Body Composition during the First Year of Life

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Abstract
Knowledge of changes in body composition is of great potential benefit to the understanding of the nutritional needs and functional outcome of nutritional management for both healthy and sick infants. This review evaluates the different methods presently available to evaluate whole-body composition analysis based on different models, i.e. 2, 3, or more compartments. Analysis of the various approaches related to age, body weight and body length suggests that the major differences observed between the techniques could be preferentially related to differences in the population and that gender is one of the major determinants of whole-body composition during the first year of life. Among the techniques dual-energy X-ray absorptiometry (DEXA) and, more recently, air displacement plethysmography appear to be major techniques that have been evaluated in infants. Determination of weight gain composition is one of the major keys to the evaluation of the nutritional requirements, whereas the dynamic aspect during the first years of life could play a fundamental role in the nutritional programming of adult morbidity. Recent data suggest that protein intake and the protein:energy ratio are the main determinants of weight gain composition in preterm infants. Nevertheless, these data need to be confirmed in larger cohorts evaluated during the first year of life. To that, DEXA appears to be a useful technique to obtain sequential analysis of weight gain composition over a longer period of time and in a less invasive fashion.

Introduction
Infancy is the period of most rapid postnatal growth and is accompanied by major changes in body composition. Knowledge of these changes in body composition in healthy infants is of great potential benefit to the understanding of the nutritional needs and functional outcome of nutritional management for both healthy and sick infants [1]. Recently much interest has been focused on the relationship between early nutrition and the future health of
humans. Poor growth during early life as well as a large weight gain during infancy have been associated with disorders up to adulthood. Accurate assessment of body composition during infancy enables the determination of weight gain composition and provides key information for evaluating nutritional requirements, the efficacy of diet and medical interventions, and the influence of chronic disease [2]. Therefore, studies on how the nutritional situation interacts with the growth process and body and weight gain composition during early life in humans are very important.

**Evaluation of Body Composition**

*Direct Measurements of Body Composition*

Most of our knowledge on the body composition of preterm infants is derived from body carcass analyses of stillborn preterm infants. The first values were reported in 1877, and thus far 169 infants have been analyzed [3]. However, not all analyzed fetuses can be considered for reference material because gestational age, and time and cause of death were either not reported or may not have been accurately obtained. Nevertheless, more recent studies using various technologies have confirmed the chemical analysis data and validated the interest in the evaluation of intrauterine reference values of whole body composition and in the determination of the postnatal nutritional requirements for preterm infants. With the exception of the composition of a 4-year-old male who died of tuberculous meningitis, no data on whole body chemical analyses are available from birth until adulthood and our knowledge during the first year of life is derived from indirect methods [4, 5].

*Indirect Measurements of Body Composition*

In infants, the only practical means of measuring body composition is by noninvasive and indirect methods. Several methods have been developed to indirectly measure body composition in vivo (table 1). Unfortunately, these methods have limited application in infants, i.e. they are relatively invasive, may involve significant radiation exposure, and/or need active cooperation of the subject. Whole body composition analysis may be based on different models, i.e. 2, 3, or more compartments. The basic 2-compartment model, which assumes that body mass is composed of adipose and non-adipose issue, i.e. fat mass (FM) and fat-free mass (FFM) or lean body mass (LBM), is the widely used. The total body fat (TBF) compartment is the most variable one and most sensitive to changes in nutritional status so most emphasis has been laid on its measurement [5]. The three-compartment model adds a value for skeletal or bone mass, whereas in the multi-component model, body composition is obtained by integrating data from various techniques (whole body density, total body water (TBW), bone mineral content (BMC) and anthropometry) [6, 7].
Among the various techniques, anthropometric measurements, total body electrical conductivity (TOBEC), bioelectrical impedance analysis (BIA), tracer dilution using stable isotopes (deuterium oxide: $^{2}$H$_2$O), dual-energy X-ray absorptiometry (DEXA) and, more recently, air displacement plethysmography (ADP) are major techniques that have been evaluated in infants.

