Body Composition in Infancy: Impact on Health Later in Life

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Abstract

From retrospective studies, there is substantial evidence that birthweight and the rate of weight gain during early infancy are associated with increased risk for adverse health outcomes later in life. Birthweight is the marker of the integrative effects of the prenatal environment, while the rate of weight gain after birth reflects both genetic potential and external postnatal influences. The adulthood-to-infancy associations constitute the basis for the ‘fetal origins’ and ‘catch-up growth’ hypotheses for some diseases. However, these findings are based on the assumption that anthropometric-based indices reflect body composition during both time periods, with the body mass index (weight/stature$^2$) being the most frequently used index. More direct measures of body composition were simply not available at the time of the births of the adults participating in these studies. Nowadays, there are a number of in vivo techniques that can be used to examine body composition in infancy. In particular, what does the body mass index reflect in terms of body composition for the infant? Is it an adequate index?

Introduction

A number of retrospective studies have well established that birthweight and rapid changes in the pattern of growth in early infancy are associated with increased risks for obesity, hypertension, cardiovascular diseases, diabetes, and some cancers later in life [1–4]. The relative impact of the prenatal and postnatal periods on these risks remains unclear, as do the underlying metabolic or physiological mechanisms. The ‘fetal origins’ and ‘catch-up growth’ hypotheses, for example, have proposed that there are ‘critical windows’ during growth that may reflect genetic/nutrient/environmental interactions that translate to phenotype programming [5].
For a majority of the retrospective studies, birthweight has been the most frequently used anthropometric marker for fetal and postnatal growth. Both low and high birthweight have been associated with increased disease risks in adults, although not necessarily of the same magnitude or for the same diseases, resulting in both J- and U-shaped response curves. Also, rapid weight gain during early infancy, whether as ‘catch-up’ growth to compensate for low birthweight or as overnutrition following a normal birthweight has been identified as a potential predictor of later adverse health. The relative birthweight and changes with growth were expressed in standardized z scores or percentile rankings using the ponderal index (PI; weight/length^3) and body mass index (BMI; weight/length^2). These anthropometric-based indices were used as surrogates for body composition, since direct measures of body composition some 50–70 years ago (at the time of the births of the adults in the retrospective studies) were not readily available. One cannot say with certainty how an infant’s PI or BMI value from 50 to 70 years ago would translate to body composition, but we can make this comparison for today’s infants. During this conference, we have seen how growth curves are constructed and used internationally. For my presentation, I hope to provide some insight into how they may be translated to body compositional information.

**Body Composition Methods and Models**

The composition of the human body can be described using a number of different models which often require multiple measurement techniques [6]. The one model that is probably the most frequently used, at least for nutrition studies, is the four-compartment model that partitions the body into the major components of water, proteins, minerals, and fat. This is the model used by Fomon et al. [7] to develop their classic Reference Children model for the description of growth for birth to age of 10 years. At least three independent assays are required for use of this model; measurements of body water, proteins, and minerals. The sum of these three compartments along with body glycogen is called the fat-free mass (FFM). The body’s fat mass is then defined as bodyweight minus FFM. That is, the fat mass is not directly measured, but is the difference between two large values. It is worthy of note that although FFM was developed only to be used as an intermediate step for determining fat mass, FFM has gained prominence over the years as though it were an important body composition parameter. That is, as in vivo assays have been developed, comparisons are often made only with the FFM when it is the subcompartments that are more important. That is, the subcompartments can independently deviate from the normal range for different diseases or illnesses, while the estimate for the overall FFM would still appear normal. Thus, caution should be taken not to overinterpret the importance of measuring only FFM. Likewise, to use a measure of only the protein or mineral
Body Composition in Infancy: Impact on Health Later in Life

compartment to estimate FFM could translate into a considerable error which would transfer to the estimate for fat mass as well. What this means is that if the two-compartment model of fat and FFM is to be used, then at least a measure of the body water compartment is needed in order to minimize the error for estimating body fat mass.

