Growth of the Breast-Fed Child

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Breast-feeding confers significant health, nutritional, immunologic, developmental, psychological, social, economic, and environmental benefits to infants, mothers, families, and society. "Human milk is uniquely superior for infant feeding and is species-specific; all substitute feeding options differ markedly from it. The breast-fed infant is the reference or normative model against which all alternative feeding methods must be measured with regard to growth, health, development, and all other short and long term outcomes" (1).

Assessing the growth of infants is important for judging the overall progress of infants at both population and individual levels (2) as well as for evaluating the adequacy of lactation (3). Assessment of infant growth generally involves comparison with a reference population, making use of an appropriate growth reference chart. The reference population should reflect the growth expected for infants who are healthy and well nourished and who have received proper care. Feeding recommendations endorsed by international agencies and academies of pediatrics specify that infants should be exclusively breast-fed for about 6 months, with breast-feeding continuing thereafter while the infant is also fed appropriate, adequate, and safe complementary foods.

As the international infant growth reference currently used was constructed primarily from the growth of infants fed formula (4), an important issue is whether the growth patterns of breast-fed infants differ sufficiently from the growth patterns of non-breast-fed infants to be of concern. The purpose of this chapter is to review published reports to address five questions relevant to this issue: (1) What are the growth patterns of healthy breast-fed infants in the first year of life? (2) How does the duration of exclusive or predominant breast-feeding affect growth? (3) How does breastfeeding relate to long-term growth status? (4) What are possible mechanisms to explain differences in growth patterns between breast-fed and non-breast-fed infants? (5) What are the implications of these growth patterns for the assessment of the adequacy of growth?

GROWTH PATTERNS OF HEALTHY BREAST-FED INFANTS IN THE FIRST YEAR

Many studies have shown that breast-fed infants grow differently during the first year of life than do formula-fed infants (5,6). This difference in growth patterns has been
seen in relation to the current international growth reference that was created using data from infants fed on formula that is no longer available and in relation to infants fed on currently available formulas (7). Typically, infants who have been breast-fed grow as rapidly as or more rapidly than formula-fed infants during the first 2–3 months. Then, during the rest of the first year, breast-fed infants grow less rapidly than formula-fed infants.

The most extensive investigation of these growth patterns combined data from seven longitudinal studies from North America and Europe (7–9). Healthy infants were included in the pooled breast-fed dataset if they were predominantly breast-fed for at least 4 months (i.e., they had no solid foods, formula, or other milks before 4 months) and were partially breast-fed for at least 12 months. In all, 226 infants met these criteria. Growth patterns were similar across the seven studies, justifying pooling the data.

Figures 1–4 show the breast-fed versus formula-fed differences in patterns of growth for girls and boys in length and weight from birth to 12 months of age. The figures were created using the data from the pooled breast-fed dataset (8) and from the current international reference (10). The figures plot the difference in growth in centimeters or kilograms (pooled breast-fed minus current international reference) against age in months. Birth length was not available in the breast-fed set. For both length and weight and for both girls and boys, attained growth for the breast-fed set was higher in the first months and then decreased relative to the current reference. The largest difference in favor of the breast-fed set was at about 2 months. The largest difference in favor of the current reference was between 10 and 12 months, depending upon the anthropometric measurement and gender.

For girls’ weight, there was a slightly higher growth rate from 1 to 2 months for the breast-fed set; this difference was not seen for girls’ length or boys’ length and weight.

![Graph](image-url)

**FIG. 1.** Difference in growth in length (cm) for girls plotted against age (mos), with difference defined as pooled breast-fed dataset (8) minus current international reference (10).
FIG. 2. Difference in growth in length (cm) for boys plotted against age (mos), with difference defined as pooled breast-fed dataset (8) minus current international reference (10).

For the weight of both girls and boys, there was a slightly higher growth rate from birth to 1 month. With the exception of girls’ weight, the average growth rate of the breast-fed set was higher than that of the current reference between 11 and 12 months.

The estimated growth gained between 1 and 12 months is shown in Table 1. Regardless of gender, the growth gained between 1 and 12 months was about 1 kg in weight and 1 cm in length less for the breast-fed set than for the current reference.

The relative magnitude of the difference between the breast-fed set and the current reference was greater for weight than for length. As a result, the relative weight of the

FIG. 3. Difference in growth in weight (kg) for girls plotted against age (mos), with difference defined as pooled breast-fed dataset (8) minus current international reference (10).
breast-fed set, as measured by weight for length, showed the same pattern of decrease over the first year as the current reference (7).

