I GENERAL CONCEPTS

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Pediatric Nutrition: A Distinct Subspecialty

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Scientific interest in nutrition has a long history.[1–3] Balance studies were conceived by Sanctorius in the 1620s. Lavoisier researched the oxidation of foods and Magendie discovered that protein was necessary for survival two centuries ago. In 1838, Franz Simon produced his classic dissertation, in Latin, on human milk biochemistry, which for the first time underpinned a rational basis for infant nutrition. It was over 100 years ago, in the late nineteenth century, that Rubner defined the energy content of foods and constructed the first calorimeter for measuring energy expenditure. By the early twentieth century, we already had a broad understanding of nutrient needs and an increasing understanding of micronutrients and of the effects of specific deficiencies. (Funk coined the term "vitamines" in 1912.) Sophisticated metabolic research on animals fed by continuous intravenous infusion flourished in the first three decades of the last century, and as early as 1944, we saw the first case of a child, age 5 months, fed successfully via the intravenous route.

In parallel with this long-term development of nutritional science has been an equally long-term appreciation of the clinical and public health importance of infant and child nutrition. In the earliest part of the last century, and well before, nutrition was a prominent and vital part of caring for infants. Unquestionably, in the eyes of early clinicians, how and what the infant was fed during health and illness were primary determinants of survival. The infant mortality rate in the United States in 1900 was 165 per 1,000.[1] The unacceptably high rate and the variability from one area of the country to the other related primarily to mode of feeding in infancy.

At that time, pediatrics, both as an academic specialty and in everyday practice, was in its own infancy. At the turn of the nineteenth century, there were probably fewer than a dozen practitioners in the United States who were exclusively devoted to pediatrics.[2] In the first presidential address to the American Pediatric Society in 1889, Abraham Jacobi discussed the rationale for having the specialty of pediatrics distinct from internal medicine: "Pediatrics deals with the entire organism at the very period during which it presents the most interesting features to the student of biology and medicine ... there is scarcely a tissue or an organ which behaves exactly alike at different periods of life."[2]

A review of the topics covered in the annual presidential addresses to the American Pediatric Society during its first 35 years shows a frequent return to nutrition and nutrition-related subjects. In 1924, David M. Cowie suggested that feeding in infancy was then sufficiently based on sound physiologic principles and that pediatrics needed to focus more on nutrition and metabolism, among other things, of the older child.[2] By 1940, when the eleventh edition of *Holt's Diseases of Infancy and Childhood* was published, the editors unhesitatingly stated, "Nutrition in its broadest sense is the most important branch of pediatrics. A knowledge of its fundamental principles is essential to the physician if he is to apply preventive and corrective measures intelligently."[4]

WHY HAS PEDIATRIC NUTRITION NOT EMERGED AS A DISTINCT SUBSPECIALTY?

Given that nutrition is the oldest branch of pediatrics based on centuries of major research, it seems paradoxical that it has never emerged as a formal, distinct academic discipline. Indeed, considering its roots in and fundamental relationships to that which makes pediatrics unique—growth and maturation—why has nutrition taken a back seat to other subspecialties? The decline in the importance of nutrition in pediatrics can be explained in two ways.

First, the urgency that fostered nutrition research and the illnesses that made nutrition a prominent part of pediatric practice decreased progressively during the last century. The causes of infantile scurvy and rickets and other deficiency diseases were delineated during the early decades of the twentieth century. In fact, with the exception of iron deficiency, primary nutritional deficiencies are now virtually unknown in the United States and other developed countries, and infant mortality rates relate more to the general level of socioeconomic development than to nutritional practices. With the advent of refrigeration and appropriate milk processing technology, survival of artificially fed infants in clean environments is now the norm.

Second, pediatrics has followed the path taken by internal medicine and surgery; the past 40 years have seen the growth of "organ-based" subspecialties: pediatric cardiology, neurology, nephrology, and so on, and, more recently, gastroenterology. The result of this evolutionary course was to imbed clinical nutrition in a variety of "organ-focused" subspecialty areas. This arguably fostered a disease-specific orientation to nutrition and fragmentation of nutrition practice and research. Thus, enteral feeding has come under the wing of gastroenterologists, parenteral nutrition has interested gastroenterologists and pediatric surgeons as well, aspects of growth have fallen into the domain of endocrinology, neonatal nutrition has been taken on by neonatologists, eating disorders by psychologists and psychiatrists, food allergy by allergists and physicians in respiratory medicine, and so forth. This fragmentation and multiple ownership of pediatric nutrition have hindered development of the field as a distinct entity.

WHY IS PEDIATRIC NUTRITION REEMERGING IN IMPORTANCE?

