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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.

INTRODUCTION

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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

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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.

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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).

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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 ^{2}H 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 $\times$ 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

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TABLE 1 1966 and 1967 versions of male reference infant (22, 23)

		Composition (gm/100 g)											
		Whole body								Fat-free mass			
		Water		Protein		Lipid		Other[a]		Water		Protein	
Age (mo)	**Weight (kg)**	**1966**	**1967**	**1966**	**1967**	**1966**	**1967**	**1966**	**1967**	**1966**	**1967**	**1966**	**1967**
Birth	3.50	75.1	75.1	11.4	11.4	11.0	11.0	2.5	2.5	84.4	84.3	12.8	12.8
2	5.45	62.1	63.7	14.1	11.4	20.3	22.4	3.5	2.5	77.8	82.0	16.4	14.7
4	7.00	60.1	60.2	15.4	11.4	22.2	25.9	2.3	2.5	77.2	81.0	19.5	15.4
6	8.28	56.7	59.9	15.0	12.3	26.5	25.3	1.8	2.5	77.1	80.0	20.4	16.5
8	9.08	56.7	59.6	15.8	13.1	25.4	24.8	2.1	2.5	76.0	79.2	21.2	17.4
10	9.82	56.7	59.3	16.6	13.7	24.4	24.5	2.3	2.5	75.0	78.5	21.6	18.1
12	10.50	56.7	59.0	17.5	14.6	23.3	23.9	2.5	2.5	73.9	77.5	22.8	19.4
Adult										72.4		21.5	

[a]Includes minerals and "residue" in 1966.

infant at 3 months of age (44%), and one infant at 18 months of age (59%). These values for fat content of adipose tissue are considerably less than those reported by Allen et al. (1) for adults. We were unable to find data on the water content of fat-free adipose tissue of infants and therefore assumed that water is 79% of fat-free adipose tissue as reported by Allen et al. for adults (70–80%). The chemical composition of muscle was calculated from the data of Dickerson & Widdowson (15), and that of bone from the data of Dickerson (14). The density (g/ml) of each component was then calculated using values proposed by Brozek et al. (3). The density of tissue not accounted for by water, protein, fat, and minerals, ("residue") was assumed to be 1.100 gm/ml. From these data, the chemical composition (g/100 g) of fresh muscle, adipose tissue, and bone was calculated for the ages for which data were available and interpolated for other ages. These data were used to calculate the chemical composition of the fresh-weight model and the FFM model of the four extremities at ages 2, 4, 6, and 12 months of age.

Values for TBW of the male reference infant between 2 and 12 months of age were taken from our own published (38, 39) and unpublished data. It was assumed that the relation between water and the other components of FFM (protein, minerals, and residue) were the same in the reference infant as in the model of the four extremities. The estimates of body composition of the 1966 male reference infant are included in Table 1. The major difficulties with the approach were that (*a*) the chemical composition of the extremities might be quite different from that of the whole body; (*b*) there were very few data points on TBW after 270 days of age, and it was therefore assumed that at 6, 8, 10, and 12 months of age body water remained at 56.7% of body weight (the mean value for the few available determinations); (*c*) in the model the water content of adipose tissue after birth was based on one data point at age 3 months and one at age 18 months.

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THE 1967 MALE REFERENCE INFANT

Almost as soon as the manuscript concerning the 1966 reference infant went to press, we identified serious difficulties with his body composition. Largely as a result of the values used for TBW at 6–12 months of age and values used for water content of adipose tissue, the water content of FFM of the 1966 male reference infant decreased to nearly the adult level by 12 months of age. Even more troubling was that the calculated protein content of FFM from 6 to 12 months of age approached or exceeded that of the adult.

Fortunately, by the time of publication of the composition of the 1966 reference infant, additional data on the composition of adipose tissue became available to us [subsequently published by Baker (2)]. We had also accumulated additional data on TBW, especially from 270 to 365 days of age. Substituting some new values for TBW and composition of adipose tissue in the model of the four extremities, the 1967 male reference infant was developed (Table 1). The major ways in which the 1967 version differed from the 1966 version were as follows: (*a*) As a percentage of FFM, TBW decreased less rapidly from 4 to 12 months of age and the value at age 12 months no longer approached that of the adult. (*b*) As a percentage of

FFM, protein increased less rapidly from birth to 12 months of age and no longer exceeded the corresponding value of the adult. (*c*) As a percentage of body weight, fat increased more rapidly during the first 4 months of age. (*d*) The component "other" was assumed to be constant at 2.5% of body weight throughout the first year of life, whereas the analogous category, minerals-plus-residue, in the 1966 version had an unbelievable high value at age 2 months.

