call the patients ‘‘intellectually normal.’’ There has always been some reservation about this, as is shown in the following excerpt from the abstract of the paper by Azen et al (4): ‘‘except for arithmetic, the scores of which declined between ages 6 and 12 y in 90% of the children in this study.’’ In the fourth paragraph, in an attempt to produce 2 groups of patients for comparison, 1 group was proposed to have a therapeutic goal of 60–332 μmol/L and a second group to have goal of 330–599 μmol/L with a 2-phase crossover. ‘‘This randomization was disrupted by some parents choosing to either continue or discontinue diet therapy regardless of assignment. However, no child was dropped from the study because of failure to comply with randomization’’ (4). There is no question that it is difficult to perform any clinical study, but information obtained under such difficulties should not be considered to have been shown without doubt.

Snyderman ignored completely references I cited as evidence that there is some damage to heterozygous fetuses born to heterozygous mothers (5–7). Such mental damage might affect one-quarter of the nieces and nephews of the mothers of children with PKU and more than one-half of the children of female siblings of PKU probands. It could affect 1% of all children and account for a large part of what is now called nonspecific retardation. It must be noted that 2 of the 3 authors of reference 7 were the Director and Assistant Director of the National Collaborative Study. Even though they agree with the evidence uncovered in the National Collaborative Study, they have been unable to initiate further studies on concurrent maternal-fetal heterozygosity with the large PKU population they study. The heterozygote phenomenon should be used to study means of helping the families of PKU children.

Snyderman’s own reference (8), a fine, but incomplete review of perinatal amino acid physiology, contains little to deny the possibility of heterozygous intraterine partial deficiency of tyrosine and nothing to deny that a homozygote, in a heterozygous mother, has a serious deficiency. Her review contains no reference to the study by Raiha (9), which showed that the phenylalanine hydroxylase activity of fetal liver was apparent at 8 wk and in the normal (adult) range after 13 wk. Page 389 in Snyderman’s (8) study reads ‘‘According to the evidence of phenylalanine hydroxylase activity in the premature is the counterpart of phenylketonuria.’’ I could not have said it better myself.

I have been accused of trying to stop the screening for PKU and the use of diet for therapy. This is not true. I believe that by screening we recruit patients. We should give the benefit of the doubt to heterozygous mothers (5–7). Such mental damage might affect one-quarter of the nieces and nephews of the mothers of children with PKU and more than one-half of the children of female siblings of PKU probands. It could affect 1% of all children and account for a large part of what is now called nonspecific retardation. It must be noted that 2 of the 3 authors of reference 7 were the Director and Assistant Director of the National Collaborative Study. Even though they agree with the evidence uncovered in the National Collaborative Study, they have been unable to initiate further studies on concurrent maternal-fetal heterozygosity with the large PKU population they study. The heterozygote phenomenon should be used to study means of helping the families of PKU children.

L-Tryptophan in maternal phenylketonuria

Dear Sir:

Rohr et al (1) reported that plasma tyrosine concentrations can be increased to normal or above normal values in maternal phenylketonuria (PKU) by L-tyrosine supplementation. Higher maternal plasma tyrosine concentrations may result in a greater availability of tyrosine to the fetus. However, another overlooked factor in the pathogenesis of maternal PKU is that an excess of circulating phenylalanine also inhibits membrane transport of L-tryptophan. This may have a deleterious effect on the fetus during gestation. Experiments with plasma membrane vesicles of human full-term placental syncytiotrophoblast showed inhibition of L-tryptophan and L-tryptophan uptake by high phenylalanine concentrations (2). In vivo studies also showed that hyperphenylalaninemic pregnant rats had fetuses with lower concentrations of L-tryptophan in blood and brain than did control rats; additionally, a labeled L-tryptophan tracer did not reach the fetal circulation and brain to the same extent in hyperphenylalaninemic rats as in controls (3). A deficiency of L-tryptophan during fetal brain development could impair serotonin synthesis in the same way that tyrosine deficiency leads to decreases in dopamine and norepinephrine biosynthesis. This has been shown in experiments with synaptosomal plasma membrane vesicles (4). The reduction of L-tryptophan intestinal absorption by hyperphenylalaninemia and its normalization after a low-phenylalanine diet was clearly shown earlier in children with PKU (5) and in an adult PKU patient (6).