In order for Fomon et al. [7] to construct the Reference Children model, they had to rely on body composition data reported in the literature for different pediatric populations of varying ages. Their remarkable efforts, however, resulted in a composite hypothetical multicompartment body composition model that was very informative, gender dependent, and covered the age range from birth to 10 years. The only restriction was that with only limited data available, the model was constructed to match the 50th percentiles of weights and stature at each age. That is, the normal variations in body composition associated with differences in body size and possibly ethnicity could not be modeled.

More recently, Butte et al. [8] revisited the original Fomon reference model, focusing on the first 2 years of life. These authors obtained longitudinal body composition data at 0.5, 3, 6, 9, 18, and 24 months for contemporary infants in order to reconstruct the same reference model, with the same set of assumptions. These investigators and others have also examined the potential differences in body composition during early infant growth for breastfeeding vs. formula feeding and variation of the protein content of infant formula [9–12]. Several representative contemporary studies in infants are listed in table 1, where different in vivo measurements and models were used.

Overlapping the time period of the study by Butte et al. [8], the development of dual-energy X-ray absorptiometry (DXA) provided a major advancement in in vivo body composition methodology. Although mainly focused on the clinical measurement of bone density of the lumbar spine, the scanners were modified to cover the length and width of the whole body. Analysis of the whole-body scan produces a pseudo three-compartment model of body composition: bone mineral, body fat, and the remaining soft tissues [6]. A number of studies in term and preterm infants have reported body composition ‘reference’ ranges based solely on DXA [13, 14]. The references provided by the earlier publications should be used with caution as a recent study has reported fat and lean tissue values are dependent on which DXA software version is used [15].

The most recent advancement in in vivo techniques, magnetic resonance imaging (MRI) can provide an excellent measurement of body fat distribution [16]. A single-slice abdominal scan can be obtained in less than a minute, and the reconstructed image providing a ‘picture’ with sufficient anatomical accuracy that the subcutaneous adipose regions can be easily traced, as well as visceral fat when there is a sufficient quantity present. Similar images can be obtained using computed tomography, but the associated radiation dose prohibits routine use of this methodology for infants. Using multiple MRI scans
along the length of the body, the volume of the whole-body subcutaneous fat volume can be estimated. Body fat mass can be calculated if one assumes the density of the adipose tissue is known. This approach has been used to examine changes in fat mass during early infancy [17, 18]. The MRI-derived estimate of fat mass, unlike that obtained with the Fomon model, does not require any knowledge of the FFM. A limitation with the MRI approach, however, is that even small movements by the infant during the scan can quickly degrade the accuracy of the reconstruction images, which in turn limits the accuracy of the subcutaneous fat and whole body fat estimates. It is mainly for this reason why MRI has not been successfully used with older infants unless the infant is sedated or significantly constrained.

The one other method specifically developed and verified for assessment of body fatness (%fat) in early infancy is based on the measurement of body volume [19]. It is based on the two-compartment model (fat mass and FFM) and requires that the density of each compartment is known. The measurement technique has several clear technical advantages over the other methods, especially if longitudinal monitoring is to be considered, and if it is to have clinical application beyond the research environment. There is minimal risk associated with the procedure which takes about 1 min to complete and is unaffected by infant movement. The results are immediately provided and have the potential

### Table 1. Contemporary studies of body composition in infants using various methods and models

<table>
<thead>
<tr>
<th>Study</th>
<th>Model</th>
<th>Methods</th>
<th>Infants</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rigo et al. [23]</td>
<td>3-C</td>
<td>DXA</td>
<td>106</td>
<td>cross-sectional (ages: &lt;0.5 months)</td>
</tr>
<tr>
<td>Butte et al. [8, 9]</td>
<td>4-C</td>
<td>D₂O, TBK¹, DXA</td>
<td>76</td>
<td>longitudinal (ages: 0.5, 3, 6, 9, 12, 24 months)</td>
</tr>
<tr>
<td>Koo et al. [24]</td>
<td>3-C</td>
<td>DXA</td>
<td>214</td>
<td>cross-sectional (ages: 0.1–13 months)</td>
</tr>
<tr>
<td>Olhager et al. [17]</td>
<td>-3-C</td>
<td>MRI, D₂O</td>
<td>46</td>
<td>longitudinal (ages: 0.13–4.4 months)</td>
</tr>
<tr>
<td>Ellis et al. [19]</td>
<td>4-C, 2-C</td>
<td>D₂O, TBK¹, DXA, PEA POD²</td>
<td>88</td>
<td>cross-sectional (ages: 0.5–6 months)</td>
</tr>
</tbody>
</table>

4-C = Four compartments (fat, water, protein, mineral); 3-C = three compartments (bone, fat, other tissues); 2-C = two compartments (fat and fat-free mass); TBW = total body water (deuterium dilution).

