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Preface

As in previous volumes in this series, subjects that may be of interest to nutritionists, usually expanding the underlying science of nutrition or its extension into application in the health arena, are covered by chapters that are listed under "Related Articles" on page x. This is not intended to be a complete list, but it represents the diversity of disciplines which accrete information that contributes to nutrition, just as the latter expands and integrates such knowledge as enhances our well-being.

The prefatory chapter of the current volume of *Annual Review of Nutrition* (*ARN*) brings us up-to-date on what we do and do not know about body composition of infants. In this one of several lifetime interests of Dr. Fomon, he and his colleagues summarize the rather scant information on which early-life composition data is based. The situation with respect to our bodies is not so simple as expressed by Anthelme Brillat-Savarin, who claimed that "Tell me what you eat, and I will tell you what you are." At the later stages of life, there are physiologic changes that reflect the aging process. Horwitz et al. document some insights from animal studies. The onset of nutritional frailty in the elderly is discussed by Bales & Ritchie.

In specific categories of nutrients, the reader can be enlightened on the nutritional and pathologic relevance of fatty acid transport across membranes as considered by Hajri & Abumrad, and be updated on health aspects of dietary conjugated linoleic acid discussed by Belury. Picard & Auwerx describe PPARγ and glucose homeostasis. The dietary regulation of enzymic systems that involve synthesis of nitric oxide is summarized by Wu & Meinenger, and control on steps in the urea cycle is covered by Morris, Jr. Several chapters bring us up-to-date with regard to micronutrients: the role of vitamin A in reproduction and development (Clagett-Dame & DeLuca), carotenoid bioavailability and conversion (Yeum & Russell), details on hydroxylases in the vitamin D pathway (Omdahl et al.), in vivo kinetics of folate (Gregory & Quinlivan), and recent work of a molecular biologic nature on biotin (McMahon). The metabolism and function of copper-binding ceruloplasmin is summarized by Hellman & Gillin. Dietary flavonoids are considered by Ross & Kasum.

In the comic strip character Ziggy (by Tom Wilson), we are reminded that "The waist is a terrible thing to mind." Yet some may learn from the studies of genetically lean mice reported by Reitman in this volume. The relationship of muscle triglyceride and insulin resistance is reviewed by Kelley et al. Newer findings with phytosterols are noted by Ostlund. The ways in which microbes alter the nutrient environment of the mammalian intestine is described by Gordon and his associates. Deleterious effects of helminths on the intestinal tract are documented by Crompton & Nesheim, whereas pre- and probiotics are discussed as protective gastrointestinal organisms by Teitelbaum & Walker. Though many in the U.S. should heed the words of Ben Franklin, among whose dictums was "To lengthen thy life, lessen thy meals," the greater number of people in our world suffer from malnutrition, most commonly as a result of poverty. This is brought forth in the chapter by Pena & Bacallao. Indeed the global problem is to even meet the requirement set by Moliere as concerns food, namely "One must eat to live, not live to eat." Finally, a "special topics" chapter on genetic effects of methylation diets is provided by Van den Veyver.

Our chapter contributors deserve such credit as concerns the content of subjects covered. They are largely suggested by our Editorial Committee but occasionally by past authors and even "volunteers." Authors usually suffer only minor indignities from editorial review and we thank them for their forbearance. For help with manuscripts, I thank my Associate Editors, Denny Bier and Bob Cousins. As always we are indebted to Lisa Dean (production editor) and Sam Gubins (president of Annual Reviews).

The current editor would note with sadness that the founding editor of the *ARN*, Dr. William J. Darby, passed away recently. Bill Darby was not only one of my mentors while I was a student in the Department of Biochemistry at Vanderbilt University, but he had ongoing interest in the evolving *ARN* mission to communicate advances in our profession. He will be missed.

Donald B. McCormick
Editor

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ERRATA

An online log of corrections to *Annual Review of Nutrition* chapters (if any, 1997 to the present) may be found at http://nutr.annualreviews.org/

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BODY COMPOSITION OF THE MALE AND FEMALE REFERENCE INFANTS[1]

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Key Words fat, fat-free mass, minerals, protein, water

■ **Abstract** During infancy, especially early infancy, a substantial proportion of the requirements for energy and specific nutrients are those needed for growth. Knowledge of the body composition of a reference infant (body size and chemical composition at the 50th centile for age) permits an estimate of the growth needs of the infant. In this communication, we review efforts from the 1960s to the present at defining the composition of the male and female reference infants. We and others have demonstrated that accumulation of fat is remarkably rapid during the first 4 or 6 months of life. As a percentage of fat-free mass, water decreases throughout infancy whereas protein and minerals increase. However, the quantitative nature of these changes remains uncertain. After identifying the areas in which further data are needed, we conclude that the single most important area for further work is determining the relation of "bone mineral content" determined by dual energy X-ray absorptiometry to the osseous mineral content of the infant.