The studies of Rohr et al (1) support the relevance of providing supplemental L-tyrosine and a low-phenylalanine diet during gestation in maternal PKU. The question remains open as to whether compensating a likely deficit of another neurotransmitter precursor, L-tryptophan, might be beneficial to a heterozygous fetus at risk. Since L-tryptophan was recalled late in 1989 because of its association with eosinophilia-myalgia syndrome, the therapeutic use of L-tryptophan has been largely in limbo. The likely contamination of L-tryptophan, which is considered to

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be responsible for that disorder, originated during its industrial biosynthesis. The contaminant has now been identified (7). High-purity L-tryptophan may again allow the use of this amino acid for well-justified purposes, such as supplementation of pregnant women with PKU during gestation.

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Both authors of this book have backgrounds in nutritional science and have had a deep interest in nutritional education. Norman Kretchmer, Editor-in-Chief of this Journal from 1991 until his untimely death in 1995, needs no introduction to readers of this Journal. Michael Zimmermann is a Senior Research Scientist in the Laboratory for Human Nutrition, Swiss Federal Institute of Technology, Zurich, where he directs the postgraduate course in human nutrition.

The book contains 10 chapters, each of which emphasizes the continuity of the life cycle and the underlying concept that health at each succeeding stage of this cycle is built on the nutritional foundation established during the earlier stages. The first chapter reviews the basic concepts of developmental biology and human nutrition as well as basic nutritional terms and concepts. Chapter 2 focuses on the influence of nutrition on fertility, particularly the importance of nutrition before conception. The third chapter deals with the effects of maternal nutrition on intrauterine growth of the fetus as well as the effects of pregnancy on maternal and maternal nutrient needs. Chapter 4 discusses the physiology of lactation and the unique composition of human milk; chapter 5 discusses the process of breastfeeding and the influence of breast-feeding on both maternal and child health. Chapters 6 through 8 focus on nutrition during infancy, childhood, and adolescence. Chapter 9 examines the effect of diet on adult health, including the rapidly expanding knowledge concerning the relation between nutrition and chronic disease. The final chapter discusses both the influence of nutrition on the physiologic changes of aging and the influence of the physiologic changes of aging on nutritional requirements.

All the chapters examine the effect of psychosocial environment and cultural influences as well as how they interact to influence dietary patterns and practices. Overall, the book provides a clear understanding of what constitutes a healthy diet at different stages in the life cycle and how nutrients act at the cellular, tissue, and whole organism level to influence human growth, development, and aging.

The book was written for students who have had introductory courses in biology and nutrition. However, the clear language used, the well-organized material, and the use of a variety of learning aids (eg, the use of a large number of figures as well as the use of boldface italics to identify important terms and concepts, which, in turn, are defined within the margins of the page on which the terms or concepts appear) make it appropriate for individuals with only a limited background in these areas. At the same time, the book is an appropriate reference for those of us with specialized interests who occasionally need a broader perspective of nutrition throughout the life cycle.

I predict that the book will become a popular text for general undergraduate and graduate courses in nutrition. It should be particularly valuable as a text for the increasing number of elective and mandatory nutrition courses for first- and second-year medical students.

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Every 4 y, experts in the area of dietary fiber meet at the Vahouny Conference (named after a pioneer in this field) to discuss the status of dietary fiber research and to explore new and emerging areas of interest. This book is the fifth in a series documenting the proceedings of this conference. In a comparison of this book with the preceding one, the reader will get a good idea of the history of dietary fiber research and how that research has changed over time. Two major changes emerge from this comparison. First, current thinking, as emphasized in this publication, is that the health benefits of dietary fiber per se should not be overemphasized. Fiber-rich foods contain health-promoting substances other than fiber and there is increasing emphasis on the nonfiber components. Of particular note is the contribution of resistant starch to colonic physiology, which is an important area of current research. Equally important is the developing field of phytochemical research, which is highlighted in a chapter on phytosterols and in one of the fiber-related nutrients and their addition to food products.

A second major emphasis of this book is a focus on the products of fiber fermentation—the short-chain fatty acids. The increasingly important area of dietary fiber research is documented in 7 chapters representing current research directions. Many of these chapters provide important insights not found in research articles. Collectively, they form an excellent overview of this field and make an important contribution to the literature. Of particular interest is the chapter by Huang and which presents the intriguing hypothesis that certain pp

inflammatory responses from colonocytes only occur in undifferentiated cells. Because butyrate is known to promote colonocyte differentiation, this may explain, in part, its ameliorative effect in ulcerative colitis. Edwards provides an excellent analysis of the effects of short-chain fatty acid production on gut motility. Also of note is a comprehensive review by Velazquez and Rombeau on the potential role of butyrate in colon cancer prevention and treatment. A chapter on butyrate production in infants as a function of infant feeding is novel, and suggests that it may be possible to affect adult colonic bacterial colonization by early feeding practices.