¹ Whole body counting. ² Body volume.
Body Composition in Infancy: Impact on Health Later in Life

to possibly aid in the nutritional management of the infant in early life. If unac-
counted for, a significantly abnormal hydration may bias the %fat estimate, and
the size of the measurement chamber will limit its use to infant weighing less
than about 8–9 kg or about 6 months of age. This size limit, however, matches
well with the fetal origin and rapid weight gain hypotheses.

**Body Composition during Early Infancy**

In most of the retrospective adult studies, the BMI has been used as the
measure of excess adiposity for both adults and infants. For full-term infants
of appropriate size, the adipose tissue constitutes the second largest propor-
tion of bodyweight, being exceeded only by the body’s water content. During
early growth, adipose tissue mass usually increases concurrent with a decrease
in body water, while there are relatively slow increases in the protein and
mineral compartments [7]. The lipid (fat) content of adipose tissues in early
infancy increases almost twofold, starting at about 39% at birth and reaching
around 63% by 6–9 months [20]. For the retrospective studies, it is implied
that changes in BMI in infants mainly reflect the increased fat storage of adi-
pose tissue. Only until recently have we had techniques that could directly
assess fat mass in vivo for the infant. I want to present some of our initial find-
ings on the relationship between BMI and body composition in early infancy.

As noted, for the retrospective adult studies, at birth it was usually only birth-
weight that was recorded, and occasionally body length. Accurate body com-
position assays were simply not available, especially for use with infants. The
only anthropometric measures related to body dimensions. The physical param-
eter used to monitor growth was weight gain, while body length measurements
were difficult to obtain and were therefore infrequent and often of questionable
reliability. Thus, a retrospective calculation of BMI, for example, may have lim-
ited accuracy for the individual infant and clearly no direct translation to the
infant’s body composition. That is, what does BMI measure in the infant? How is
it related to body composition? To answer these questions, we have examined a
group of contemporary infants, both preterm and full-term birth.

When compared with standardized weight-for-age and length-for-age
charts, our infants were within the percentiles expected for preterm and full-
term infants, respectively. To measure body composition, the DXA, total body
potassium (TBK), total body water, and PEA POD techniques described above
were used, not necessarily all of the assays at all visits and for all infants. Each
infant, however, had at least one of the independent assays performed at
each visit. A series of anthropometric measurements was performed, includ-
ing BMI. The correlations for BMI and the PI with various body composition
compartments are given in table 2 for the contemporary full-term infants in
three age groups. The PI was included because it has often been used as a
measure of the growth status of term newborn infants. For all three ages, PI
Table 2. Correlation of BMI and PI with body composition

<table>
<thead>
<tr>
<th></th>
<th>0.5 months</th>
<th></th>
<th>6 months</th>
<th></th>
<th>12 months</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI</td>
<td>PI</td>
<td>BMI</td>
<td>PI</td>
<td>BMI</td>
<td>PI</td>
</tr>
<tr>
<td>%fat</td>
<td>0.51</td>
<td>0.36</td>
<td>0.81</td>
<td>0.65</td>
<td>0.74</td>
<td>0.75</td>
</tr>
<tr>
<td>Fat</td>
<td>0.68</td>
<td>0.42</td>
<td>0.89</td>
<td>0.6</td>
<td>0.85</td>
<td>0.78</td>
</tr>
<tr>
<td>FFM</td>
<td>0.68</td>
<td>0.30</td>
<td>0.23</td>
<td>-0.29</td>
<td>0.15</td>
<td>-0.09</td>
</tr>
<tr>
<td>TBK</td>
<td>0.62</td>
<td>0.35</td>
<td>0.40</td>
<td>-0.07</td>
<td>0.58</td>
<td>0.37</td>
</tr>
<tr>
<td>BMC</td>
<td>0.70</td>
<td>0.36</td>
<td>0.75</td>
<td>0.32</td>
<td>0.67</td>
<td>0.50</td>
</tr>
<tr>
<td>Length</td>
<td>0.40</td>
<td>-0.12</td>
<td>0.26</td>
<td>-0.35</td>
<td>-0.12</td>
<td>-0.42</td>
</tr>
</tbody>
</table>

