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Carbohydrate Intolerance in Infancy

edited by
Fima Lifshitz

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Volume 1 Carbohydrate Intolerance in Infancy, *edited by Fima Lifshitz*

Other Volumes in Preparation

DEDICATION

To the Memory of Horacio Toccalino

Dr. Horacio Toccalino, Argentinean pediatrician, was a modern pioneer of pediatric gastroenterology and nutrition in South America. He served at The "Alejandro Posadas" Polyclinic in Buenos Aires, Argentina. In the early sixties Horacio Toccalino started his career at the Hospital de Niños of Buenos Aires, where he studied food intolerances which affected a large number of his patients. Specifically, he worked on carbohydrate intolerance in both acute and chronic diarrhea, with special emphasis on secondary disaccharidase deficiencies and the bacterial overgrowth syndrome in children with malnutrition and diarrhea. Later he studied the absorption of potential antigens through the small intestine as a cause of food allergy. Thus, years before these subjects attained general interest, he was pioneering the field covered in this book.

Dr. Toccalino was a man of fascinating personal characteristics which gave him charisma. His extremely remarkable personality, enterprising character, permanent desire to teach, involve, and stimulate young doctors in research, and his sincere friendship with his students were his most notable characteristics. All of these personal attributes gave him a great power of attracting numerous people of unquestionable natural leadership; thus, he trained many of the pediatric gastroenterologists in South America. Unfortunately, he died on December 28, 1977, at 45 years of age at the apex of his professional career. In spite of his early death, he carried out work sufficiently important to have his name perpetuated in the history of pediatric gastroenterology and nutrition. His philosophy of work is embodied in the Latin American Society of Pediatric Gastroenterology and Nutrition, which he founded in 1974.

Ulysses Fagundes-Neto
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FOREWORD

Since the beginning of this century, protein feedings and formulas, with simple sugars or sugar-free, have been utilized for the management of diarrhea. It was in the early 1900s that Finkelstein, in Germany, published his observations about the failure of selected infants to tolerate complex sugars, especially after acute diarrhea. Even earlier, empirical dietary changes were utilized for the nutritional rehabilitation of infants with diarrhea and other illnesses. Since those astute early clinical observations, researchers have made impressive gains in the knowledge of infant feedings in health and disease states. Application of this knowledge has helped in some regions of the world to decrease the mortality rate, secondary to severe diarrhea, to a nearly irreducible point. However, much more remains to be learned about the proper nutritional rehabilitation of infants that are premature or suffer from several diseases, including acquired monosaccharide intolerance and cow's milk protein hypersensitivity.

In response to research findings through the past five decades, a number of special formulas for infant feedings have been made available to medical practitioners. In 1911, Mead Johnson introduced its first product, Dextri-Maltose, to help physicians in the dietary rehabilitation of infants who were not able to tolerate milk sugar, as well as those who were not thriving appropriately. The carbohydrate content is the single most important formula ingredient in determining the acceptance and tolerance of the product. Furthermore, a number of infant formulas are now available which contain different types and concentration of other ingredients, including protein and fat. Thus, for rational nutritional rehabilitation, the pediatrician must be familiar with all the possible alterations in specific and generalized dietary intolerances that may occur. Therefore, the pediatrician must also be familiar with the different formulas available for proper prescription in specific instances.

This book focuses on the most recent advances in the knowledge of carbohydrate intolerance in infancy. This most important aspect of infant nutrition and pediatric gastroenterology is reviewed from the vantage point of many well-known experts in the field. Their collective efforts update our knowledge in carbohydrate digestion and tolerance in infancy and, therefore, constitute an important contribution for all those who care for infants. Dr. Lifshitz deserves our thanks for editing this book by a distinguished panel of experts.

Angel Cordano

SYMPOSIUM REFLECTIONS

In this book we have an excellent mixture of results, from clinical and applied research, on the subject of carbohydrate intolerance in infancy, making the contents informative to students of nutrition and pediatrics alike. To the contributors of this book we owe a debt of gratitude.

I am thrilled at the attention being given to the subject of carbohydrate malabsorption, including monosaccharide absorptive defects. In Chapter 2 (Veda N. Nichols) there is a summary of factors which have been found to be higher in incidence in infants with acquired monosaccharide intolerance (AMI). While reading that information, I recalled a classic volume published by Miller and Merritt in 1979.* They summarized maternal practices and their effect upon fetal growth and development. Most of their factors are paralleled by those identified in the AMI patient group. This leads me to conclude that (a) perhaps obstetricians should be included in future seminars on the prevention of diarrhea, malnutrition, and/or acquired monosaccharide intolerance, and (b) infants are not all the same when delivered, but subtle changes may occur in their molecular biological function due to gestational exposures which may result, among other hazards, in increased susceptibility to carbohydrate intolerance in infancy.

I pose for this august group two questions which when answered will make this symposium's results increasingly applicable by the generalist and pediatrician. (a) What is the difference in the risk of generating an immune response to dietary antigens when a protein hydrolysate diet compared to an intact protein diet is used as the first *enteral* feeding to diarrheal patients? (b) How can we clarify the role of bacteria, viruses, antibiotics, enzyme deficits, and allergy to tailor the therapy to the individual patient who has had protracted diarrhea with resultant intestinal mucosa damage?

I trust that the information exchanged in this book will stimulate each of us to further pursuits in search of answers to questions raised regarding carbohydrate intolerance in infancy.

Harold W. Hermann

*Miller, H. C., and Merritt, T. A. (1979). *Fetal Growth in Humans,* Year Book Medical Publishers, Chicago.