In the past, the major focus in the field of nutrition has been one of meeting nutrient needs and the prevention of nutrient deficiencies. There has

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now been a fundamental sea change in orientation in this field. The major current interest in nutrition is its impact on health.[5] Our new understanding of the potential biologic impacts of nutrition on health has led us to frame two key new questions: Does nutrition matter in terms of patients' responses to their disease? Does it matter for long-term health and development?

With regard to the first, increasing evidence now indicates that good nutritional care may improve the clinical course of disease, reduce hospital stay, reduce the need for more expensive treatments, and, indeed, result in major reduction in health care costs. Such benefits of nutritional care are emerging over a broad range of pediatric domains such as gastroenterology (eg, Crohn's disease, short-bowel syndrome), surgery, renal medicine, care of disabled children (eg, cerebral palsy), infectious disease (eg, human immunodeficiency virus [HIV]), and oncology. Neonatology provides good examples of the effects of good nutrition on clinical course: Nutritional practices may have a major influence on the incidence of life-threatening diseases (necrotizing enterocolitis and systemic sepsis),[6] may influence the need for expensive and potentially hazardous parenteral nutrition, and may significantly impact length of hospital stay.

However, the factor that has most influenced the reemergence of interest in pediatric nutrition is the increasing evidence for its effects on long-term health and development. The idea that early nutrition could have long-term consequences is part of a broader concept concerning the impact of early life events in general. To focus attention in this area, Lucas proposed using the term "programming,"[7] the idea that a stimulus or insult applied during a critical or sensitive period of development could have a long-lasting or lifetime impact on the structure or function of the organism. The first description of programming during a sensitive or critical period of development was by Spalding, who in 1873 defined the critical period for imprinting in newborn chicks.[8] Since then, developmentalists have described numerous examples of short-lived stimuli—both endogenous and exogenous—that have had lifetime effects.

What is the evidence that nutrition may behave in this programming way? Since the first studies by McCance in the 1960s, the evidence for such programming in animals is overwhelming. Brief periods of experimental nutritional manipulation in early life influence in adult life many outcomes of potential relevance to humans,[9] including blood pressure, insulin resistance, blood lipids, vascular disease, body fatness, bone health, gut function, endocrine status, learning, behavior, and longevity.[9–13] Nutritional programming effects have been seen in all species studied, including nonhuman primates.[10,11]

In the past 25 years, increasing evidence has shown that humans, like other species, may be highly sensitive to early nutrition in terms of later health outcomes. Deficiencies of single nutrients at critical periods can have long-lasting effects. Animal studies have documented the role of zinc deficiency in the development of neural tube defects in the fetus. Choline deficiency in the rat in utero or in the early weeks of life has long-term effects on brain function, specifically memory.[14] Decreased folic acid intake in the periconceptional period also has been linked to neural tube defects in the human.[15]

Iron is another trace element that appears to play a critical role in development. Iron deficiency in rats, for example, produces reversed sleep cycles, altered pain threshold, and difficulty in learning. Dopamine D_2 receptors also are decreased. When the iron-deficient diet is begun at 10 days of age, later iron repletion is unable to reverse these defects completely.[16] In the human, the mechanisms of the detrimental effects of severe iron deficiency in early childhood on subsequent mental development are yet to be elucidated, but several studies suggest that such effects may be permanent and may affect both cognitive ability and behavior.[17–19] On a molecular level, it is possible that iron is required at a critical time for the expression of one or several genes, and if this opportunity is lost, iron sufficiency is unable to reverse the path of development.

Many observational studies have linked growth, size, or nutrition in early life to the types of health outcome influenced by early nutrition in animals. Human studies now point to effects of birth weight, early growth rate, and weight at 1 or 2 years of age on such outcomes as bone mass and coronary events in later life.[20–22] Such observational data might be confounded, but in more recent years, there has been long-term investment in randomized intervention studies. These trials have now shown that early diet during obesity, bone health, and cognitive performance.[9,22–24]

The effects of brief early nutritional interventions are often surprisingly large. Studies in the preterm infant show that feeding a standard versus preterm formula for just 1 month may result in a 12-point deficit in verbal IQ (in males) and a more than doubling of motor or cognitive impairment (both sexes) 7 to 8 years later.[22] In the same population, random assignment to banked donated breast milk rather than infant formula resulted in a reduction in diastolic blood pressure 13 to 16 years later of a magnitude greater than that induced by nonpharmacologic interventions used to manage hypertension in adult life (weight loss, exercise, salt restriction).[23] A small follow-up study of full-term infants who had been randomized to be fed infant formula with or without added arachidonic acid and docosahexaenoic acid for the early months of life found that diastolic blood pressure was significantly lower at 6 years of age in previously supplemented infants.[25] These data require confirmation with larger numbers of subjects. Such data have major biologic and public health implications. They show that nutrition cannot simply be seen in terms of meeting nutritional needs. Rather, nutrition emerges as a major environmental influence on the genome, influencing lifetime health. It is also apparent that there is now a new onus on health professionals to ensure proper nutrition to optimize the short- and long-term health of sick individuals and healthy populations.