Skin-fold thickness is a simple way of measuring FM. This approach makes two assumptions: i.e. the thickness of the subcutaneous adipose tissue reflects a constant proportion of the TBF and the sites selected for measurement represent the average thickness of the subcutaneous adipose tissue. Soft tissue composition, derived from anthropometric measurements, shows good correlation with several other techniques for in vivo body composition measurement, including isotope dilution, TOBEC, and DEXA [1]. However, the rapidly changing distribution of fat accretion in young infants makes it difficult to generate a consistent equation for predicting TBF [5, 8]. In addition, body composition data from anthropometric measurements have a poor predictive value for individual measurements of body composition [1].

FM Evaluation Derived from LBM Determination

FM can also be estimated indirectly by determining LBM using methods such as TBW [9], TOBEC [10] and BIA [11]. TBW may be measured by isotope dilution using deuterium ($^{2}$H$_2$O) or oxygen 18 (H$_2$O$_{18}$). Assuming that the ratio of TBW to LBM is constant [12], LBM may then be estimated. However, TBW varies with gestation and changes rapidly in the first few weeks of life, limiting application in the neonate, particularly the preterm infant. In addition, the water content of LBM in infants is higher than that generally considered for adults and decreases progressively during the first 2 years of life [7].

The principle underlying TOBEC is that lean tissue is more electrically conductive than fat, and the greater the LBM the greater the electromagnetic disturbance when a weak homogeneous electromagnetic field is applied. With this technique normative data close to older reference values have been

**Table 1.** Indirect in vivo techniques for measuring body composition in infants

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<td>Tracer dilution: chemicals, stable isotopes</td>
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<td>Total body potassium</td>
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reported in term infants between birth and 1 year of age [13]. However, this method is also sensitive to the hydration status factor of FFM. The error of estimation is inversely related to FM and therefore is relatively inappropriate for infants weighing <2,800 g [10].

BIA has the advantage that it can be used across a broad age spectrum and in a variety of settings. It appears to be a simple, cheap and easily available technique requiring little cooperation of infants. It has been widely used for measuring TBW and extracellular volume in preterm and term infants. Various algorithms have been proposed in order to improve the accuracy of TBW and extracellular volume estimations in infants [8, 11, 14]. Unfortunately, data are influenced by the hydration coefficient of FFM, whereas the precision and accuracy are still being questioned [15].

Densitometry is considered to be among the most accurate indirect body composition methods. Body composition assessment by densitometry involves measurement of the density of the whole body. Body density (body mass divided by body volume) is then used in a two-compartment model to calculate the percentage of fat, FM, and FFM. Body mass is easily measured using an accurate weighing device. Body volume is a more difficult measurement and is commonly determined either by hydrodensitometry performed in water using Archimedes’ principle or ADP performed in air using gas laws. Because hydrodensitometry requires subjects to be totally submerged during a test, compliance and safety issues prevent the implementation of this technique in the infant population [16].

ADP has been successfully used to measure the body composition of children and adults, and recently a new ADP system has been developed (the PEA POD Infant Body Composition System, Life Measurement, Inc.; fig. 1). Using body mass and volume measurements, the ADP system automatically calculates the percent body fat by using a classic densitometric approach and age- and sex-specific FFM density values obtained from a multi-compartmental study [7]. The ADP system has recently been evaluated in infants, and the reliability and accuracy results of these studies indicate that ADP is easily used by operators, comfortable for infants, reliable, and accurate compared to the deuterium ($^2$H$_2$O) dilution technique taken as reference. Future studies are needed to determine ADP reference values compared to other reference methods and to further evaluate weight gain composition during infancy [17].