Fig. 1. Relationship of %fat (a) and fat mass (b) and BMI for term infants at 2 weeks of age. %fat = (2.30 – 0.24 × sex) × BMI – 12.00, and fat = (154 – 8.79 × sex) × BMI – 1,339, where sex = 1 for males, 0 for females. Prediction errors for %fat and fat are 3.5% and 160 g, respectively.
tended to have the lower correlations. Somewhat surprising, BMI at 2 weeks of age was correlated with all of the body composition compartments (p < 0.001). That is, BMI could equally predict lean tissue mass as well as body fat. If BMI is to be considered a measure of body fatness, then one would expect it would be more significantly correlated with %fat. However, we observed the lowest correlations were for %fat and fat mass. This may indicate that in early infancy, BMI may be a better predictor of the components of the FFM, fat mass or of body fatness. This may not be too surprising since body water is about 80–85% of the total FFM, which makes it also the largest component of bodyweight. Hence, it is possible that the associations found in the retrospective adult studies that had infant BMI information may be equally related to lean tissue mass as to fat mass.

The relationship of BMI with fat mass and %fat for 2-week-old term infants is shown in figure 1. There is no gender-specific difference in BMI at this age, while girls have higher fat mass and %fat than boys (p < 0.001). This reinforces the proposition that BMI in early infancy is related to more than only body fatness. To illustrate this point, the relationship between BMI and TBK, an index of skeletal muscle mass, is shown in figure 2. Since there is no gender-specific difference in the BMI-TBK relationship, this may indicate that a portion of BMI is related to the adipose cellular component and additional lean tissues associated with increased adiposity.

As epidemiology studies continue to find associations between body size in early infancy and risks for diseases in adulthood, other studies are focused on cellular mechanisms that may contribute to our understanding of this associa-

Fig. 2. Relationship of TBK and BMI for term infants at 2 weeks of age. TBK = 11.4 × BMI + 6.12 × sex, where sex = 1 for males, and 0 for females, and fat = (154 – 8.79 × sex) × prediction error for TBK, 16.6 mEq.
It remains unknown whether it is the fat or lean tissue compartment that has a major role in this relationship.

References

**Discussion**

_Dr. Davies_: You showed some data that show that BMI in babies was not particularly well correlated with anything and changed markedly across the 1st year of life. I don't think we should forget that when Quetelet proposed the BMI, it was an attempt to adjust weight for height in adults, and it wasn't an attempt to measure adiposity. So I think we are not surprised that BMI doesn't work in babies because it was never designed to.

_Dr. Ellis_: I don't disagree. Basically, if you look at the origin of BMI from anthropology studies, one finds it was a way to adjust for differences in body size. But over the years, BMI or its z score or percentile has become a marker for defining excess adiposity. We published a paper 10 years ago that showed that the relationship between the percentage body fat and BMI in children was too broad to consider BMI for this application. Yes, if your BMI is above the 97th percentile, your excess weight is most likely due to excess fat. But what is the case at the 85th or the 70th BMI percentile? There are about equal numbers of children with normal vs. excess fat, when defined as a percentage of bodyweight, at these levels.

_Dr. Domellöf_: I have two questions. When measuring body fat in small infants, is there an influence of brain fat? We usually think of body fat as a negative outcome, but brain growth would obviously be a good outcome, so that's my first question. The second one is, since body mass index does not work very well in determining body fat in these infants, could you make another formula, perhaps also including head circumference to better estimate body fat?