RATIONALE FOR A SEPARATE DISCIPLINE

Viewed in the historical context of a changing subspecialty paradigm and a new appreciation of nutrition's role at the molecular level with profound implications for health, the time would seem right for nutrition to be recognized as a distinct area of pediatric practice. But what other criteria should be fulfilled for nutrition to be formally developed as a pediatric subspecialty? Two questions must be addressed: Is there a defined area of pediatric care that requires specific nutritional expertise and are there readily identifiable deficiencies in current pediatric nutritional patient teaching and research that would benefit from such a development?

Defined Area of Expertise

There is a defined area of pediatric care that requires nutritional expertise. Nutritional advice is one of the most common categories of advice sought by parents. Nutritional management problems are possibly the most common problems in pediatric hospital practice; virtually every sick premature infant and a high proportion of sick older children could benefit from specific and expert nutritional attention. Walk on any general ward and the number of patients needing advice from a pediatric cardiologist, nephrologist, or gastroenterologist will be far exceeded by those who would benefit from sound nutritional care.

However, beyond the routine practice of what we know, there are potentially important areas of new expertise that need to be sewn into nutrition practice. Just as a field such as cardiology owes its specialty status in part to the development of specialized techniques—catheterization, diagnostic imaging, etc—so could pediatric nutrition be underpinned by new tools awaiting exploitation in a clinical setting.[7] Isotope probes are available for exploring metabolic process and energy expenditure. Body composition devices (dual X-ray absorptiometry, impedance, isotope dilution, air displacement plethysmography, three-dimensional photonic scanning, ultrasonography, magnetic resonance imaging, etc) are ready to be pioneered in the complex management of sick infants and children. They are also likely to prove useful in the assessment of the impact of public health policy on the nutritional status of the childhood population (for instance, the value of interventions to reduce obesity, which are currently monitored by inappropriately nonspecific and crude methods). New tools are also available to measure and plot growth that will make the diagnosis and management of growth disorders, failure to thrive, and overweight less arbitrary and more precise. Such techniques require trained specialists.

Deficiencies in Patient Care

Subspecialists trained in pediatric nutrition would improve patient care. Specialty advice in nutrition

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is often sought from physicians whose primary interest is in another area.[26] This results in fragmentation of care and creates a lack of uniformity in how conditions are managed. A "standard of practice" does not exist. Nutrition knowledge has exploded to the point where clinicians in individual subspecialties no longer can be expected to have a comprehensive grasp of all aspects relevant to their own increasingly complex practice. There is an increasing number of children with obesity and latent or overt metabolic syndrome, which will complicate the course of other diseases. In addition, there continues to be a high percentage of inpatients in any general or pediatric hospital who are found to be malnourished by "world-class" criteria as a result of their primary disease. With efforts to contain costs and the move to home care, patients often are leaving hospital with more profound nutritional deficits than before, and the situation can be expected to become worse.

For many years in the United States, parenteral nutrition support in many hospitals was overseen by the surgical service, whereas enteral nutrition was handled by virtually any pediatrician. Even with the advent of nutrition support teams, most of the physicians involved have acquired their nutritional skills in an ad hoc fashion. If consultation about enteral nutrition is needed, the gastroenterologist, by default, has assumed responsibility and is likely to be called. To be sure, gastroenterology and nutrition are closely linked, and most pediatric gastroenterologists have considerable expertise in nutrition, especially as it affects their "organ system." But the pediatric gastroenterologist should not be expected to be well versed in all areas of nutrition, because only a small part of nutrition science and practice is related directly to gastroenterology.