The ratios of the standard deviations for the breast-fed set divided by the current reference are presented in Fig. 5 for weight for girls. Plots of the ratios for each gender and measurement were very similar to this figure. For weight, standard deviations were close to 1.0 at birth but were much smaller thereafter for the breast-fed set than for the current reference.

The results of this investigation are consistent with those of other studies (5,11,12). On the whole, as documented in the comprehensive review by Dewey (5), these studies have found that the growth patterns of breast-fed infants differ substantially from those of infants fed modern as well as older formulas. Most studies have reported that breast-fed infants gain less weight in the first year. For infants breast-fed through 12 months, this difference in weight gain is particularly apparent in the second half of the first year, resulting in a difference in attained weight at 12 months of 600–650 g.

TABLE 1. Growth gained between 1 and 12 months for infants from pooled breast-fed set (8) and current international reference (10)

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Gender</th>
<th>Pooled breast-fed data</th>
<th>Current reference data</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length (cm)</td>
<td>F</td>
<td>19.6</td>
<td>20.8</td>
<td>-1.2</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>20.3</td>
<td>21.5</td>
<td>-1.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>F</td>
<td>4.65</td>
<td>5.50</td>
<td>-0.85</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>5.04</td>
<td>5.90</td>
<td>-0.86</td>
</tr>
</tbody>
</table>

From WHO Working Group on Infant Growth (8) and World Health Organization (10).
In contrast, fewer than half of the studies showed a significant difference in length by feeding mode. Even when a difference in length has been observed, the difference in length has been proportionally much less than in weight. Consequently, the weight relative to height of breast-fed infants is less at the end of the first year. Measures of adiposity such as skinfold thickness are consistent with the explanation that the weight difference reflects differences in fat deposition. Growth in head circumference is not related to feeding mode (5).

DURATION OF EXCLUSIVE AND PREDOMINANT BREAST-FEEDING AND GROWTH

As documented in the previous section, growth patterns of exclusively or predominantly breast-fed infants differ from those of infants who are not breast-fed in the first year of life. Another question of interest is whether there are differences in growth patterns due to varying duration of breast-feeding. Several studies have examined this question.

A study in Honduras randomized 141 infants at 4 months of age to either continue breast-feeding and receive solid food or continue exclusive breast-feeding to 6 months (13). The complementary solid food given was hygienically prepared and nutritionally adequate. This study found small differences in length gain of 0.5 mm/month and weight gain of 32 g/month with longer exclusive breast-feeding during 4–6 months; these differences were not statistically significant. Length and weight gain after the intervention, from 6 to 12 months, was very similar between the groups provided solid foods at 4 months and those exclusively breast-fed throughout the first 6 months (14). There was a higher dropout rate in the group with breast-feed-
ing than in the group with solid foods (15). This may or may not have affected the growth estimates somewhat, but it is unlikely to have altered the conclusion that there was no difference in growth between the two feeding modes.

The results from several observational studies can be compared with these results. Stuff and Nichols (16) examined the effect of the timing of the introduction of solid foods (i.e., stopping predominant breast-feeding) on energy intake and growth. Forty-five infants from Texas were divided into three self-selected groups based on when solid foods were introduced: 16–20 weeks, 20–24 weeks, and after 24 weeks. They reported that energy intake did not increase with the introduction of solid foods and also that there was no relation between energy intake and growth.

Heinig et al. (17) studied 60 breast-fed infants in California who were given solid foods (i.e., stopped predominant breast-feeding) either before or after 6 months. For four periods defined over the first year, differences between the two groups (late solid group minus early solid group) in length gain (mm/month) ranged from −1 to 1 and in weight gain (g/month) from −63 to 84.

In Brazil, infants who were predominantly or partially breast-fed for 3 months were larger in weight at the beginning of the fourth month but grew more slowly during the fourth month than infants who were breast-fed for 0, 1, or 2 months (18). The differences for 3-month versus 1-month breast-feeding duration were 260 g in weight at 4 months and −90 g during the fourth month. Growth rates from 1 to 4 months were greater for infants who were predominantly or partially breast-fed versus those not breast-fed (particularly for those without indoor tap water); the reverse was true for growth rates from 4 to 6 months.

