Cholestasis may be defined physiologically as a reduction in canalicular bile flow. Although it is clinically manifested as jaundice due to conjugated hyperbilirubinemia, its main consequences are due, on the one hand, to the cellular toxicity of accumulated bile acids, ultimately leading to biliary cirrhosis and, on the other hand, to decreased intraluminal bile acid concentration responsible for fat and fat-soluble vitamin malabsorption. Because the hepatobiliary excretory system is functionally immature at birth, the neonate has a particular tendency to develop cholestasis. Indeed, cholestatic diseases have been central in the development of pediatric hepatology. Around biliary atresia, the main cause of cholestasis in infants, multiple other causes have been recognized, related either to anatomic or genetic anomalies or to infectious or toxic agents, with very different prognoses.

Several reasons justify why this issue of *Annales Nestlé* is dedicated to cholestasis in childhood: (1) impressive progresses have been made in the past 10 years in the characterization of several genetic defects affecting biliary secretion at the molecular level as well as in the clinical evaluation of their treatment and prognosis; (2) on clinical grounds, the difficulty remains to recognize cholestasis and identify, as early as possible, a cause that could be amenable to medical therapy (e.g., galactosemia, inborn error of bile acid synthesis) or to early surgical intervention (biliary atresia) for an infant presenting with various degrees of jaundice, dark urines, pale or acholic stools and often hepatomegaly; (3) early and adapted medical interventions may avoid the need for liver transplantation which, although life saving, remains a difficult procedure, with frequent side effects.

This background explains the selection of topics covered in this issue.

The first article, by Muriel Girard and Florence Lacaille from the Department of Pediatric Gastroenterology, Hepatology and Nutrition at Necker-Enfants Malades University Hospital, Paris, France, is logically devoted to the diagnosis of cholestasis, mainly in neonates, because it is at that age that it is crucial to ascertain or eliminate biliary atresia as early as possible. Their vast clinical experience allows them to write a comprehensive chapter ending with useful diagnostic algorithms and basic advice on how not to miss biliary atresia.

Then, Dr. Richard Thompson, Senior Lecturer in Pediatric Hepatology at King's College London School of Medicine, London, UK, well known for his studies on the genetics of progressive familial intrahepatic cholestasis, describes the various genetic defects affecting biliary secretion. He explains clearly why certain conditions are multisystem disorders whereas others are confined to the liver, according to the organ expression of the gene involved, and how the prognosis is linked to the genetic defect, particularly in the case of bile sort export pump deficiency whose prognosis is darkened by the risk of hepatocellular carcinoma. Of additional interest, this chapter highlights the relations between clinical phenotype and genotype and, more specifically, demonstrates that knowing the genetic cause of a disease makes it easier to identify phenotype variations.
Once the correct diagnosis is made, the adapted treatment should be initiated; this is the subject of the last 2 articles.

In his chapter, Dr. Fernando Alvarez, Professor of Pediatrics at Saint Justine University Hospital, University of Montreal, Montreal, Canada, senior pediatric hepatologist, deals with the specific treatments available for children with chronic cholestasis, emphasizing that very few of its causes have a specific treatment and that in most cases, therapeutic medical or surgical strategies are aimed at preventing or treating complications of bile (mostly bile acids) retention. The unique role of ursodeoxycholic acid in improving cholestasis is well explained; its rapid efficacy on liver tests is stressed as well as our ignorance of the benefit of its long-term administration. In addition to the drugs used to treat pruritus and malabsorption, the place of surgical procedures is well described and the necessity of an early Kasai intervention again underlined.

Because of the nutritional risks linked to chronic cholestasis and the importance of a good nutritional status when liver transplantation is envisaged, it is logical that the last chapter of the issue deals with the nutritional management of cholestatic syndromes in childhood. Dr. Piotr Socha, Professor of Pediatrics at the Children’s Memorial Health Institute in Warsaw, Poland, an expert in nutrition in this field, has written a comprehensive review of the causes of malnutrition in these children, the diagnosis of specific deficiencies and of their treatment. The importance of bringing to these children enough protein and energy to achieve catch-up growth, either orally, by tube feeding or even by a central line, is well stressed as is the necessity of following the lipid-soluble vitamin status to correct possible deficiencies. The difficulties in polyunsaturated fatty acid and vitamin E supplementation are emphasized.

This issue does not deal with liver transplantation because, although an often necessary life-saving end-stage treatment of some of the causes of cholestasis in childhood, it represents another chapter in the story of these diseases, a chapter that is postponed as long as possible.

On the contrary, some of the congenital causes of cholestasis are a good example of conditions where the knowledge of their genetic defect may lead to new therapeutic strategies such as gene therapy or hepatocyte transplantation.

The Editorial Committee