‘Intractable diarrehas’ in infancy emerged from the medical literature 40 years ago, in the early 1960s; the term was coined to define a group of infants (less than 3 months of age) who had diarreha for more than 14 days, had negative stool culture and whose diarreha persisted despite medical intervention. During the following years it became apparent that this clinical entity was heterogeneous including both cases of severe post enteritis diarreha more or less complicated by food allergy (‘protracted diarreha’) and cases of diarreha that persisted despite bowel rest during weeks or months and resisted any pharmacological treatment (steroids, loperamide, somatostatin, …).

In developed countries, the increasing hygiene standards and the liberal use of formulas made of partially hydrolyzed (peptides, oligosaccharides) or easily absorbable (MCT) nutrients by mouth or via constant rate enteral nutrition allowed the first subgroup of patients to eventually be cured. On the contrary, the development of total parenteral nutrition favored the emergence of a small residual group of patients who would have died before the advent of this intensive care technique.

Indeed, it is from the late 1970s, early 1980s that the various entities that will be discussed in this issue of the Annales Nestlé were described for the first time. Ten years later a careful analysis of these patients using both clinical and immunohistochemical criteria enabled the design of algorithms that would help to differentiate enteropathies due to congenital enterocyte defects, the earliest and most severe ones from those secondary to an abnormal (sometimes congenital) immune activation of lamina propria T cells and occurring usually somewhat later (usually before the end of the second year) in the life of the child.

The long-term treatment of these children is one of the greatest challenges facing pediatric gastroenterology: although home total parenteral nutrition allows some of these children to live a nearly normal life, it is often complicated by episodes of life-threatening central catheter-linked sepsis, the progressive shortage of venous access, and above all hepatic failure. These risks, which were recognized as TPN developed, led early to the project of small bowel transplantation which, however, has only recently come to maturity. It is now a reasonable alternative to TPN in these cases of intestinal failure.

It is the fascinating history of this recent chapter of pediatric gastroenterology that this issue of Annales Nestlé wishes to bring to its readers.

Alan D. Phillips from the Centre for Paediatric Gastroenterology of the Royal Free Hospital, in London, UK, is one of those who first described the anatomical (histological and ultrastructural) lesions of the congenital enterocyte defects responsible for the most severe forms of intractable diarreha, and particularly of familial microvillous atrophy (or microvillous inclusion disease). The later condition summarizes the problems raised by these diarrehas: extreme severity (up to 300 ml/kg/day of stool output), difficulties in maintaining water and electrolyte balance and a normal growth while preventing hepatic failure, inescapable discussion of intestinal transplantation.
Philip M. Sherman and Ernest Cutz from the Hospital for Sick Children in Toronto, Canada, and Olivier Goulet from Necker-Enfants Malades Hospital in Paris, France, present the main features of the other group of intractable diarrhea due to immune or autoimmune enteropathies. The great interest of differentiating this group of patients from the previous one is that, although it may also induce extremely severe diarrhea (usually in somewhat older children), the therapeutic approach, once the diagnosis is made, is completely different, based on the use of immunosuppressive drugs and, in the most severe cases (IPEX syndrome), on bone marrow transplantation.

Olivier Goulet from Necker-Enfants Malades Hospital in Paris, France, participated in the description of some of these new entities (epithelial dysplasia, syndromic diarrhea) and is a leader in the field of intestinal transplantation. He introduces the concept of intestinal failure, the ultimate consequence of these intractable diarrheas, as well as other anatomical situations (short bowel syndrome in particular), which often would impose intestinal transplantation. However, he shows here that whereas intestinal transplantation did not raise unusual technical difficulties, it did raise serious immunological problems until the advent of immunosuppressor drugs such as tacrolimus, which recently allowed this transplantation to reach acceptable 1-year survival rates.

Finally Zulfiqar A. Bhutta from the Department of Paediatrics and Child Health of the Aga Khan University in Karachi, Pakistan, usefully recalls that, in developing countries, most cases of protracted diarrhea still occur as a complication of infectious diarrhea linked to preexisting malnutrition, micronutrient deficiency, decreased immune defenses, inadequate treatment, elevated infectious burden. He shows that protracted diarrhea is the background from which the rare cases of intractable diarrheas described in the Western world emerged. After having precisely reviewed our current knowledge concerning the mechanisms leading to protracted diarrhea, Zulfiqar A. Bhutta summarizes the rules to be followed to avoid such situations.

It is hoped that this issue of Annales Nestlé will help all pediatricians to prevent diarrhea from becoming protracted, and to recognize and correctly take in charge the rare cases that are intractable and need the assistance of specialized teams dedicated to their long-term treatment.

The Editorial Committee