In Ghana, 30 infants were divided in the first month according to whether they were exclusively breast-fed or received complementary foods (19). From 1 to 6 months, weight gain for the first group was 3.2 kg and for the second group 3.7 kg, a difference of 100 g/month in favor of the group receiving complementary foods.

In Sudan, 341 infants were followed from birth to 32 weeks (20). In each 4-week period during that time, infants were classified according to whether they were exclusively breast-fed or received complementary foods. For each of the periods, the differences (exclusive minus complemented) in weight gains ranged from −1 to 3 g/day. A follow-up analysis on 122 infants using multiple regression to examine the effects of illness, weaning age, birthweight, and income on the first year’s increment in weight found a significant positive relation between weaning age and weight gain, such that each additional 28 days of breast-feeding was associated with an additional 132 g of weight gain (21).

A study in India found no differences in monthly attained weight for infants aged 1–12 months who either were solely breast-fed or were breast-fed with complementary foods (22); infants were reclassified as to breast-feeding status at each month. Although this study used a longitudinal design, of the 287 infants who started at 1 month, only 107 were examined at 12 months and only 182 at 6 months. Also, this study did not evaluate growth increments or control for other possibly influential factors. A study of similar design in Chile categorized 207 infants into those receiving breast-feeding, mixed feeding, or artificial feeding for each month from 1 to 12
months. The results appeared to show greater weight gains until 8 months and greater length gains until 4 months for breast-fed infants, but they were presented as cumulative weight and length gains and so are difficult to interpret (23).

The differences in growth related to duration of exclusive or predominant breast-feeding across these studies are all small and are not consistent. Furthermore, the inconsistency in the results cannot be explained by the fact that some studies were done in good versus poor environments. These studies taken together indicate that postnatal growth in length and weight appears not to be very sensitive to the duration of exclusive or predominant breast-feeding between about 4 and 6 months.

**BREAST-FEEDING AND LONG-TERM GROWTH STATUS**

Long-term effects on growth status of differences in infant feeding have been relatively little studied (4). Birkbeck et al. (24) compared the growth at 7 years of age between children who had been breast-fed to at least 12 weeks and those formula-fed from birth. Pomerance (25) compared the growth rate from 3 to 12 years of age between children who had been breast-fed to at least 2 months and those formula-fed from birth. In both studies, no differences were found. Similarly, no differences have been found in four other studies (3). Of the studies that provided data for the pooled breast-fed dataset and collected data past 12 months, most showed that the growth of the breast-fed infants reached that of the current reference at 24 months (7).

A recent study with a large sample has raised interest in the possibility that breast-feeding may have an impact on later attained weight and obesity (26). Three earlier studies had used much smaller samples and found no effect. A larger study of 1,320 adolescents in Canada born in the 1960s found that obesity was less among children who had been breast-fed (27). In this case-control study, the odds of being obese were 2.25 times lower for breast-fed infants than for non-breast-fed infants after controlling for potential confounding factors.

In the recent study, 9,357 children of German ancestry aged 5 and 6 years had weight and height assessed at entry to school in Bavaria. A survey questionnaire completed by the parents assessed early feeding, diet, and lifestyle factors. Obesity and overweight were defined as a body mass index [weight (kg) divided by height squared (m²)] greater than the 97th and 90th centiles, respectively, of all enrolled German children. The prevalence of obesity was 4.5% among children never breast-fed compared with 2.8% among children who were breast-fed. A dose–response relation was found between duration of breast-feeding and prevalence. Even after adjusting for potentially confounding social and lifestyle factors, breast-feeding was associated with reduced obesity and overweight, the odds ratios being 0.75 and 0.79. The report states that the study assessed the history of exclusive breast-feeding “defined as the child being fed no food other than breast milk.” However, 863 children were reported to have been exclusively breast-fed for 6–12 months and 121 for >12 months, which is highly unlikely to be the case. Apparently, parents interpreted the question asked of them as whether the milk fed to their infant had been exclusively breast milk (R. von Kries, personal communication).
POSSIBLE MECHANISMS TO EXPLAIN DIFFERENCES IN GROWTH PATTERNS

In healthy infants living in good environments, the differences in growth patterns between breast-fed and formula-fed infants in the first year are consistent with what is known about energy intakes of infants in these two groups (4,5,28,29). Breast-fed infants have lower intakes that are governed primarily by infant demand, not by inadequate milk volume (4,5,30). It is not understood why formula-fed infants have higher energy intakes than breast-fed infants (5).

