40. Hu Z, Jing Y, Xue Y, Wang L, Vanyukov M, Kirisci L, et al. Analysis of substance use and its outcomes by machine learning: II: derivation and prediction of the trajectory of substance use severity. Drug Alcohol Depend 2020;206:107604.
41. Kelly NJ, Bergman B, Hoeppner BB, Vilsaint C, White WL. Prevalence and pathways of recovery from drug and alcohol problems in the United States population: implications for practice, research, and policy. Drug Alcohol Depend 2017;181:162-9.
42. Ridenour T, White D, Bogen D, Novak S, Scherer J, Reynolds M, et al. Detecting initiation or risk for initiation of substance use before high school during pediatric well-child check-ups. Drug Alcohol Depend 2015;150:54-62.
43. Committee on Substance Use. Substance use screening, brief intervention, and referral to treatment for pediatricians. Pediatrics 2019;128:1330-40.
44. Vanyukov MM, Cornelius MD, De Genna NM, Reynolds MD, Kirillova GP, Maher BS, et al. Measurement of liability to addiction: Dimensional approaches. Int J Person Cent Med 2016;6L:250-9.
45. Sanchis-Segura C, Becker JB. Why we should consider sex (and study sex differences) in addiction research. Addict Biol 2016;21:995-1006.
46. Becker JB, McClellan ML, Reed BG. Sex differences, gender and addiction. J Neuroscie Res 2017;95:136-47.
47. Becker JB, Hu M. Sex differences in drug abuse. Front Neuroendocrin 2008;29:36-47.

50 Years Ago in *The Journal of Pediatrics*

Infantile Diarrhea

Lifshitz F, Coello-Ramírez P, Gutiérrez-Topete G. Monosaccharide intolerance and hypoglycemia in infants with diarrhea I. Clinical course of 23 infants. J Pediatr 1970;77:595-603.
Lifshitz F, Coello-Ramírez P, Gutiérrez-Topete G. Monosaccharide intolerance and hypoglycemia in infants with diarrhea. II. Metabolic studies in 23 infants. J Pediatr 1970;77:604-2.

In 1970, Lifshitz et al described the clinical course of 23 infants with gastroenteritis, carbohydrate intolerance, and diarrhea. In these infants, diarrhea resolved after removal of dietary carbohydrates. Notably, 17 infants experienced hypoglycemia, which improved with diarrhea resolution. Dietary glucose re-introduction was tolerated in all but 9 infants who died before proving full tolerance. The study concluded that patients with diarrhea had monosaccharide and disaccharide intolerance that improved with total dietary carbohydrate elimination. Thus, impairment of carbohydrate absorption by the small intestine causes the carbohydrate load to pass into the colon. There, bacterial fermentation promotes the production of lactic acid, which decreases the intraluminal pH, causing an osmotic diarrhea. However, further metabolic studies concerning the nature of hypoglycemia were needed. This was described in the second article; the authors determined that factors affecting blood glucose include carbohydrate intolerance, glucose amount introduced, and dietary intake, as well as glycogen stores in the liver.

The question of what to feed a child with acute diarrhea still arises in everyday practice. We now have more information on the causes of nutrient malabsorption during acute diarrheal illness. In 1983, Lo and Walker described chronic protracted diarrhea of infancy as an iatrogenic, nutritional disease.[1] They described diarrheal diseases that improved with bowel rest—in effect, removal of high osmolality contents from the intestinal lumen. However, bowel rest must be accompanied by appropriate nutrition provision, either intravenously only, or intravenously plus small amounts of continuous intraluminal feeds, which allows mucosal healing. In 1984, Fagundes-Neto et al provided insight on the histology of the small intestine during protracted diarrhea.[2] They reported alterations of the intestinal mucosa, disaccharidase deficiency, and disruption of the intestinal permeability barrier; they proposed that severe deterioration of nutritional status and death is possible if appropriate treatment is not established. In 2018, a Clinical Guideline from the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition reviewed recommendations on the management of acute diarrhea in nonmalnourished children and determined that elimination diets are usually not indicated for children with acute gastroenteritis because this may further impair the child's nutritional status.[3]

In summary, the key best practice point over the past 50 years is that appropriate early nutrition during diarrheal illness is essential for recovery. If oral or enteral nutrition is limited owing to the disease process, appropriate temporary parenteral provision of nutrients is necessary to allow for appropriate healing and recovery.

A. Adjowa Amevor, MD
Stephanie B. Oliveira, MD, CNSC
Pediatric Gastroenterology, Hepatology and Nutrition
Cincinnati Children's Hospital Medical Center
Cincinnati, Ohio

References

1. Lo CW, Walker WA. Chronic protracted diarrhea of infancy: a nutritional disease. Pediatrics 1983;72:786-800.
2. Fagundes-Neto U, Pacheco I, Patricio FR, Wehba J. Ultrastructural study of alterations in the small intestinal epithelium of children with acute diarrhea. J Pediatr Gastroenterol Nutr 1984;3:510-5.
3. Guarino A, Lo Vecchio A, Dias JA, Berkley JA, Boey C, Bruzzese D, et al. Universal recommendations for the management of acute diarrhea in nonmalnourished children. J Pediatr Gastroenterol Nutr 2018;67:586-93.