1982 MALE AND FEMALE REFERENCE INFANTS

In 1981 Haschke et al. (29) used data from the literature to construct a 9-year-old reference boy, and in 1982 Fomon et al. (25) presented a first effort in estimating the body composition of male and female reference individuals from birth to 10 years of age. Because estimates of the body composition of preadolescent children had not previously been attempted, this was the focus of the presentation. However, we had access to unpublished data on body composition of stillborn infants [published soon afterward by Widdowson (47)], and Romahn & Burmeister (43) had summarized their studies of total body potassium (TBK) during infancy. Thus, with inclusion of new data, the composition of the male reference infant (23) differed from that presented previously and, for the first time, the composition of a female reference infant was included (Tables 2a and 2b).

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Composition at Birth

Birth weight of the male reference infant was set at 3.5 kg and that of the female reference infant at 3.35 kg. The data of Widdowson (47) were used to obtain values of fat, protein (nitrogen $\times$ 6.25), and calcium. The content of osseous minerals (the minerals and mineral salts of bone cortex and teeth) was calculated from the calcium content (calcium/osseous minerals $=$ 0.34) as documented for bone cortex of the adult by Brozek et al. (3). Because the data of Widdowson were not gender specific, we made the assumptions (*a*) that the ratio of fat to body weight was the same as the ratio of truncal skinfold thickness to body weight as reported by McGowan et al. (35) and (*b*) that the composition of FFM at birth was the same for males and females. TBW was calculated from the deuterium dilution data of Yssing & Friis-Hansen (49) and W_{ec} from the thiosulfate space data of Burmeister (6, 7). From the known mineral composition of W_{ec} and W_c, we calculated the body content of nonosseous minerals. On the basis of these data and assumptions we arrived at the composition of the reference male and female infants at birth with respect to body weight, fat, FFM (body weight minus fat), TBW, W_{ec} and W_c, minerals, and protein. We assumed that carbohydrate (predominantly glycogen) accounted for 0.6% of FFM.

Composition at Age 6 Months

In estimating the composition of the male and female reference infants at age 6 months, we used the median body weight of males and females from the National Center for Health Statistics data (28), our own data on TBW, and the data of

TABLE 2a Body composition of reference infants[a]

	Length (cm)		Weight (g)		Components (% of body weight)									
					Fat		Protein		TBW		W_{EC}		W_C	
Age	**F**[b]	**B**[c]	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**
Males														
Birth	51.6		3545		13.7		12.9		69.6		42.5		27.0	
0.5 mo		52.5		3760		11.4		12.5		73.9		46.3		27.6
1 mo	54.8		4452		15.1		12.9		68.4		41.1		27.3	
2 mo	58.2		5509		19.9		12.3		64.3		38.0		26.3	
3 mo	61.5	61.2	6435	6330	23.2	30.2	12.0	10.6	61.4	56.5	35.7	32.9	25.8	23.6
4 mo	63.9		7060		24.7		11.9		60.1		34.5		25.7	
5 mo	65.9		7575		25.3		11.9		59.6		33.8		25.8	
6 mo	67.6	67.9	8030	8040	25.4	29.1	12.0	10.9	59.4	57.2	33.4	32.9	26.0	24.3
9 mo	72.3	72.2	9180	9130	24.0	25.7	12.4	12.0	60.3	59.2	33.0	32.6	27.2	26.9
12 mo	76.1	76.1	10150	10030	22.5	25.6	12.9	12.3	61.2	59.0	32.9	31.6	28.3	27.4
Females														
Birth	50.5		3325		14.9		12.8		68.6		42.0		26.7	
0.5 mo		52.0		3640		14.2		12.2		73.2		47.0		26.2
1 mo	53.4		4131		16.2		12.7		67.5		40.5		26.9	
2 mo	56.7		4989		21.1		12.2		63.2		37.1		26.1	
3 mo	59.6	60.7	5743	6030	23.8	31.5	12.0	10.2	60.9	55.6	35.1	32.8	25.8	22.8
4 mo	61.9		6300		25.2		11.9		59.6		33.8		25.8	
5 mo	63.9		6800		26.0		11.9		58.8		33.0		25.9	
6 mo	65.8	66.5	7250	7600	26.4	32.0	12.0	10.4	58.4	54.9	32.4	31.7	26.0	23.2
9 mo	70.4	71.0	8270	8620	25.0	28.8	12.5	11.4	59.3	56.9	32.0	31.4	27.3	25.5
12 mo	74.3	75.3	9180	9500	23.7	27.6	12.9	12.2	60.1	56.9	31.8	29.7	28.3	27.4