There is some discussion in published reports that protein intakes of breast-fed infants may be below requirements after the second month of life, which corresponds to the period when the linear growth of breast-fed infants occurs more slowly than in formula-fed infants (28). Recent evidence, however, suggests that protein is not limiting (5). Other possible explanations for differences in growth patterns in the first 4–6 months, such as intakes of minerals, are unlikely (5). When complementary foods are introduced after this period, it is possible the combination of breast milk and complementary foods is not completely adequate in all nutrients. Whether this is so and whether any inadequacies may affect linear growth are just beginning to be investigated (5).

Human milk contains many nonnutritional substances such as hormones and growth factors. Hormones in human milk include cortisol, somatostatin, thyroid hormones, oxytocin, and prolactin (4,31,32). Growth factors include epidermal growth factor, insulin, and lactoferrin (4,31). Other substances such as long-chain polyunsaturated fatty acids may relate to growth (33). In addition, human milk contains other factors that are inducers of certain biological processes (4). The significance of these hormones and factors for growth patterns, however, is not understood (31).

The apparently protective effect of breast-feeding for school-age obesity in the German study was not likely to have been due to lifestyle factors, as these were controlled (26). This study did not assess family history of obesity, but this is unlikely to be the explanation of the association. In the Canadian study, sociodemographic variables and family history of obesity were controlled (27). Possible explanations for the association between breast-feeding and later obesity are behavioral and biological, related to the process of breast-feeding or the properties of breast milk (26). Perhaps breast-feeding, which is an intense caring behavior, leads to other forms of differential caring behaviors. Breast-feeding or breast milk may have a programming effect. Breast-fed infants have lower plasma concentrations of insulin than formula-fed infants, which might result in less fat deposition and fewer adipocytes developing. The other bioactive factors that are present in breast milk might modulate growth factors that are known to inhibit adipocyte differentiation. The lower protein intake associated with breast-feeding may decrease the risk of later obesity. These possible explanations have not been investigated (26).

IMPLICATIONS FOR ASSESSMENT OF ADEQUACY OF GROWTH

Anthropometric information is used for assessing growth that has been and is being attained. Growth can be indicative of nutritional status, overall health, and feeding
and other care behaviors. Judgments about infant growth may be strongly influenced by the choice of the reference population. As a growth reference chart conveys information about the growth that is expected, the use of an inappropriate chart means that an unrealistic or misleading expectation may result, and consequently incorrect decisions about infant care may be made. Because of the marked differences between the growth of breast-fed infants and the current international growth reference, it is important to examine how likely it is that incorrect public health and clinical decisions are made when the current reference is used in comparison with the growth of breast-fed infants.

Several datasets have been used to compare the assessment of the adequacy of growth in the first year of life using both the pooled breast-fed dataset as if it were a reference and the current international reference (8,9,34). These datasets have come from India, Peru, Chile, a group of formula-fed infants from the USA and Europe, and a multicountry study.

When the breast-fed set was used as a reference and applied to formula-fed infants from the USA and Europe, a larger proportion of infants was classified as overweight at ages 10–12 months than when the current reference was used (8,9). Therefore, if the growth of breast-fed infants is considered to be normative, then the use of the current reference underestimated the extent of overweight. When the breast-fed set was used as a reference and applied to malnourished populations, a larger proportion of infants was classified as underweight or stunted during the first 6 months of life than when the current reference was used (8,9,34). For population assessment, both the shape of the reference growth curve and the variance of the curve are influential in classifying infants.

At the individual level, data from India and Peru indicate that the diagnosis of poor weight gain using the current reference would occur at 3 months of age on average (8,9). If, on the other hand, the breast-fed set is used as a reference, poor weight gain will be diagnosed on average at 5 months. For individual assessment, it is primarily the shape of the curve that influences the diagnosis of growth faltering as an infant’s growth is tracked over time, although the placement of the growth measurements on the growth chart also influences judgment.

**RESEARCH RECOMMENDATIONS**

There is now strong evidence that the growth patterns of breast-fed infants differ from those of formula-fed infants in the first year of life and that growth patterns are not sensitive to the duration of exclusive or predominant breast-feeding during 4–6 months of age. There is much less evidence documenting growth patterns of breast-fed and formula-fed infants in the second year and beyond and about any possible functional consequences (35). Further information about some of these issues will probably come from the longitudinal component of the World Health Organization (WHO) multicenter growth reference study currently underway (36,37).