Advances in imaging techniques have allowed more direct in vivo measurement of body composition. These methods include computed axial tomography, nuclear magnetic resonance imaging (MRI) and ultrasonography [18]. Computed tomography scanning requires significant radiation exposure in contrast to MRI and ultrasonography. However, all three methods share the problem of extrapolating cross-sectional slices from a part of the body to whole body composition slices. There are also very little data on infants using these techniques. However, data in infants during the first months of life using MRI and isotope dilution have recently been reported [2, 19].
In contrast, DEXA requires minimum radiation exposure (<0.3 mrem) and performs whole body rather than slice measurements. Given the short scanning time (6–10 min) this method is becoming the most widely used method for the in vivo measurement of whole body composition in humans. Determinations are performed without sedation, but the naked infant is swaddled in a paper blanket to minimize the movement artifact. During a DEXA determination an X-ray source generates two different energy levels and, depending upon the differential absorption of the two photon emissions, body composition (lean mass, FM, bone mineral density) is determined. In addition, total bone area is also determined and BMC can be calculated. However, the accuracy and precision of the determinations may be affected by the type of DEXA instrument [1], scan mode [20] and software programs used [21]. Using the QDR 2000 (Hologic Inc., Waltham, Mass., USA) equipped with an infant table pad and the infant whole body software V5.65P, we have performed validation studies in piglets and clinical studies in preterm and term infants. In validation studies on piglets we observed that DEXA was accurate and precise in measuring lean mass and BMC but not FM [22, 23]. However,
further evaluation indicated that FM measurements, which were overestimated, were highly improved using a correction factor [22, 23]. Using this technique and correction factor, we have obtained reference values of body composition in ‘normal’ preterm and term infants (fig. 2). Unfortunately, DEXA accuracy and precision are device- and software-dependant and up to now an optimal instrument specially designed for infants is not widely available. Thus, in a comparative study, we found that the use of the more recent QDR 4500A (Hologic Inc.) appears to underestimate FM compared to the QDR 2000 (unpublished data).

**Body Composition during the First Year of Life**

In 1982 Fomon et al. [24] published their classical body composition model that provided age- and gender-specific data for TBF, FFW, TBW, and the degree of hydration in FFW. The latter is of particular importance, as TBF is often calculated as the difference between body weight and FFW, obtained using direct or indirect estimates of TBW and a value for the degree of hydration in FFW.
However, the Fomon model, which provided data from birth to 10 years of age, was presented as preliminary and crude because it was based on quite a limited data set. Since that time, several studies have evaluated whole body composition during infancy using different techniques. TOBEC reference values were provided by de Bruin et al. [13]. DEXA reference values were determined by Koo et al. [25] as well by our group [23]. More recently Olhager et al. [2] evaluated MRI data during the first 4 months of life, and a longitudinal study of human body composition during the first 2 years of life was reported by Butte et al. [7] using a multi-compartmental system.

As shown in figure 3, there is good agreement between the various approaches. In addition, analysis of the data related to age, body weight and body length suggest that the major differences observed between the techniques could be related to differences in the population evaluated in the study. Nevertheless, these studies suggest that gender is one of the major determinants of whole body composition during the first year of life and that separate data references need to be provided.

Evaluating body composition in infants and toddlers using various techniques, Butte et al. [26] suggested that methods are not interchangeable for group or individual estimations. The magnitude of method difference is a function of age which makes it difficult for systematic biases.

Considering that the sequential evaluation of body composition is of interest for monitoring and evaluating growth patterns, efficacy of diet and medical interventions, progression of chronic disease, and recovery from malnutrition, DEXA may be considered as one of the gold standards. It is a precise, safe, noninvasive, easy to perform and widely available method providing accurate information not only on FM and FFM but also on LBM, BMC and bone mineral density in infants and toddlers. However, the accuracy of the instrument and software used remain to be validated.

**Weight Gain Composition during the First Year of Life**

Evaluation of weight gain composition is of major importance in the assessment of the nutritional requirements of preterm and term infants. Up to now, duplicate analyses of 3-day metabolic and energy balances have been performed to estimate energy expenditure in association with nitrogen and energy retention in order to estimate FM deposition, LBM gain and protein accretion in preterm and term infants according to the feeding regimen. In addition, measurement of calcium and phosphorus retention enabled estimation of the adequacy of mineral deposition compared to reference values. Those data were considered as representative of growth quality over a larger period.