Deficiencies in Teaching

Teaching of nutrition in medical schools also is fragmented at best: "To almost everyone expressing an opinion about the teaching of nutrition in medical schools, it appears to be entirely unsatisfactory. Rare successes prove to be ephemeral and crucially dependent on individual commitment and outside funding."[27] In most medical schools, the basic science pertaining to nutrition is embedded in biochemistry and, perhaps, physiology. A survey of 126 US medical schools in 2004 found that a separate course in nutrition was required in only 32 of the 106 schools responding.[28] Formal teaching of clinical nutrition is nearly nonexistent. The same survey reported that the average contact hours of required nutrition instruction in the third and fourth years of medical school was 5.1 $\pm$ 0.7 hours. What teaching there is generally done as a part of primary care rotations or by subspecialists in other areas in pediatrics. Many medical students never observe breast-feeding and are never trained to make up a formula feed. Most house staff leave training with less than adequate understanding of the physiology and management of breast-feeding, the composition and appropriate use of standard or special infant formulas, or the appraisal of simple feeding problems and the rationale for nutrition advice or care during the second 6 months of life and beyond. Public health and preventive nutrition are equally neglected. The provision of 5-year Nutrition Academic Awards to 21 US medical schools since 1998 to foster nutrition education during medical school is a step in the right direction and appears to have produced a number of innovative approaches in nutrition education.[29] The 2004 survey previously referred to, however, concluded the following: "With the move to a more integrated curriculum and problem-based learning at many medical schools, a substantial portion of the total nutrition instruction is occurring outside courses specifically dedicated to nutrition. The amount of nutrition education in medical schools remains inadequate."[28,*]

Nutrition education and practice continue to relate primarily to organ-based specialties. Although this may be acceptable from the point of view of clinical practice, from the point of view of research it will ultimately impede inquiry into the important areas.

Deficiencies in Research

The area that perhaps stands to gain most from the development of nutrition as a distinct discipline is research. Although basic laboratory and animal research in nutrition has been active, the key clinical research questions in pediatric nutrition are unlikely to be addressed as long as nutrition is divided among the traditional specialties. This is so because the orientation toward disease of most subspecialties will favor research to answer questions related to therapeutic dietetics (ie, treatment of disease). With infant survival from a nutritional point of view assured in most Western countries, the issue of how early nutrition should be optimized in terms of its effects on later health becomes of paramount importance.

The objective for clinical research in any field of health policy or clinical practice should be to prove outcome benefits for recommended approaches to management, generally by use of formal clinical trials that test the safety and efficacy of the intervention. This would be standard in established clinical areas. Thus, whether or not a clinician should treat high blood pressure, remove a malignancy rather than give chemotherapy, or repair a heart defect at birth rather than later in childhood and other decisions depend on proven clinical benefit for each management option. For example, physicians routinely treat high blood pressure precisely because lowering blood pressure has been shown to reduce morbidity and mortality from cardiovascular disease.

Research in childhood nutrition has been largely unsatisfactory in this respect. Dietary recommendations fluctuate as new expert groups examine the data. The data that underpin the recommendations for dietary reference nutrient intakes in adults are often inadequate, and recommendations for children frequently are based on even less secure data. In addition, research over the past 50 years has largely failed to address adequately whether adhering to the nutritional recommendations made by ad hoc groups and governmental bodies confers outcome benefits.[7] The critical issue of whether early nutrition, either in health or in disease, influences long-term health or development has, until the last two decades, barely been approached in formal studies. Thus, most recommendations of expert bodies on fundamental areas of practice are based largely on theoretic considerations derived from short-term physiologic experiments and epidemiologic studies rather than on outcome findings from intervention trials. Both physiology and epidemiology can be useful in identifying questions and framing hypotheses for such outcome trials, but neither can replace them.

The paucity of clinical outcome studies in pediatric nutrition contrasts sharply with the major research investment that has been made in pediatric nutritional physiology. Possibly more research effort has been applied here than in any other area of pediatrics. For instance, as far back as 1953, Macy and colleagues summarized the contents of 1,500 publications on the composition of breast milk—just one small area of infant nutrition.[30] The profusion of pediatric nutritional studies in the face of the paucity of outcome data justifying clinical practice suggests that clinical pediatric nutritional research has lacked direction. This lack of research direction, not seen to nearly the same extent in the recognized pediatric specialties, can be traced in part to the absence of guidance on research priorities from specialists trained in nutrition and from centers of excellence in pediatric nutrition.

CONCLUSION

Like the blind men approaching the elephant, each subspecialty comes up with a different view of nutrition. Each subspecialty creates a paradigm that determines how questions are framed and results are interpreted. Depending on one's primary interest, taurine may be thought of as a critical nutrient for neural development and function, a primary determinant of bile acid conjugation, or an osmoregulator of the brain during dehydration. Someone needs to see the elephant for what it is—to collate our knowledge in the field of nutrition, understand its significance for development, and apply it to clinical practice.

Functional specialties in medicine increasingly are interacting in a matrix fashion with organ-based specialties. Clinical nutrition fits comfortably into this new paradigm. The time appears to be right to foster clinical nutrition within pediatrics as a unique discipline. Such a development would address currently identifiable deficiencies in patient care, training, and, especially, research in clinical nutrition.

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[*] For a comprehensive look at the state of nutrition education in medical school curricula, see "An evidenced-based approach to medical nutrition education. Am J Clin Nutr 2006;83:929S–87S."

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