The overwhelming and diverse advantages of breast-feeding for infants have been well documented. Two reports (26,27) suggest yet another advantage for breast-feeding, namely, that it is protective against childhood and adolescent obesity. Additional
research on the role and impact of breast-feeding on long-term growth status will be important to further document and understand this protective effect, especially given the rapid increase in obesity, even among children, in many countries, and the ill health and costs associated with obesity (38–40).

The mechanisms that might explain differences in growth patterns with feeding mode are poorly understood. Research is needed to investigate the possible nutritional and hormonal bases for these differences (35). Research is also needed to understand why infants who are breast-fed are less likely to be obese in later childhood and adolescence. The biological and behavioral explanations that could emerge may in turn contribute to a larger understanding of the causes of obesity.

One of the striking findings from the comparison of the pooled breast-fed dataset and the current international growth reference was the marked difference in variability between them (8,9). This observation is counter to the general assumption that has been made that populations may be shifted in terms of average growth, but that the variability of growth across individuals of a given age is relatively constant from one population to another. Although ample data exist to document the variability of attained growth from a large number of published studies, there needs to be a systematic evaluation of this variability and the factors that affect variation in growth.

One purpose of growth references is to provide a tool for effective caring for and health management of infants and children (2). An important part of the rationale for constructing a new international growth reference is that it will improve the nutritional management of infants (8). Because healthy breast-fed infants appear to falter relative to the current international reference, the current reference may undermine efforts to promote and maintain prolonged exclusive breast-feeding. The assumption is that changing to a new reference that reflects the growth of infants fed according to current recommendations will lead to better support for breast-feeding and other accepted healthy practices. If the new reference has similar characteristics to the pooled breast-fed dataset, however, formula-fed infants may be more likely to be identified as being overweight (8), with the risk that parents may react by placing the child on a low-energy diet, which is not recommended during infancy (8). Nevertheless, the potential risks to formula-fed infants of changing the growth reference are judged to be much lower than those faced by breast-fed infants whose management is based on the current international reference (8). The argument that a new reference will lead to better management rests on assumptions about how policymakers, health workers, and child caregivers understand growth information and how they will respond to a new growth reference. The research base to support these assumptions is quite limited, however. Therefore, a critical research need is to investigate the following: how decision makers and agency officials, health workers, and caregivers understand the concept of child growth, information from measurement on child growth (individual and population levels), and information from growth references; how and why they interpret and use information from child growth measurements and reference curves; and what challenges and barriers users at different levels will encounter in making a transition from the
growth reference charts in current use to the new growth reference charts under
development.

POLICY IMPLICATIONS

The slower weight gain of breast-fed infants in the first year of life is not associated
with any adverse functional outcomes regarding activity or behavioral development
(3). In all populations, breast-feeding confers significant health advantages. Policies
must continue to emphasize the importance of breast-feeding in all societies and en-
vvironments so that infants and mothers gain these advantages.

The current international reference was based on data from a well-nourished and
healthy population. This reference was presumed to be descriptive of that population,
and its rationale for use as a reference was that a reference should represent the growth
observed in a geographically defined population. The new international growth refer-
ence under development has adopted a different rationale. This is that a reference
should instead be representative of a population defined on the basis of having fol-
lowed widely endorsed health and nutritional recommendations (8,9). This rationale
has been strongly endorsed by the WHO and its member states, although undoubtedly
further policy efforts will be required to encourage its acceptance at various levels.

A basis for the current international reference is the assumption that optimal
growth is equivalent to maximal growth (8). Given that breast-feeding is clearly op-
timal for infants and that it does not result in maximal growth in the first year of life,
we can now understand that these two concepts are, in fact, not equivalent.
Furthermore, the fact that populations of children can have a high prevalence of obe-
sity (38–40) contributes to the realization that, although in poor environments, better
nutrition and care are associated with greater child growth, “bigger” is not always
“better.” This decoupling of the concepts of optimal and maximal will necessitate
careful thinking at various levels to ensure that policies that may be inherently based
on the assumption of their equivalence are re-examined.