Analysis of the data presently available for preterm infants made it possible to evaluate the main determinants of weight gain, nitrogen retention and FM deposition [27]. Protein intake and the protein energy ratio are the main
Determinants of weight gain. Protein intake is the only determinant of LBM gain in contrast to FM gain that is positively related to energy intake and negatively to protein energy ratio. Thus, protein and energy needs are reciprocally limiting. If there is a surfeit, one affecting the ability of the infant to assimilate

Fig. 3. Evolution of fat mass (FM) and fat-free mass (FFM) related to age, weight and length. From De Bruin et al. [13], Olhager et al. [2], Rigo et al. [5], Fomon and Nelson [4] and Butte et al. [7].
the other, and if energy intake is insufficient, protein is used as an energy source and nitrogen balance becomes less positive. Increasing the caloric intake will spare protein loss and improve nitrogen retention, but with limited protein intake, protein retention reaches a plateau and the energy excess is used only for fat deposition. Nevertheless, when protein supply is in the range of the protein requirement, the effect of the energy increase on protein retention appears to be minimal. Therefore, with a view to increasing the LBM accretion and limiting the FM deposition in the premature infant, an increase in the protein energy ratio is mandatory.

Unfortunately energy and metabolic balances, requiring the use of a metabolic bed, infant relative contention and a reduction in nursing, are relatively limited. Therefore, we recently suggested that DEXA might also be used to analyze weight gain composition over a longer period of time and in a less invasive fashion [28–30].

DEXA body composition was measured at the beginning of the study and then 3 weeks later. Lean, fat and bone mass gain was determined by subtracting the second from the first determination. In preterm infants (birth weight <1,750 g) fed either fortified human milk or preterm infant formula, the weight gain composition evaluated between a mean of 34 and 37 weeks of post-conceptional age was in the range of the data obtained previously using energy and nutrient balance (fig. 4) [30]. Formula-fed infants showed a
greater weight gain, FM deposition, BMC gain and bone area increase compared with the fortified human milk group. In contrast, calcium retention estimated from bone mineral gain was greater than that determined with nutrient balance techniques. The reasons for the latter observation are not entirely clear but might be explained by the low threshold level of bone mineral detection necessary to estimate bone mass in preterm infants [5].

In term infants, the growth pattern of breast-fed infants is known to deviate from that of formula-fed infants. Mainly after 3 months of life, breast-fed infants grow more slowly than formula-fed infants even if a relative catch-up growth tends to occur during the 2nd year of life. Evaluating body composition, Butte et al. [31] recently suggested that FFM was lower in breast-fed infants compared to formula-fed infants at 3, 6 and 9 months of age. In addition, a gender effect was also reported. Similarly, weight gain composition was also estimated in term infants breast-fed and formula-fed during the first 2 months of life.

The use of DEXA allows evaluation of the weight gain composition in term infants. From birth to 2 months of age, we compared body composition in a limited number of breast-fed (n = 16) and formula-fed (n = 47) infants. From birth up to 2 months, weight gain (31.3 ± 6.9 vs. 35.8 ± 7.4 g/day; p = 0.04) and FFM gain (19.7 ± 3.9 vs. 22.7 ± 4.5 g/day) were significantly lower in breast-fed than formula-fed infants. The percent FM increased in the 2 groups from 15.1 to 23.8% in breast-fed infants and from 14.8 to 24.0% in formula-fed infants. During the study period, weight gain corresponded to about 75% of the birth weight and was similar in the 2 groups. FM deposition accounted for 36.3 and 35.8% of the weight gain in breast-fed and formula-fed infants, respectively [29].

During these studies [29, 30], it was also possible to determine the minimal detectable changes in weight gain composition according to time in preterm and term infants in relation to the size of the population. In 3 weeks, between 1,500 and 2,200 g body weight at the time of discharge, the minimal detectable differences in body weight gain were 2.3 g for weight, 2.1 g for LBM, 1.2 g for FM, and 76 mg/kg for BMC between the 2 groups of 20 very low birth weight infants. Considering the relatively low FM content at the time of discharge, this sensitivity (±30%) appears to be better than could be obtained by other indirect methods in preterm infants [30].

