systems are induced and begin to strike a balance conducive to the enzymatic work of life on the surface of our planet to enhance survival. This transition is usually completed over the first several days of life. However, there are several factors that can alter this transition and place an infant at risk for injury caused by rapid buildup of the pigment in the blood, which can exceed binding capacity and lead to its accumulation outside of the circulation in tissues. If excessive, bilirubin may accumulate in the brain and lead to neurologic dysfunction, manifested as "acute bilirubin encephalopathy" (ABE) or sometimes permanent damage, called kernicterus or chronic bilirubin encephalopathy (CBE).

This series of papers in this special issue on newborn jaundice addresses most of the important topics with which the clinician needs to be familiar to practice safely, as well as summarizes the extent of knowledge of experts on the causes of jaundice and hyperbilirubinemia, the nature of bilirubin's potential toxicity because of limited or compromised binding to albumin ("*Narrative Review of Bilirubin Measurement and Binding*" by Markee and Amin), and management strategies, including decision tools ("*A Narrative Review of Electronic Clinical Decision Support Tools for Hyperbilirubinemia Management*" by Palma and Arain). Of course, all pediatricians should be familiar with the epidemiology of newborn jaundice ("*The Epidemiology of Neonatal Jaundice*" by Hansen), and in particular, the hemolytic causes of neonatal hyperbilirubinemia ("*Hemolytic Causes of Neonatal Jaundice*: *Diagnosis and Treatment*" by Bahr, Christensen, and Kaplan). Moreover, they should also be familiar with the use of phototherapy to prevent the need for exchange transfusion and its limitations, including its possible risks when applied to extremely immature infants ("*Phototherapy for Preterm Newborns—Historical Controversies and RCT Evidence*" by Arnold and Tyson). Reviews of the biology of bilirubin production ("*The Biology of Bilirubin Production*: *Detection and Inhibition*" by Stevenson and Wong), the phenomenon fundamental to the development of all jaundice, and the genetics of hyperbilirubinemia ("*The Contribution of Genetic Factors to Hyperbilirubinemia and Kernicterus Risk in Neonates*: *A Targeted Update*" by Watchko), an essential ingredient in the causation of the various patterns of newborn jaundice, provide a background of information essential to understanding the clinical syndromes encountered by pediatricians. Finally, and most importantly, the possible toxicity of bilirubin is discussed with a focus on bilirubin-induced neurologic dysfunction (BIND) ("*Severe Neonatal Hyperbilirubinemia and the Brain*: *the Old but Still Evolving Story*" by Jayanti, Ghersi-Egea, Strazielle, Tiribelli, and Gazzin) and the hypothesized mechanisms of permanent brain injury ("*Bilirubin Neurotoxicity*: *A Narrative Review on Long Lasting*, *Insidious*, *and Dangerous Effects*" by Brites and Silva).

Although there is necessarily some overlap of subject matter because of the nature of the selected topical foci, each article in the series can stand on its own as a reference, and together they represent a compendium of evidence-based information and expert opinion on newborn jaundice.

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David K. Stevenson

Ronald J. Wong

David K. Stevenson
(*Email: dstevenson@stanford.edu*)
Ronald J. Wong
(*Email: rjwong@stanford.edu*)
Department of Pediatrics, Division of Neonatal and Developmental Medicine, Stanford University School of Medicine, Stanford, CA, USA.

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