"inborn errors of bile acid synthesis causing metabolic liver disease and, development of a life-saving therapy"

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Genetics defects in the cholesterol-bile acid biosynthetic pathway are now recognized as a specific class of metabolic liver disease. Bile acid synthesis disorders due to single enzyme defects generally present in infancy or early childhood with progressive cholestatic hepatitis that, unchecked, leads to cirrhosis, liver failure, and death. Prior to their discovery as discrete entities, and conceiving of an effective therapy, children with these autosomal recessive diseases either underwent liver transplantation, or more commonly, were given supportive care until they dies of liver failure of unknown origin. The elucidation of the biochemical basis of this new entity of liver disease, the development of an international diagnostic screening program, and a therapeutic approach based on primary bile acid replacement therapy that recently gained regulatory approval from the FDA will be described. This translational approach from the bench to bedside has been a game-changer that has led to a radical change in the evaluation and treatment of patients with idiopatic progressive familial intrahepatic cholestasis syndromes.