The finding that breast-feeding in the first year of life is associated with a de-
creased risk of obesity among school-age and adolescent children is an example of
how early experiences may have consequences that can last a lifetime. These find-
ings suggest that promotion of breast-feeding may decrease obesity in childhood and
adult life. As childhood obesity is related to adult obesity and chronic disease, breast-
fed infants may have better health status as adults (26). Policies and educational ef-
forts that support this promotion are warranted.

The facts that breast-fed infants grow differently from formula-fed infants in the
first year and that a new international growth reference will be based on breast-fed
infants have important implications for education in use of growth information and
nutritional management of infants and young children. The views and perspectives of
decision makers and agency officials, health workers, and caregivers will need to be
understood, and then educational activities may be devised to promote and encour-
ge the appropriate use and interpretation of anthropometric information for the wel-
fare of infants and young children.
GROWTH OF THE BREAST-FED CHILD

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REFERENCES

DISCUSSION

Dr. Guesry: I am strongly in favor of exclusive breast-feeding for as long as possible, as long as the mother is comfortable with it. However, I would like to know how you cope with the fact that in industrialized countries, the exclusively breast-fed cohort is one of the most biased and selected populations. Breast-feeding mothers are of higher socioeconomic class, are more educated, and are healthier. If you get
tuberculosis or AIDS or if you are mentally sick, you don’t breast-feed. And any incident during the course of breast-feeding, like hospital admission of the baby for surgery or for infection, or any slowing down of the growth curve will lead the majority of the pediatricians to switch from breast-feeding to bottle-feeding. So, you end up with a highly selected population.

Dr. Frongillo: One of the most contentious issues over the decision to have a new WHO growth reference based on breast-fed infants involved just this. There was a lot of concern about whether we would be developing a growth reference for a rather peculiar set of infants. The compromise that was made after much discussion was to ensure that in the countries involved—and there are six countries in the multicenter growth reference study—there would be a substantial population of women of higher socioeconomic status who were exclusively breast-feeding or breast-feeding with support for a minimum of 4 months, so that it would not be a very selected group. Of course, that only partially addresses your question. It may still be the case that infants who are breast-fed differ from infants who are not breast-fed in certain characteristics, and those characteristics may have played a part in determining why the decision was made on how the infant should be fed. But, in the end, the decision was made that, because there is now universal agreement that infants should be breast-fed, the growth reference should describe the growth of infants who are fed in that way.

Dr. Flores: We now seem to be clear about growth norms in the first year, but what is the position of the WHO in relation to growth from 13 months onward?

Dr. Frongillo: There are two components of the WHO multicenter growth reference study: a longitudinal component from birth to 24 months and a cross-sectional component, sometimes a mixed longitudinal component, from 18 months to the sixth year of life. So, there will be data available all the way from birth up to about 71 months. That will allow the construction of a reference from birth up to 5 years, maybe a little bit beyond.

Dr. Räthä: Related to the possible mechanisms for the difference in growth in breast-fed and formula-fed infants, you mentioned that you didn’t think protein intake was important in this connection. We have some data in breast-fed and formula-fed infants between 4 and 12 months getting the same supplementary foods, which show that the formula-fed infants have a very high protein intake, sometimes two to three times higher than the breast-fed infants. They have a significantly higher level of insulin-stimulating amino acids, and they also excrete more C peptides in the urine. Furthermore, there are some studies from France (1) showing that infants who have protein energy intakes of more than 15% have higher levels of insulin-like growth factor-1, and the authors speculate that this may increase the growth of adipose tissue. Indeed, they found obesity in these infants later on. So, I would not completely rule out the protein intake as a factor both in the increased growth and possibly in the obesity.

Dr. Haschke: How is it planned to follow subjects who do not adhere to the feeding recommendations? You will have a lot of mothers who exclusively breast-feed their infants for 4–6 months, but you will also have a lot who drop out for one reason or another. How will you treat those in the data analysis?

Dr. Frongillo: One of the things I’m happiest about is the attention that has been paid to this issue, because it is a limitation of other studies. There are five groups of infants apart from the group that adheres precisely to the protocol. There is a dropout group, who agreed to participate but then moved away or some such; there is a group
of infants who started off breast-feeding according to the protocol but did not achieve the required length of breast-feeding; and there are three additional groups showing various other types of divergence from the protocol. All of these will be followed. The intention was that each participating site would recruit about 300 infants and that all these infants would be followed all the way to 24 months, regardless of their adherence to the feeding recommendations. Thus, at the end of that time, we will be able to use the data to tell us whether any type of self-selection has resulted in different growth patterns. We will be able to learn a lot about how these kinds of variation in behavior are related to growth.