Other areas of dietary fiber research were covered in the 4 preceding books in this series, but not as well as in the current publication. Humble contributes a comprehensive and highly critical review of the evolving epidemiologic data on fiber and heart disease. He makes a good case that the protective effect of dietary fiber is not due to confounding by fat displacement, as often stated. However, the book is not without its controversial aspects, including a convincing argument by Wolever and Jenkins that current recommendations for fiber intake (20–35 g/d) are insufficient. In fact, these investigators select foods on the basis of the food pyramid and current dietary guidelines and show that the recommendation to eat only 20–35 g fiber/d is inconsistent with current dietary recommendations. In summary, this book is important to anyone working in the area of carbohydrate or fiber research, or anyone wanting a good overview of current research in the field.

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There has been an enormous amount of research on various aspects of eating and obesity. Unfortunately, research on nutrition and macronutrient intake is rarely integrated with research on genetic and learning influences on eating and obesity. This slim volume is an admirable attempt to remedy this situation. As the authors note in the preface, the book focuses on the relations between people and food that might give rise to positive energy balance.

The book has 9 chapters. Chapter 1 is a brief overview of the concepts of homeostasis and set point that provides a context for the remaining chapters. Chapter 2 discusses the roles of hunger, palatability, and satiety on the initiation, maintenance, and termination of eating and includes a discussion of the confusion about terms such as palatability and satiety in the literature. Chapter 3 provides an overview of energy intake, energy expenditure, and energy balance. Chapter 4 discusses the genetics of obesity and energy balance and chapter 5 reviews the short- and long-term influences of macronutrients and food intake on energy balance. Chapter 6 reviews the evidence for increased preferences for specific types of foods (mainly sweets and fats) in obese persons. Chapter 7 reviews the literature on patterns of food intake and their relation to obesity. Chapter 8 reviews the influence of external food-related cues and dietary restraint on eating and chapter 9 discusses the evidence for and against the roles of mood, food craving, and food addiction as causes of overeating.

The authors do a good job of pointing out areas of controversy and methodologic problems in the literature and suggest further directions for researchers to explore. However, the authors themselves also point out the primary shortcoming of this book: it does not directly address the health implications of food intake and weight change. Despite this shortcoming, the book is a good summary of the literature to date and is a useful starting point for those interested in discovering the links between particular macronutrients and eating patterns, behavioral acts of food consumption, and obesity. This book would be a valuable resource for any researcher seeking to uncover or understand these links.

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Vitamin D is a new and comprehensive review of knowledge about vitamin D—both its role and its metabolism—gained over the past 35 y. In general, the chapters are well written and the topics covered are comprehensive. The figures are also extremely clear and molecular structures are well represented. Certain chapters in this book deserve comment because of their clarity; especially recommended are chapters 1 and 2, “Historical Overview” and “Vitamin D Metabolism,” by DeLuca and by Horst and Reinhardt, respectively. The chapters “Vitamin D Physiology on the Regulation of Phosphate Transport” by Hruska et al and “Perinatal Vitamin D Actions” by Bishop and Salle are especially informative and contain a great deal of information from widely dispersed sources. The explosion of information that has occurred in the area of vitamin D over the past 3 decades is well known to all students of nutrition. A potential therapeutic role for vitamin D has emerged for many areas of both mammalian and human nutrition and may be important in terms of therapy of leukemia, cancer therapy, breast cancer, normal and abnormal hematopoiesis, transplantation, and psoriasis and other skin conditions. All of these topics are critically reviewed in a series of chapters that examine the expanding literature in this area. Another strong feature of this book is that the discussion of rickets is separated into the various forms of the disease, including discussion of the importance of vitamin D and its metabolites in each of these forms. The authors of all of the
sections on the vitamin D endocrine system and its disorders are
world experts who have extensive experience in the diagnosis
and treatment of these disorders.

In conclusion, Feldman, Glorieux, and Pike have gathered a
group of experts to discuss the topic of vitamin D. The role of
vitamin D as a steroid hormone has been elucidated over the
past 35 y. This volume documents the extraordinary advances in
our understanding of this secosteroid vitamin hormone. I recom-
mend this text to all students of calcium, phosphorus, and vita-
min D metabolism; this textbook will be also valuable to all stu-
dents of calcium endocrinology.

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