_Dr. Ellis_: I will answer the second question first. The answer is yes, we could attempt to establish some other correlation or regression models that could include a parameter related to head size. However, it may be easier to use something other than the power of 2 for the height term. If one does a log-log regression of weight vs. height, the exponent for the height term is closer to 2.78 than it is to 2.0. And as for your first question, you are absolutely right because the brain region from the DXA technologies' prospective is closer to fat than to lean tissue. Some investigators have excluded the head region for DXA scans for older children, but I am not aware of it being excluded for infant scans. It would be interesting to see how much the head region contributes to the whole body fat estimate provided by DXA for infants.

_Dr. Wang_: Although DXA examination is safe in babies, what is the response from the parents regarding DXA examination according to your experience? My second question is related to infant feeding. As mentioned by Dr. Lucas on the 1st day of this workshop, the energy and protein level in breast milk may be overestimated. Do you think there is a need to reduce the energy and protein content of full-term infant formula for a healthy development and safety of the babies?

_Dr. Ellis_: When we explain the risks associated with DXA in comparison with other routing risks in life, like traveling in a car, for example, the parents understand the risks involved better. I think the second question was whether we should be changing the composition of the diet if babies become fatter. This is an area that I have no expertise in, but I think there are ongoing studies looking at that question now, by varying the energy density as well as the protein content and different sources of protein.

_Dr. Cooke_: Just some comments. Our group sequentially measured body composition in 150 preterm infants between hospital discharge and 12 months corrected age [1]. Lean mass was greater but no differences were detected in absolute fat mass while percent fat mass was less in boys than girls. As you have suggested, it is also important to consider changes in lean mass. Although fat mass is increased in infants fed a nutrient-enriched formula, it is explained by increased fat deposition on the legs, not centrally. In effect, differences in fat mass and lean mass can be directly related
to differences in energy and protein intake. Whether these changes persist later on remains to be determined.

**Dr. Ellis:** You are right about the fat distributions, they are different, and DXA gives you some information, but I don't think people should be misleading by saying that DXA can separate subcutaneous from visceral fat for the abdomen. What you are saying about the legs vs. trunk or arms can be somewhat shown, but it is very difficult to do this for young infants. I just did some calculations and realize that in babies the cellular component of the adipose tissue can be as much as 30–50% of the total lean mass. It doesn't seem right at first, but an infant's adipose tissue is only about 60% fat as compared with 80–85% for adults, 90% for very obese. So for the infant, a large part of adipose tissue mass is the cellular mass, not fat mass.

**Dr. Ziegler:** I would like to answer the question from the gentleman from China about the protein content of formula. We think the best evidence indicates that the protein concentration of formula should be similar to that of breast milk, and breast milk in the 1st month of lactation has a protein energy ratio of approximately 1.8–1.9 g per 100 calories, and the most advanced formulas in Europe and in the United States have that protein content, which provides very little if any excess over the need of the infant at 1 month of age. In the past, the formulas were much higher in protein and that puts a metabolic burden on the baby. For later ages, like 4 months, the protein content of formula should be lower just like the protein content of human milk is much lower at 4 months of lactation. Some companies are working in that direction to have follow-on formulas for the 4- to 5-month-old infant that are lower in protein content than the starter formulas.

**Dr. Ellis:** And we too are looking at those kinds of babies now, and again that's why for us the potassium measurement is so important. It is a direct measure of body cell mass, the active metabolizing compartment of the total lean mass. It is a measure of the true changes in the lean tissues, and we are very curious to see how this is going to come out.

**Dr. Ziegler:** What do you think about skinfold thickness? How good a predictor is it of fatness?

**Dr. Ellis:** I think if you do multiple skinfold thicknesses, you can get a pretty good measure of the subcutaneous fat. It won't tell you much about the visceral fat, but then the visceral fat is a small component of total fat for infants. Subcutaneous fat is probably 80% or more. However, if you can't do the sophisticated methods I presented, then some measure of skinfolds will probably be better than nothing.

**Dr. Zulkifi:** I just want to follow up on what Dr. Ziegler said earlier about protein. Correct me if I am wrong, at the moment all the follow-on formulas are higher in protein compared to the infant formulas, am I right? And what's the reason for that?