In comparison, in term infants from birth to 2 months of age, the minimal detectable differences in body weight gain were 1.9 g for weight, 0.8 g for LBM, 1.5 g for FM and 50 mg/kg for BMC between the 2 groups of 15 infants. In our study, the highest differences were for weight gain (0.7 g/kg/day; p = 0.37) and FM gain (0.5 g/kg/day; p = 0.39). These values, corresponding to 27 and 33% of the minimal significant differences, should be reevaluated in a larger cohort of infants [29].

In conclusion, determination of whole body and weight gain composition is one of the major keys to the evaluation of the nutritional requirements of preterm and term infants, whereas the dynamic aspect of body composition
during the first years of life plays a fundamental role in the nutritional programming of adult morbidity. In preterm and term infants, the only practical means of measuring body composition is by noninvasive and indirect methods. Of the various techniques presently available, anthropometry and impedancemetry have not yet been appropriately validated in young infants. TOBEC and stable isotope tracer dilution techniques appear more appropriate but difficult to adapt for widespread use in infants. In contrast, although in investigation, ADP seems easy to use, comfortable, reliable, and accurate in infants, but further investigations are needed to establish normative values and to validate weight gain determination. DXA, a widely available technique using the three-compartment model, is now considered by some as the reference technique for determining body and weight gain composition. The technical procedure for DXA scan acquisition and analysis is quite simple. Radiation exposure to the infant is minimal. DXA techniques have been validated for measuring body composition in infants. Unfortunately, commercial DXA instruments have major differences, and software especially adapted to preterm and term infants is not always available.

References

\textbf{Discussion}

\textit{Dr. Dewey:} In Dr. Butte's study the babies were exclusively breastfed during the first 4 months, but after that the infants may or may not have continued to be breastfed and I think by 1 year of age less than half of them were still being breastfed and they were mainly being supplemented with formula. So when we try to draw conclusions about whether breastfeeding affects fatness beyond 6 months for example, I think we have to be very careful about how we define what we mean by breastfed. When we look at babies who are breastfed for the whole first year of life it is fairly consistently shown that there are differences, at least in skinfold thickness which is lower in breastfed children. But again it is those who are breastfed for a whole year and not getting infant formula. The question I have has to do with methods for measuring body composition. I was involved in a validation study of air displacement plethysmography using an instrument called the PEA POD. The PEA POD is nice because it is relatively insensitive to the babies moving around a little bit or urinating or crying, i.e. you still get a good
measurement. But I am not sure about dual-energy X-ray absorptiometry (DEXA), and I wonder if you could tell us how much it is affected by movement or crying or other activities of the babies? What do you have to do to use it under these circumstances?

**Dr. Rigo:** It is difficult to compare breastfed infants and formula-fed infants because breastfed is not completely a homogenous group. In our study we limited the data on the first 2 months of life in order to obtain exclusively breastfed and formula-fed infants. In my presentation, I stress the point that not only body composition, but also weight gain composition are very important referring to the studies evaluating the influence of protein-energy ratio on weight gain composition.

Techniques evaluating body composition are also promising for weight gain evaluation. Techniques need to be useful, practical, and not time-consuming if we want to evaluate relatively large cohorts with sequential evaluations. The problem of DEXA is that presently, the technique is still device and software dependent.

DEXA is relatively sensitive to movements but in small babies it is possible to wrap the baby very carefully in a paper sheet to induce quietness and immobilization. The present technique is relatively fast, and it is so possible to obtain data without any movement. In addition, movements are recorded during the examination enabled the exclusion of the database or a second evaluation. I have never used the PEA POD, but I consider that it is a promising technique.

**Dr. Roggero:** Regarding exclusive breastfeeding, the UNICEF definition of exclusive breastfeeding is related to a baby who is only breastfed. The exclusively breastfed infant does not receive any other sort of food or water. I have another comment on a new air displacement system (PEA POD). I routinely determine the body composition in neonatal intensive care unit babies using this technique and usually we have no difficulties performing this measurement. Generally the babies don’t cry because the place where they are measured is comfortable. The temperature inside the box is adequate for them. At birth, term newborns have a mean fat mass of 6% and at 15 days of life it is 12%. Preterm infants, at term-adjusted age, have a fat mass of close to 16%. This is significantly different to that found in term neonates.