[a]Abbreviations: TBW, total body water; W_{EC}, extracellular water; W_C, cellular water.

[b]Fomon et al. 1982 (25).

[c]Butte et al. 2000 (8).

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Romahn & Burmeister (43) on TBK. We assumed that the nitrogen to potassium ratio of tissue synthesized between birth and 6 months was 0.461 g/meq (the ratio in the adult) and obtained total body protein by adding the increment in total body protein from birth to age 6 months to the protein content at birth. The data of Dickerson (14) suggested that the ratio of calcium to nitrogen in the cortex of the femur does not increase until after 12 months of age and, on this basis, we assumed that the ratio of osseous minerals to FFM is constant from birth to 12 months of age. W_{ec} and W_c were calculated from TBW and TBK, and nonosseous minerals were calculated from the known concentrations in W_{ec} and W_c. FFM was calculated as the sum of weights of water, protein, minerals and carbohydrate, and fat mass was calculated as body weight minus FFM.

We noted that in males the ratio of percent body fat to the sum of truncal skinfold thickness [data from (31)] was similar at 6 months and 9 years of age (24.5%/13.2 mm and 13.2%/8.0 mm). From the truncal skinfold thickness data we calculated the fat (percentage of body weight) for each age from birth to 9 years and

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TABLE 2b Body composition of reference infants[a]

	Components (% of body weight)					
	OM		NOM		CHO	
	F[b]	B[c]	F	B	F	B
Males						
Birth	2.6		0.6		0.5	
0.5 mo		1.8		0.68		0.45
1 mo	2.6		0.6		0.5	
2 mo	2.4		0.6		0.5	
3 mo	2.3	1.7	0.6	0.52	0.5	0.45
4 mo	2.3		0.5		0.4	
5 mo	2.3		0.5		0.4	
6 mo	2.3	1.9	0.5	0.53	0.4	0.45
9 mo	2.3	2.1	0.6	0.55	0.5	0.45
12 mo	2.3	2.2	0.6	0.54	0.5	0.45
Females						
Birth	2.6		0.6		0.5	
0.5 mo		1.9		0.68		0.45
1 mo	2.5		0.6		0.5	
2 mo	2.4		0.6		0.5	
3 mo	2.3	1.7	0.6	0.51	0.5	0.45
4 mo	2.3		0.5		0.4	
5 mo	2.2		0.5		0.4	
6 mo	2.2	1.8	0.5	0.51	0.4	0.45
9 mo	2.3	2.0	0.5	0.52	0.4	0.45
12 mo	2.3	2.2	0.5	0.53	0.5	0.45

[a]Abbreviations: OM, osseous minerals; NOM, non-osseous minerals; CHO, carbohydrate.

[b]Fomon et al. 1982 (25).

[c]Butte et al. 2000 (8).

constructed a smoothed curve for fat content of the body, interpolating between birth and 3 months of age and extrapolating from 9 years to 10 years of age.

We arrived at the composition of a 6-month-old reference female in a manner similar to that used for the male and arrived at the composition of a 10-year-old reference female in a manner similar to that used in developing the 9-year-old reference male. Values at other ages were obtained by interpolation as described for the male. The data for infancy are presented in relation to body weight in Tables 2a and 2b and in relation to FFM in Table 3.

