PEDiatric Nutrition research at iowa (1954-94)

The research conducted in the Pediatric Nutrition Unit since Dr. Fomon's arrival in 1954 has had national and international impact. Policy statements of the Committee on Nutrition of the American Academy of Pediatrics have in a number of instances reflected changes in thinking brought about by results of studies conducted in the unit. Similarly, the World Health Organization has used the publications of the Unit as a basis for several of its recommendations, and, most recently, the National Center for Health Statistics has requested permission to use the Unit's data on early infant growth to supplement national survey data to be used in construction of revised NCHS growth charts. Manufacturers of infant formulas have at times relied on studies conducted in the unit as a basis for formula modifications. Throughout the US and in many other countries, the Unit is well known and is highly regarded as a center of research and teaching in infant nutrition. Many pediatric researchers have been introduced to nutrition research in the Unit.

Although research in the Unit has ranged broadly over topics of practical interest in infant nutrition, the following areas are particularly noteworthy:

- Physical growth of infants
- Body composition of the fetus, infant and child
- Infant requirements for protein and amino acids
- Renal solute load
- Factors affecting food consumption by infants
- Cow milk-provoked intestinal blood loss
- Iron absorption by infants and children
- Zinc metabolism of infants
- Fluoride metabolism of infants
- Carnitine metabolism and requirements of infants and children

Physical Growth of Infants

The most sensitive indices of nutritional adequacy of the infant's diet during the early months of life are gains in weight and length. Using standardized techniques, data on gains in length and weight of normal term infants have been measured in the Unit and accumulated on a gender-specific and feeding-specific (breast-fed, fed milk-based formula, fed isolated soy protein-based formula) basis. Summaries of the data concerning growth during the early months of life have been published (Fomon et al., 1970a, 1971a, 1978, 1986; Fomon and Ziegler, 1979; Nelson et al., 1989). The data have also been combined with the Fels data pertaining to later infancy and early childhood to provide reference data on gains in length and weight during the first two years of life (Guo et al., 1991).
Body Composition of the Fetus, Infant and Child

Contributions in the area of body composition of the infant began in the Unit with studies of total body water (Owen et al., 1962, 1963; Fomon and Owen, 1964) and led to development of the "reference infant" (Fomon, 1966, 1967a, 1974; Fomon and Nelson, 1993), the "reference fetus" (Ziegler et al., 1976) and the "reference child" (Haschke et al., 1981; Fomon et al., 1981a, 1982). These models have been essential in the use of the factorial method for estimating nutrient requirements of the term and preterm infant, and in interpretation of body density data of the child. Because the density of fat-free body mass of children is much lower than that of adults, the estimates of body composition of the child led to revision of previously used equations to estimate percent body fat from body density data. A recently completed project compared the growth of fat free body mass of breast-fed and formula-fed infants. Other researchers, both on campus and at other institutions, seek out our collaboration in a wide range of ongoing projects related to body composition.

Infant Requirements for Protein and Amino Acids

Defining and understanding the protein and amino acid needs of the infant has for many years occupied the interests of the Unit (Fomon and May, 1958a and b, 1959; Fomon et al., 1958, 1964, 1965, 1971b and c, 1973, 1975a, 1977, 1979; Fomon, 1959, 1960a and b, 1961, 1986, 1991, 1993; Fomon and Owen, 1962; Fomon and Filer, 1967; Fomon and Ziegler, 1979). Several of these studies have been guided by estimates of needs for growth as indicated by growth in body components of the reference infant. A recent study (Fomon et al., submitted for publication) was designed to test the adequacy of protein-energy ratios of infant formulas. The ratios (declining with age), based on theoretic calculations of protein requirement, were found to be slightly inadequate, forcing us to revise upwards our previous estimate of requirements. This study exemplifies how theoretical estimates guide experimental studies, and how, in turn, results of experimental studies lead to reexamination of theoretical estimates. Currently, we are preparing to begin another study with slightly higher protein intakes in an attempt to answer the question: What is the safe level of protein in infant formulas? Such information is important in providing guidance for feeding normal and ill infants.

Renal Solute Load

The first edition of Dr. Fomon's book, "Infant Nutrition," included a chapter on renal solute load (Fomon, 1967b). Drs. Ziegler and Fomon have continued their interest in this topic (Ziegler and Fomon, 1971, 1989; Fomon and Ziegler, 1972, 1993; Bergman et al., 1974), and estimates of potential renal solute load are now widely applied in judging the safety of infant diets.
Factors Affecting Food Consumption by Infants

Although infants eat primarily to satisfy energy needs, food consumption is also influenced by other factors. Study of factors influencing food consumption by infants has been a continuing topic of interest to the investigators in the Pediatric Nutrition Unit. Studies have concerned the effect on food consumption of energy density (Fomon et al., 1969, 1971d, 1975b, 1977), saltiness (Fomon et al., 1970b), sweetness (Ziegler and Fomon, 1982; Fomon et al., 1983) and the ratio of fat to carbohydrate (Fomon et al., 1976). Overviews of the topic have been presented (Fomon, 1980; Fomon and Bell, 1993).