CONTENTS

[1]Abbreviations: BMC, "bone mineral content" determined by DEXA; DEXA, dual energy X-ray absorptiometry; FFM, fat-free mass; TBK, total body potassium; TBW, total body water; W_{ec}, extracellular water; W_c, cellular water.

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INTRODUCTION

Since the early 1960s, one of the authors (SJF) has had a major interest in the body composition of infants. In the mid 1960s he published crude estimates of the chemical composition of the infant at various ages and, subsequently, in collaboration with a number of his colleagues, presented estimates of body composition of infants and children. From knowledge of the body content of a nutrient at two selected ages, one can calculate the increment of the nutrient during the relevant age interval—a value essential for use of the "factorial" approach to estimating nutrient requirements. As will be discussed, the factorial approach is particularly useful for infants because, especially during the early months of life, requirements for various nutrients for growth comprise a substantial fraction of the total requirements. This communication reviews the progress that has been made in defining the composition of the "male and female reference infants," and identifies areas in which further work is needed.

Six approaches, with some overlap, may be used to estimate nutrient requirements during infancy: (*a*) direct experimental evidence; (*b*) extrapolation from experimental evidence relating to human subjects of other ages, to subjects of the opposite sex, or to animal models; (*c*) analogy with the breast-fed infant; (*d*) metabolic balance studies; (*e*) clinical observations; and (*f*) theoretically based calculations (23). In estimating nutrient requirements of the infant, the last of these approaches is, in many cases, the first to be applied. As early as 1957 Hegsted (30) used a theoretic approach to estimate protein requirements of children, and it seemed feasible to apply a similar approach to the requirements for other nutrients. By adding the estimated requirement of a nutrient for growth to that for maintenance (nongrowth), one can derive a tentative value for requirement of the nutrient. As now applied, this theoretic approach is generally based on the estimated requirements for growth and maintenance of a "reference infant" (an infant with weight and length and body composition believed to be at the 50th centile for age). The estimated requirement is then increased by some factor to arrive at a recommended intake believed to be adequate for all or nearly all infants. The major value of this theoretic approach is that it provides a specific target for experimental testing.

The approach to estimating nutrient requirements of the infant differs considerably from that for adults. The normal adult requires regular intake of energy and specific nutrients to maintain the size and composition of the body (i.e., requirements for maintenance), whereas infants and children need, in addition, energy and nutrients for growth. The ratio of need for growth to need for maintenance is greatest for the fetus, the rapidly growing preterm infant, and the term infant during the early months of life. Therefore, to obtain reasonable estimates of the requirements for energy and nutrients of the infant, it is desirable to have quantitative data on the increments in energy storage and the increments in specific nutrients needed for synthesis of new tissue. The importance of defining the requirements of energy or nutrients for growth is much less important for children over the age of 2 years and for adolescents because the requirements for growth are quite small fractions of total requirements.

A simple conception of body composition is a two-compartment model composed of fat and fat-free mass (FFM). Fat in this model is ether-extractable fat and FFM is the remainder (nonfat), which includes the stroma of adipose tissue. It is now much more clearly established than it was in the early 1960s that in adult subjects the composition of FFM varies with gender and age (45). Nevertheless, in the early 1960s it was recognized that the changes with age in composition of FFM of the adult are rather modest. Little was known about the extent of changes in composition of the whole body or of FFM of the infant.

WHAT WE KNEW IN THE EARLY 1960s

Chemical Analyses

Whole body chemical analyses were available for stillborn infants as summarized by Owen et al. (37) and for five adults as summarized by Widdowson & Dickerson (48). It was evident from these data that the percentage of water in FFM was considerably greater and the percentage of protein in FFM was considerably less in the newborn than in the adult. Limited data from tissue analyses were available for various ages during infancy. The most important were analyses of fresh muscle (15), adipose tissue (16–18), and bone (14).

Total Body Water and Extracellular Water

A number of reports of total body water (TBW) and chloride or bromide space [from which the quantity of extracellular water (W_{ec}) can be calculated] in the infant were available (12, 13, 19, 21, 27). These studies demonstrated a decrease in TBW with age and a decrease in W_{ec} as a fraction of TBW. Our own studies (38, 39) demonstrated that the decrease in TBW as percent of body weight was rapid during the first 130 days of life and was quite modest from 131–270 days. W_{ec} decreased more rapidly than did TBW during the first 130 days of life. Thus, during the first few months of life there was a major decrease in the ratio of W_{ec} to cellular water (W_c). Moreover, TBW and W_{ec} were greater per unit of body weight in males than in females. Only a few values for TBW were available for infants from 270–365 days of age.