We believed that even with the limited data available to us, we would be able to arrive at useful age-specific and gender-specific constants for infants and children regarding the components of FFM: TBW, TBK, protein, W_{ec}, W_c, osseous minerals and nonosseous minerals. Nevertheless, we stated that, “although we believe that

TABLE 3 Composition of fat-free mass (FFM) of reference infants[a]

	Components (% of FFM)															
	Protein		TBW		W_{EC}		W_C		OM		NOM		CHO		TBK (meq/kg FFM)	
Age	**F**[b]	**B**[c]	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**	**F**	**B**
Males																
Birth	15.0		80.6		49.3		31.3		3.0		0.7		0.6		49.0	
0.5 mo		13.9		82.7		51.6		31.0		2.0		0.8		0.5		48.6
1 mo	15.1		80.5		48.4		32.1		3.0		0.7		0.6		50.1	
2 mo	15.4		80.3		47.4		32.9		3.0		0.7		0.6		51.2	
3 mo	15.6	15.1	80.0	81.0	46.4	47.2	33.6	33.8	3.0	2.5	0.7	0.7	0.6	0.6	52.2	52.5
4 mo	15.8		79.9		45.8		34.1		3.0		0.7		0.6		53.0	
5 mo	15.9		79.7		45.2		34.5		3.0		0.7		0.6		53.6	
6 mo	16.0	15.3	79.6	80.7	44.7	46.4	34.9	34.2	3.0	2.6	0.7	0.7	0.6	0.6	54.1	53.2
9 mo	16.4	16.1	79.3	79.7	43.5	43.6	35.8	36.2	3.0	2.8	0.7	0.7	0.6	0.6	55.5	55.9
12 mo	16.6	16.4	79.0	79.3	42.5	42.5	36.5	36.9	3.0	2.9	0.7	0.7	0.6	0.6	56.5	57.0
Females																
Birth	15.0		80.6		49.3		31.3		3.0		0.7		0.6		49.0	
0.5 mo		13.5		83.1		53.2		29.9		2.1		0.8		0.5		46.9
1 mo	15.2		80.5		48.3		32.1		3.0		0.7		0.6		50.2	
2 mo	15.5		80.2		47.1		33.1		3.0		0.7		0.6		51.5	
3 mo	15.8	15.0	79.9	81.1	46.0	47.7	33.9	33.4	3.0	2.4	0.7	0.7	0.6	0.6	52.7	52.0
4 mo	15.9		79.7		45.2		34.5		3.0		0.7		0.6		53.5	
5 mo	16.1		79.5		44.6		34.9		3.0		0.7		0.6		54.2	
6 mo	16.3	15.3	79.4	80.7	44.0	46.5	35.4	34.2	3.0	2.6	0.7	0.7	0.6	0.7	54.8	53.1
9 mo	16.6	16.0	79.0	79.8	42.7	43.9	36.4	35.9	3.0	2.8	0.7	0.7	0.6	0.6	56.3	55.5
12 mo	16.9	16.8	78.8	78.8	41.6	40.9	37.1	37.9	3.0	3.1	0.7	0.7	0.6	0.6	57.4	58.4

[a]Abbreviations: TBW, total body water; W_{EC}, extracellular water; W_C, cellular water; OM, osseous minerals; NOM, nonosseous minerals; CHO, carbohydrate; TBK, total body potassium.

[b]Fomon et al. 1982 (25).

[c]Butte et al. 2000 (8).

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these constants are more suitable than constants based on the composition of the adult reference man, the constants and other estimates of body composition presented here must be considered preliminary and crude because of uncertainties about the data and because of the large number of assumptions that have been required." In 2000 Butte et al. (8) used a more satisfactory approach to determining body composition of individuals less than 2 years of age.

BUTTE ET AL. (8) REFERENCE SUBJECTS: BIRTH TO AGE 2 YEARS

Butte et al. (8) determined TBW and TBK longitudinally with 76 subjects at ages 0.5, 3, 6, 9, 12, 18, and 24 months and determined bone mineral content (BMC) by DEXA at ages 0.5, 12, and 24 months. BMC at other ages was based on a prediction equation relating it to age, length, and TBK. The assumptions needed to arrive at composition of FFM (except for BMC) were the same as those of our

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1982 publication (25). Fat was determined as body weight minus the sum of the components of FFM.