PREFACE

Knowledge is of two kinds. We know a subject ourselves or we know where we can find information upon it. (Samuel Johnson)

The subject of carbohydrate intolerance in infancy refers to the alterations which result from carbohydrate malabsorption. It is not to be confused with the subject of carbohydrate intolerance which pertains to diabetes mellitus and/or impaired carbohydrate metabolism. In the past, the latter was referred to as "glucose intolerance" manifested by hyperglycemia and glycosuria. Today this syndrome is referred to as "impaired glucose tolerance" of various types. Thus, this modern nomenclature clearly distinguishes it from the alterations in carbohydrate absorption leading to carbohydrate intolerance, which is the subject of this book.

Since carbohydrates provide 40–50% of the total calories ingested by infants, there must be an adequate digestion and absorption of these foodstuffs to attain optimum growth and development. Unabsorbed carbohydrates may lead to malnutrition and diarrhea as well as other gastrointestinal alterations. *Carbohydrate Intolerance in Infancy* brings together the state-of-the-art knowledge by 23 recognized experts in this field. A particular emphasis is made on the acquired form of carbohydrate intolerance which frequently complicates diarrheal disease of infancy. The presence of carbohydrate intolerance is an important issue to be considered in the nutritional rehabilitation of the large number of patients who are affected by diarrheal disease. The epidemiology and pathophysiology of the most severe form of this complication, namely, acquired monosaccharide intolerance, are discussed in detail. These patients constitute the majority of infants with chronic diarrhea in hospital wards in developed countries.

The frequent association of carbohydrate intolerance with rotavirus infection and the current state of the "lactase hypothesis" regarding the infectivity of this virus is also reviewed. The problem of lactose intolerance, lactose malabsorption, and lactase deficiency in infancy is addressed in detail since lactose, the carbohydrate found in milk, is broadly consumed from birth. However, other intestinal oligodisaccharidase deficiencies and other carbohydrate intolerance syndromes are also reviewed. These include sucrase-isomaltase deficiency, resulting in sucrose intolerance, and starch intolerance, which is important in the planning of supplementation with solids or other foodstuffs in infancy. The clinical role of carbohydrate intolerance in the premature infant and in other nondiarrheal syndromes is also discussed.

The dual role of intestinal microflora in the syndrome of carbohydrate intolerance is brought to light. On the one hand, proliferation of fecal and colonic bacteria resulting from malabsorbed carbohydrates may be injurious to the bowel. On the other hand, colonic flora may assist in the metabolism of unabsorbed carbohydrates and alleviate some of the symptoms of carbohydrate intolerance. The kinetic effects of malabsorbed carbohydrates on water secretion and the possible modes of correcting these derangements are reviewed.

The possible relationships between carbohydrate intolerance and protein hypersensitivity are examined. This topic includes reviews of the clinical association of lactose intolerance with cow's milk protein hypersensitivity, the potential role of unabsorbed lactose in stimulating intestinal macromolecular absorption that could lead to antigen uptake, and the production of hypersensitivity in a susceptible host, as well as the role of oligodisaccharides in soy protein intolerance.

Finally, the use of breath hydrogen testing in diarrheal disease for the diagnosis of carbohydrate intolerance, and the use of different infant formulas available for treatment of carbohydrate intolerance are discussed.

The recent advances in our understanding of carbohydrate intolerance in infancy are many, but much remains to be learned. The symposium held at Key Largo, Florida, in January 1982, sponsored by Mead Johnson Nutritional Division, brought together the contributors of this book in an attempt to integrate current knowledge and to disseminate it to the practicing physician and to others who care for infants.

I am grateful to Dr. Angel Cordano and Mr. David Wallace as well as to all other directors of Mead Johnson for all their efforts and support in organizing this symposium and in the publication of this volume. I also acknowledge the contribution of my former and present associates who have published with me much of our work in this field, Drs. Gerald H. Holman, Pedro Coello-Ramirez, Gillermo Guttierrez Topete, Raul A. Wapnir, Saul Teichberg, Mrs. Silvia Diaz Bensussen, and Mary Ann Bayne. Similarly, I want to thank those who behind the scenes have been instrumental in allowing us to pursue this work: Drs. Herbert C. Miller, Gonzalo Gutierrez Trujillo, and Mervin Silverberg. For secretarial assistance thanks to Jan M. Coyle, Cynthia Aquila, and Lauren Strand.

Progress to date on the subject of carbohydrate intolerance in infancy, as documented in this book, is impressive. However, we are only at the threshold of the acquisition of greater knowledge in infant nutrition. Those who wish to learn may find in this volume substantive information which may help in the nutritional rehabilitation and the care of their patients.

Fima Lifshitz

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CARBOHYDRATE INTOLERANCE IN INFANCY

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PERSPECTIVES OF CARBOHYDRATE INTOLERANCE IN INFANTS WITH DIARRHEA

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Milk is the major food of infancy. Therefore, lactose, the carbohydrate found in milk, is broadly consumed from the time of birth. However, it is well known that there may be lactose malabsorption in the immediate neonatal period and beyond 3-5 years in many ethnic groups (1,2). This is due to a widespread selective ontogenetic lactase deficiency now considered to be the normal state of mankind (3,4). In mammals the ontogenetic changes in intestinal lactase activity from high levels at birth, to decreased levels at the time of weaning, diminishing to trace levels in the adult has been known to occur since the early part of this century (Chapters 4, 6). It was then recognized that younger calves had a greater concentration of lactase activity in the small intestine than older ones (5,6). This ontogenetic sequence of events, with low adult lactase levels, occurs in all but a few ethnic and racial groups