Cow Milk-Provoked Intestinal Blood Loss

Another area of long-term interest of the Pediatric Nutrition Unit is the occult intestinal blood loss induced by consumption of cow milk. Several reports on this topic have been published (Fomon et al., 1981b, 1990) and the data were the major factor that led the Committee on Nutrition of the American Academy of Pediatrics to recommend that consumption of cow milk be avoided during the first year of life. In current studies, we are attempting to answer the following questions: What specific cow milk component causes the bleeding? Does previous breast-feeding affect the frequency or intensity of the response to cow milk? At what age does the responsiveness diminish and at what age does it cease?

Iron Absorption by Infants and Children

With the advent of inductively coupled plasma mass spectrometry several years ago, the use of stable isotopes of iron and zinc as tracers became possible. Because previously the only tracers available were radioisotopes, which many investigators believed to be inappropriate for study of normal infants, knowledge of important aspects of iron and zinc metabolism of infants and children was very limited. In collaboration with Dr. Morteza Janghorbani at the University of Chicago and Dr. Robert Serfass at Iowa State University, methods and procedures for the use of stable isotopes have been developed and a series of studies conducted. A wealth of new information concerning iron absorption of infants (Janghorbani et al., 1986; Fomon et al., 1988, 1989, 1993) and children (Woodhead et al., 1988, 1991) has been obtained. Additional reports are being prepared for publication, and further studies of iron absorption by infants are in progress. The data provide a basis for developing strategies for the prevention of iron deficiency both in industrialized and in non-industrialized countries. Although decreasing in prevalence, iron deficiency remains the most common nutritional deficiency disease among infants and young children.
Zinc Metabolism of Infants

Similar to iron, the availability of stable isotopes has revolutionized the study of zinc metabolism in infants. The Unit was the first to use stable isotopes of zinc in nutritional studies of infants. Methods and procedures were developed in collaboration with Dr. Robert Serfass at Iowa State University. In a first series of studies it was established that the isotopic tracer behaves the same way the intrinsic milk zinc behaves (Serfass et al., 1989) and that the infant is capable of defending zinc balance in the face of low zinc intake by increasing absorptive efficiency and decreasing losses of endogenous zinc (Ziegler et al., 1989). Subsequent studies explored the effects of various diet components on zinc absorption (Ziegler et al., 1990; Serfass et al., 1993) and showed that zinc is better absorbed from breast milk than from formulas (Ziegler et al., 1993). In a recently completed study (to be published) the effect of meat on zinc absorption was determined. Because there is reason to believe that zinc in breast milk is so low that it limits the growth of some infants, an ongoing prospective trial is conducted in which breast-fed infants receive either a small daily supplement of zinc or a placebo (drops with similar taste but without zinc).

Fluoride Metabolism of Infants

Fluoride metabolism and pharmacokinetics in infants are being investigated in collaboration with Dr. Jan Ekstrand of the Karolinska Institute, Stockholm, Sweden. Two reports have been published (Ekstrand et al., 1994a and b) and additional studies are in progress. The data are of particular importance because of increases in the prevalence of dental fluorosis among adolescents in communities with nonfluoridated water as well as in those with fluoridated water. Drs. Fomon and Ekstrand have argued that a portion of this increase may be the result of excessive fluoride intake during early infancy (Fomon and Ekstrand, 1993, 1994; Ekstrand and Fomon, in press), and have been instrumental in changing the recommendations for administering fluoride supplements to infants.

Carnitine Metabolism

Since joining the Pediatric Nutrition Unit in 1984, Dr. Rebouché has shown that endogenous synthesis of carnitine by infants and adults is limited by the availability of the precursor, e-N-trimethyllysine ( Olson & Rebouché, 1987; Rebouché et al, 1989), and that lipid metabolism is altered in infants fed a formula low in carnitine ( Olson et al, 1989; Rebouché et al, 1990). Carnitine status has been shown to differ between vegetarian and non-vegetarian children (Lombard et al, 1989). Using radioactive tracers, kinetics of carnitine absorption and metabolism have been investigated in human adults (Rebouché & Chenard, 1991; Rebouché, 1991). Recent investigations have been directed toward quantifying the effects of dietary components (macronutrient composition, amount of carnitine) on the efficiency with which carnitine is reabsorbed (Rebouché et al, 1993; Stadler et al, 1993). A computerized modelling program is currently being used to
develop mathematical models for carnitine absorption and metabolism, and studies of absorption and metabolism of carnitine in infants and children will be carried out with stable isotopes of carnitine ($^{13}$C and $^{2}$H).

References