This approach offers a remarkable opportunity for advancing our knowledge of the body composition of infants and is obviously much to be preferred to the approach that we had used, in which calculations were based on data obtained from a variety of sources in the literature. Furthermore, in our 1966, 1967, and 1982 reference infants, the estimates relating to osseous minerals were based on extremely little data, and therefore the inclusion of data on BMC in the reference infants of Butte et al. seemed to offer a major opportunity for improvement. The Butte et al. (8) data are presented in relation to body weight in Tables 2a and 2b and Figure 1, and in relation to FFM in Table 3, and may be compared with the earlier data of Fomon et al. (25). The large discrepancy in fat content of the reference infants of Fomon et al. and Butte et al. is evident from inspection of Tables 2a and 2b and Figure 1.

In spite of the soundness of the approach used by Butte et al. (8), the values presented for fat, TBK, and osseous minerals raise questions. Two observations about the fat content reported by Butte et al. are difficult to explain: (*a*) At age 0.5 months, fat accounts for 11.7% of body weight in males and 14.3% in females. Thus, fat content is 22.2% greater in females than in males, whereas the gender-related difference in peripheral adipose tissue as measured from skinfolds (e.g., 31) or roentgenograms (34) is generally no more than 9%. It is difficult to imagine that there is a large gender-related difference in fat depots other than peripherally (e.g., intra-abdominal sites). (*b*) Gain in weight by males from 0.5 to 3 months of age is reported to be 33.8 g/d and gain in fat 19.3 g/d (1470 g in 76 days). Because fat is

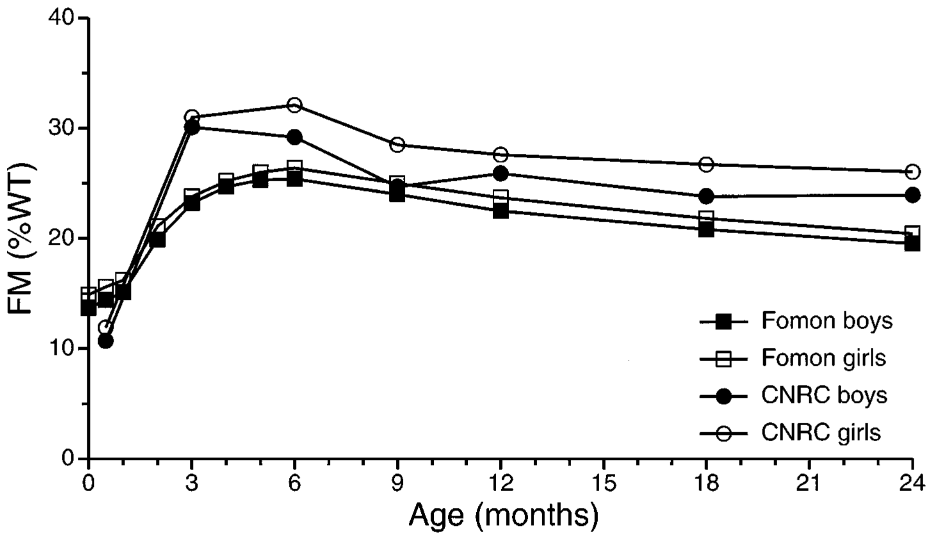

Figure 1 Fat as percentage of body weight of reference individuals described by Fomon et al. (25) and Butte et al. (8). From Butte et al. (8), reproduced by permission of the publisher.

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primarily deposited in adipose tissue, which during early infancy is about 45–60% fat (2), and because fat-free adipose tissue is relatively low in protein and minerals, the increase in adipose tissue of males from 0.5 months to 3 months of age seems to account for an extraordinarily high percentage of the increase in weight.

The values for TBK at 0.5 months of age may be correct but should be independently verified. The TBK values reported by Butte et al. (8) are greater than those reported by Romahn & Burmeister (43) for the same age and greater than the values obtained for the newborn by whole body chemical analysis (47).