Dr. Ulijaszek: In identifying differences in growth between breast-fed and non-breast-fed infants, have you controlled for the potential impact of infection? You mentioned growth factors and breast-feeding. We know that growth factors are involved in gut maturity and maturation. Does this link to resistance to infection and then to differences in growth performance?

Dr. Fromiglio: Well, we know that severe illness does relate to growth performance. In the studies that I reviewed, illness either was at such a low level that it was not relevant or was controlled. So, we are not seeing differences that are explainable by illness, but certainly in many environments, growth is substantially affected by illness.

Dr. Rivera-Dommarco: What efforts have been made to ensure that the complementary feeding was adequate in the population that will be used as a reference? From 6 months on, differences between the breast-fed infants and the reference infants could be the result of differences in complementary feeding practices.

Dr. Fromiglio: In the three studies that I particularly cited, a lot of attention was paid to that issue. We know quite a lot about what foods were given and their frequency and amounts in relation to comparisons of growth patterns. In the pooled breast-fed set, most of the studies were from the USA or Europe, where our assumption is that the adequacy of complementary foods wasn’t a limitation. However, I don’t think we have the degree of documentation you are asking for in any of those studies.

Dr. Arato: I should like to comment on linear growth in breast-fed infants. An interesting study was published recently in the British Medical Journal (2) where it was found that girls with greater than normal length increments in infancy had an increased incidence of coronary heart disease in later life. Maybe it is an advantage of breast-feeding that there is somewhat reduced linear growth in infancy.

Dr. Stolzflug: Do you know of any studies of cytokine profiles in formula-fed and breast-fed infants, particularly the cytokines that we know regulate appetite and anorexia? The cytokine profile associated with anorexia is now becoming quite well described in adults (3,4). Has anybody tried to look at that in this particular situation?

Dr. Fromiglio: I’m not the most informed person to answer this question. The last time I looked at this issue was a few years ago, but I believe it is still true to say that we don’t understand very much about the regulation of growth in infancy. Most of what we do know comes from animal studies, particularly in agricultural animals. There are some very interesting ideas about differences in regulation that occur very early on versus later on, at puberty, for example. But I don’t know of any work that really helps us understand these differences. Perhaps Dr. Ulijaszek could comment?

Dr. Ulijaszek: I am not aware of anybody looking at cytokines in this context, probably because it is notoriously difficult to do this sort of study in humans. It has
been done in the context of the linkages between growth, infection, and appetite, but to be able to make regular cytokine measurements in a noninvasive way is hugely problematic. I don’t think anybody has been doing it.

**Dr. Ramakrishnan:** The new standards will clearly affect the timing of a diagnosis of growth faltering; in a breast-fed child, this would shift from 3 to 6 months. The prevalence of malnutrition, defined by stunting or underweight, would probably go up significantly if you are going to use these standards at a national level in the first 6 months of life. What are the policy implications of that?

**Dr. Frongillo:** The implications will be substantial. I think there is no question that there is substantial gain to be made in moving to a new reference for the management of infant feeding, but you are absolutely right in raising the possibility that this will alter the apparent prevalence of conditions such as obesity, underweight, and stunting. When we start changing growth references, we are heading for a difficult period, particularly for those people who are trying to advise agencies and government officials on nutritional problems. We need to continue with dialogue on these matters to find the best way forward until everything settles down.

**Dr. Martorell:** I would like to provide some additional information about the WHO multicountry study. The countries involved are India (Delhi), Brazil, USA (California), Norway, Ghana, and Oman. The populations from which this study is being drawn are well-to-do. The study site investigators have to collect preliminary data to demonstrate that such a population exists and to show that there are no constraints on growth, using indicators such as socioeconomic status, income, and education. So, we are dealing with a very selected population in each of these countries. The effort is prescriptive, in the sense that the mothers agree to follow the WHO breast-feeding recommendations, there is lactation support provided, and, in fact, it almost becomes an intervention. For example, in Pelotas in Brazil, the breast-feeding rate in the participating group is much higher than the norm for Pelotas, so the study itself has changed behaviors. But everybody is being followed, including those who don’t adhere the protocol, so this will permit proper analysis. Infection is being assessed, but incidences are likely to be low.

**REFERENCES**