**Dr. Butte:** With the PEA POD you can combine a dilution technique with the density. So when you are uncertain of the hydration concentration the deuterium dilution is quite easy to use as well. Dr. Ellis is in the process of validating the PEA POD in both preterm and term infants and hopefully the results will be out soon. I really appreciate all the emphasis put on body composition. I think that is what we have to do and not simply look at weight gain. I was just trying to emerge the two talks of Dr. Ziegler and yourself, and it is time that we look beyond just weight gain. When we are thinking about the growth potential of the infant we have to think not only of linear growth but also ponderal growth. I wanted to ask Dr. Ziegler if he really was referring to obtaining the growth potential in terms of linear growth or in terms of ponderal growth. As we know very well from animal studies, we can manipulate the composition of ponderal growth dramatically, and I don’t think infants are any different. What we are doing with formulas, trying to look at the optimal PDE ratio and all the other nutrients and macronutrients that are present, is influencing that ponderal growth and the composition of it. Dr. Dewey and I have compared our studies over the years because they were very parallel studies. They are quite similar, but from 6 to 12 months we have some very significant differences. In our studies we didn’t control what the mothers fed and many of our mothers continued to breastfeed up to 12 months. The medium breastfeeding rate was up to 12 months, but many of the mothers were working and used formula when they were at work. That is a difference, and so we have a definition of what the predominantly breastfed infant is but we have not defined what those complementary foods are. The big debate is not about differences in breastfeeding but about differences in how the children were complementarily fed. Again we have not spent a lot of time to see what the optimal way is to feed infants from 6 to 24 months.
Dr. Lafeber: I would like to ask you a question about gender differences in the first year regarding body composition. It is not so much related to the breastfed and bottle-fed differences, but let us concentrate on the differences between preterm, post-discharge preterm and term formula. For instance if we look at the results of older studies on body composition using the post-discharge formula, we see differences in the body composition of boys and girls when post-discharge formula is given, and post-discharge formula seems to make boys a bit fatter and to have less influence on the girls [1, 2]. Can you speculate on the mechanism underlying the changes in body composition? You suggest very much that it would be a relation not with energy but with protein. I can understand that, but how do you explain differences between boys and girls? Is that just the physiology of the changes?

Dr. Rigo: There is a large difference in body composition between boys and girls. Analyzing now the weight gain in preterm infants from 1.5 g to 2.5 kg, gender appears as one of the major determinants of weight gain composition. Girls seem programmed to make more fat, but also more bone mineral deposition than boys. It is relatively the same if you investigate term and post-discharge formulas.

Nevertheless, there is some discrepancies in the published data. Using enriched post-discharge formulas. Cooke et al. [3, 4] reported a positive effect on growth rate in boys but not in girls suggesting that an increase in protein energy ratio has some influence in boys. In contrast, Lucas et al. [2], evaluating weight gain and enriched formula in intrauterine growth retarded infants, found a significant difference in girls but not boys. So it was an inverse relationship to gender between the two studies, and it is very difficult to interpret the two studies. Are the results directly related to the diet composition or to a difference in programming between boys and girls, and preterm and IUGR term infants.

Dr. Turck: My question is related to the model. What should be the model if we look carefully at the body composition of a formula-fed infant, should it be the breastfed infant? If you study the body composition on a clinical standpoint of a formula-fed infant, what would you do if let us say the fat content of the infant is higher than the breastfed model? Would you decrease the volume intake or would you change the formula?

Dr. Rigo: Your question is first about the reference; what is the body composition references that we need to take into account for formula fed infants. Presently the reference is still the breastfed infant, at least during the first 6 months of life but probably also during the second part of the first year of life. Nevertheless, it is important to accumulate data and particularly to investigate all the factors that can influence body composition during the first year of life such as exclusive breast feeding and weaning diet.

The second part of your question is related to the influence of diet content on body and weight gain composition. Is it possible to correct the differences between breast-fed and formula-fed infants, by manipulations of the formula content? Up to now, limited results suggest that protein energy ratio could be major factor influencing body and weight gain composition. But we need additional investigations, and the E.U. childhood obesity project could partially answer to that question.

References