**Dr. Ziegler:** I think you are correct, most follow-on formulas are higher in protein content and I can only guess what the reason for that is because they are not modeling human milk. I think the reason is that the older infant consumes complementary foods that tend to be low in protein and therefore the follow-on formula should be relatively high in protein. I don't know of any other reason.

**Dr. Zulkifi:** I was wondering whether anybody has actually looked at what happens to the kidney of the children who have been fed these higher protein follow-on formulas.

**Dr. Cooke:** Can I comment on that? The idea that one formula can meet the needs of all infants, particularly the follow-on formula, is perhaps a bit facile. Nutrient requirements may vary widely in very low birthweight infancy during infancy again. Thus, smaller more immature infants acquire a greater nutrient deficit than the larger more mature infant. Needs for catch-up growth are, therefore, different [2]. Differences in the nature of the complementary foods may make no difference in the otherwise
normal infant but may have significant effect in the high-risk infant who has accrued a major nutritional deficit. Under these circumstances, a diet that's relatively low in protein but high in energy may significantly alter body composition. As Dr. Ziegler has pointed, breastfed infants have lower IGF-I levels when compared to formula-fed infants. One interpretation is that protein intake is borderline to inadequate in the former. This is an area that needs to be examined more rigorously.

Dr. Norris: The PEA POD really does offer some interesting methodology in terms of collecting body composition frequently in infancy, particularly in developing country settings as you said because it's portable and so forth. I have two questions on the methodology. The one is in terms of the hydration factor which may be a potential confounder. Do you standardize that in the sense that you scan them after feeding, or how do you deal with that? The second question is, if one wants to get longitudinal data from very close after birth through to at least 1 year of age and one has got to then cross over between say 6 months when size becomes an issue, do you then recommend moving onto DXA and how do you bridge the two methodologies in terms of producing longitudinal data?

Dr. Ellis: To your second question first. You are right, at present there is a problem in that the PEA POD has a body size limit that is at about 8 kg, which is about 6 months of age. Above that, PEA POD can't be used, so one has to go to something like DXA. In our studies, we will do both PEA POD and DXA when the infant is near this range. Concerning the other question, in any two-compartment model, irrespective of what two-compartment model you pick, hydration is an issue. The way the PEA POD works, you basically assume there is an average hydration for age and gender of the infant. In the first 6–7 days of life, there can be wide fluctuations in hydration, and that is why we don't routinely make PEA POD until 1st week of age. There may be a way to get around this or to reduce the influence is a way to accounting for some of the variation. Maybe a measurement like BIA can be developed to monitor rapid fluid changes in early infancy. If I can use BIA to measure body water, it then eliminates the issues about hydration and I can now use a three-compartment model, where the variations seen by the PEA POD can be more directly related to the protein compartment. Alternatively, I can just measure body potassium and forget about using BIA completely.

Dr. Moelgaard: I can see that you use a Hologic DXA scanner. Do you think that you would get the same results if you used a different DXA machine?

Dr. Ellis: Unfortunately, all DXA machines, even though they all claim to measure the same thing, give different numbers. So, unfortunately each machine has to have its own reference set.

Dr. Moelgaard: And it's not possible to calibrate them or something like that?

Dr. Ellis: What we do, when involved with multicenter studies using different DXA machines, is to circulate a common set of phantoms that each center scans. You can make some adjustments based on these reference phantoms; I don't think there is one specifically designed for infant measurements.

Dr. Hüppi: We are all interested in nutrition, how it changes body composition, but we never really talk about the expenditure of small babies, how that would change body composition. In a way, we have observed with the back to sleep recommendations that babies move much less in the supine than in the prone position. Can we use the DXA measurements or any body composition measurements in the regional way to separate out what is fat deposition in the context of less spontaneous movement vs. real fat deposition that you would call too much.

Dr. Ellis: You are asking about energy intake and expenditure along with changes in body composition. I can measure only the net changes in body composition. It would be difficult to assign the changes to a specific physical activity such as placing
Ellis

an infant in a supine vs. prone position, considering all of the other contributions to energy expenditure.

References