Sodium, Chloride, Potassium, Calcium, Phosphorus, and Magnesium

Concentrations of various elements per unit of FFM in the newborn and the adult were summarized by Forbes (26). In this summary the concentration of sodium was the same in FFM of the newborn and the adult and that of chloride was only slightly greater in FFM of the adult than of the newborn. Concentrations of potassium, calcium, phosphorus, and magnesium were all considerably greater in FFM of the adult than of the newborn.

Peripheral Adipose Tissue

Data on peripheral adipose tissue were available from measurements made on roentgenograms of the extremities by Maresh (34). Fifty infants were studied longitudinally at ages 2, 4, 6, 12, and 18 months. The mid-arm, mid-thigh, and mid-calf roentgenograms permitted measurement of an outer layer of skin-plus-adipose tissue, a central area of bone, and an area of muscle between the skin-plus-adipose tissue layer and bone. At the three sites, the width of the muscle layer increased progressively with age, whereas the width of the skin-plus-adipose tissue layer increased to age 6 months and decreased slightly thereafter. For the sum of the three sites, the ratios of skin-plus-adipose tissue to muscle in males at 2, 4, 6, and 12 months of age were 0.56, 0.71, 0.80, and 0.69, respectively. The ratio at a specified age was greater for females than for males. We suspected that peripheral adipose tissue of the infant contained a high percentage of the body fat and we therefore speculated that body fat as a percentage of body weight increased until about 6 months of age and decreased thereafter.

Chemical Maturation of Fat-Free Mass

Moulton (36) summarized earlier reports on chemical maturation of FFM in a number of species of mammals and added new data, including relevant reports concerning humans. For the nine species with the most available data, chemical maturation of FFM progressed most rapidly early in life, then decelerated until chemical maturity was reached at 4.3–4.6% of the life span. For a human with a 70-year life expectancy, this corresponded to 3–3.2 years of age.

1966 MALE REFERENCE INFANT

Data relevant to determining various aspects of body composition of the infant at specified ages were available from whole body chemical analyses (birth only), anthropometry, roentgenograms of the extremities, and determinations of TBW. Although data were also available on W_{ec}, these were ignored in developing the 1966 and 1967 reference infants. Because we were aware of gender-related differences in body composition during infancy and had available somewhat more data on males than on females, the 1966 reference infant was male (22).

Composition at Birth

Owen et al. (37) summarized data from whole body chemical analyses of stillborn infants believed to be born at term (9–11, 17, 48). Mean body weight of six male infants was 3197 g, fat 382 g, protein 435 g, and water 2331 g. TBW of males was 73% of body weight and that of females was 70% of body weight. These values did not agree with the data of Yssing & Friis-Hansen (49) on TBW of 88 term newborn infants (51 males and 37 females) determined by the deuterium dilution method and, because of the likelihood of loss of water from the bodies of the stillborn infants between the time of death and the time of chemical analysis, it seemed probable that the in vivo data on TBW were more acceptable. Yssing & Friis-Hansen reported a mean value for 37 determinations of deuterium distribution space of male newborns to be 76.6% of body weight. Taking into account that deuterium dilution space slightly overestimates TBW because of exchange of the administered ^2H with the hydrogen of organic molecules, the mean value of Yssing & Friis-Hansen was decreased by 2%; believed to be the best estimate of the overestimation of TBW by measurement of deuterium space. Thus, water content of the male reference infant was assumed to be 75.1% of body weight rather than the 73% reported from chemical analyses. After adjustment of the values obtained by whole body chemical analysis to reflect a presumed loss of water between death and the time of chemical analysis, the composition of the male reference infant was 75.1% water, 11.0% fat, 11.4% protein (nitrogen × 6.25), 1.7% mineral, and 0.8% "residue" (Table 1).

Whole Body Chemical Analyses Beyond the Newborn Period

With the exception of the composition of a 4-year-old male who died of tuberculous meningitis (46), no data from whole body chemical analyses were available from birth until adulthood. Results of analyses of the 4-year-old male suggested that water and potassium had been lost from the body during the illness. Chemical analyses of five adult cadavers had been reported from 1951 to 1956 (48). After adjustment for probable excess water (as the result of heart failure) in two cadavers, TBW was 72% of FFM and protein was 21.3% of FFM (Table 1).

Model Chosen for Maturation of Fat-Free Mass

Based on the roentgenographic data of Maresh (34), we constructed a model of the FFM of the infant from birth to 12 months of age (37). We assumed that each thigh is a cylinder with length equal to that of the femur between epiphyseal plates and cross section as calculated from measurements of bone, muscle, (twice the lateral width), and skin-plus-adipose tissue (twice the lateral width). The volumes of skin-plus-adipose, muscle, and bone in the thigh were calculated at ages 2, 4, 6, and 12 months. In an analogous manner, the volumes of skin-plus-adipose tissue, muscle, and bone were calculated for the leg, arm, and forearm (37).

The fat content of adipose tissue was based on the limited data of Dju et al. (16–18), concerning four infants at birth (fat 40% of adipose tissue weight), one