Dual Energy X-Ray Absorptiometry, Bone Mineral Content, and Osseous Minerals

As defined by Brozek et al. (3) and used in our 1982 presentation (25), osseous minerals are defined chemically and calcium makes up 34% by weight. BMC as measured by DEXA has been interpreted by relating the measurement in pigs to the results of whole body chemical analysis of the pigs (4, 5, 20, 40–42). Picaud et al. (41) reported that calcium is 46.5% of BMC, and Rigo et al. (42) used this value. Other investigators have not specified the calcium content of BMC. Koo et al. (32) and apparently Butte et al. (8) assumed that BMC is identical to osseous minerals and that calcium accounts for 34% of BMC. Koo et al. (32) reported a mean total body calcium of 23.2 g at 1–8 days of age, and based on the reported values for osseous minerals, total body calcium at 0.5 months of age in the Butte et al. (8) reference infants is 23.0 g for males and 23.5 g for females. Thus, total body calcium values soon after birth as reported by Koo et al. and Butte et al. are in good agreement but are considerably less than the 30.4 g reported from two separate series of whole body chemical analyses (47, 50).

THE STATE OF THE REFERENCE INFANTS IN 2000

As already noted, the purpose of determining the body composition of reference infants is to permit initial estimates of the gain in energy and specific nutrients during selected age intervals. The estimated requirement for growth may then be added to the estimated requirement for maintenance (nongrowth) to provide a target value for design of studies of infant requirements for energy and specific nutrients. The reference infants of Fomon et al. (25) and Butte et al. (8) demonstrate that the body increment in fat is remarkably large during the first four (25) or six (8) months of life, indicating that energy requirements for growth are a quite large fraction of the total energy requirement.

FFM has been presented on a gender-specific basis both by Fomon et al. (25) and Butte et al. (8), and there is every reason to suspect that, as in the adult (45), such differences are present during infancy. However, gender-related differences in FFM during infancy are likely to be rather trivial in comparison with the whole body gender-related differences at a selected age or the age-related differences. Thus, until the methodology has advanced considerably beyond its current state, it may not be desirable to attempt to identify gender-related differences in FFM of infants.

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The TBW values of Butte et al. (8) are greater per unit of body weight than those of Fomon et al. (25) and, as pointed out by Butte et al., the Fomon et al. values are low because of the assumption that the quantity of ^{2}H incorporated into organic molecules is 1.3% of the dose rather than 4% of the dose as documented by Schoeller (44).

The protein content of the body was obtained both by Fomon et al. and Butte et al. on the assumption that the ratio of nitrogen to potassium is 0.461 g/meq and protein is nitrogen $\times$ 6.25. In the Fomon et al. model, the value at birth was taken from whole body chemical analysis and the value at 6 months from TBK as reported by Romahn & Burmeister (43). Gain in protein in the Fomon et al. model is 3.4 g/d from birth to 3 months of age and in the Butte et al. model it is 2.6 g/d from 0.5 to 3 months of age. The discrepancy, which results from the considerably lower TBK values of Butte et al. than of Romahn & Burmeister, will require further studies for resolution.

Although DEXA is a promising tool for estimating osseous minerals of human infants, its usefulness will be greatly limited until it is possible to relate BMC determined by DEXA to osseous mineral content of the infant. There would appear to be no easy way to do this because, unfortunately, the relation between BMC and osseous minerals of the human infant may not be the same as that of a pig of similar weight. Moreover, the relation between BMC and osseous minerals may change with age. Thus, after more than 35 years of attempting to estimate the chemical composition of the human infant, many uncertainties remain.

Although the models presented by Fomon et al. (25) and Butte et al. (8) represent improvements over the earlier models (22, 23), neither seems close to being definitive. Whole body chemical studies of infants who died after the neonatal period have not been carried out and are probably unlikely to be carried out. Additional determinations of TBK are needed to resolve the difference between the data of Romahn & Burmeister (43) and the data of Butte et al. (8). The factor relating total body nitrogen to TBK (0.461 g nitrogen/meq potassium) used by Fomon et al. and Butte et al. needs to be reevaluated. The relation of total body nitrogen to TBK at birth and in adulthood rests on relatively few analyses, and additional data are needed. Perhaps most of all we need to find a way to relate BMC determined by DEXA to osseous minerals (and therefore to calcium content of the body) throughout infancy.

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