Influence of Early Nutrition on Growth

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Realization of the genetically determined growth potential of normal infants and children depends, among other factors, on the availability and consumption of adequate amounts of nutrients. The World Health Organization (WHO) recommends that normal infants be breast-fed exclusively from birth to 4–6 months of age; that is, they should be given no liquids or solids other than breast milk during this period. After this initial period of exclusive breast-feeding, infants should continue to be breast-fed up to 2 years of age or beyond while receiving nutritionally adequate and safe complementary foods (1,2). It is well documented that the growth pattern of formula-fed infants differs from that of breast-fed infants (3–13), at least until 12 months of age.

Assessment of growth comprises two components: measurement (anthropometry) and interpretation of the measurements. Interpretation consists of comparisons of child measurement data with normative (reference) data. The validity of the normative data is therefore crucial. The universally used National Center for Health Statistics (NCHS)/WHO growth references (14,15) suffer from lack of detailed information about feeding during infancy in the subjects who provided the anthropometric data. It is of particular relevance that during early life, most of the subjects providing the data were fed formula. Another concern is that for the first 3 years of life, the NCHS/WHO standards are based on data derived from a longitudinal study with measurements made only every 3 months. The paucity of datapoints is responsible for the fact that the standards for the first year of life do not accurately reflect the dynamic nature of infant growth. Further areas of concern are as follows: (a) There were a lack of representativeness and excess homogeneity of the data between 0 and 2 years; (b) sample sizes were small, and there was a lack of repeated
measurements on the same children; (c) the curve-fitting procedures were outdated; and (d) a length–height disjunction occurred at 24 months (3–5).

One consequence of the shortcomings of the NCHS/WHO standards is that weights and lengths of normal infants regularly exceed the NCHS/WHO standards during the first 2–3 months of life, but a subsequent falloff occurs that gives the false impression that growth is faltering (11–13,16). During late infancy, the discrepancy in weight for age is large enough to lead to faulty conclusions about the adequacy of growth. These concerns have resulted in a WHO recommendation (11,16,17) that the NCHS/WHO reference data be replaced. As an interim step, the WHO Working Group on Infant Growth published references (10,11) that were based on data from infants fed according to the present WHO recommendations. Furthermore, WHO also provided guidelines for collecting data to develop a new international growth reference and started the data collection (16).

In 1988, the European Union initiated concerted action in the field of nutrition and health (EURONUT). Owing to the recognized shortcomings of the NCHS/WHO references (10–12,16,17), the steering committee of EURONUT launched a European growth study (Euro-Growth) (18). The main objectives of Euro-Growth, the multicenter study of infants and young children, were as follows:

- To record in a longitudinal fashion the growth of contemporary European children who were presumably fed in accordance with prevailing feeding recommendations and to construct growth and growth velocity reference tables [for weight, length, body mass index (BMI), and so on] (19–21).
- To assess dietary habits [e.g., the duration of exclusive breast-feeding, time of introduction of solids (22)].
- To evaluate the influences of nutrition and of genetic factors (e.g., midparental height, BMI at birth and at 1 month of age), socioeconomic factors (e.g., maternal education, number of siblings), and lifestyle factors (e.g., smoking) on growth (19,20,22).

A longitudinal study design was chosen because, among other advantages, it is suitable for linking growth data with observational data on diet and lifestyle.

**NEW GROWTH REFERENCES: EURO-GROWTH AND EURO-GROWTH FOR BREAST-FED BOYS AND GIRLS**

The Euro-Growth study was designed as a multicenter, longitudinal, observational study using standardized methodology (18,19). Healthy term infants (gestational ages between 37 and 44 weeks) without signs of intrauterine growth pathology and not meeting the other exclusion criteria (18) were enrolled before 30 days of age. The cohort consisted of 2,245 subjects (1,154 boys and 1,091 girls) from 22 study centers in 12 European countries. Information on parental weight and height (reported), educational achievement, family demographics and socioeconomic factors, and infant characteristics at birth was obtained at enrollment.

Target ages for interviews about the subjects' nutrition (23) and anthropometric measurements (19) were 1, 2, 3, 4, 5, 6, 9, 12, 18, 24, 30, and 36 months. Information
about socioeconomic factors and about family lifestyle was obtained at all target ages. The sample of the Euro-Growth study was approximately representative of the background population surrounding the 21 study sites and included children from a range of European regions with a diversity of socioeconomic characteristics (18,19). The educational level of the mothers in the Euro-Growth population was only slightly biased (+1 year) toward an above-average educational stratum of the European population (19).

Breast-feeding was defined according to WHO (24) as follows: full breast-feeding, taking no milk other than breast milk; partial breast-feeding, taking formula milk in addition to breast milk. Exclusive breast-feeding (breast milk only) could be derived from the data. Solid foods were recorded semiquantitatively during the first 2 years [never, sometimes (once or twice a week), every day] (23).

The large sample size of the Euro-Growth cohort and the detailed information on feeding between 1 and 12 months of age (Table 1) (19,22,23) provided an opportunity to assess the influence of the type of feeding on growth. In particular, it was possible to identify a large group of infants who were fed according to the present WHO recommendations (1,2). The growth of those children (22) was compared with the Euro-Growth references (19).

Figure 1 indicates that differences in mean length between birth and 24 months of age were small and ranged from −5 to +4 mm at all target ages. Differences in mean weight were also small, ranging from −148 to +199 g at all target ages (Fig. 2). Our study confirmed that infants who are fed according to WHO recommendations (1,2) have slightly greater weight and length during the first 2–3 months of age than infants fed in other ways. Between 4 and 18 months, boys and girls tend to be shorter and lighter, but the differences between breast-fed children and the Euro-Growth references are small and not clinically relevant, being smaller than the usual measurement errors for length (6 mm) and weight (239 g) in that age range (11). The variances for length (1 SD, 0.93–1.04) and weight (1 SD, 0.92–1.02) of the breast-fed children were similar to the Euro-Growth reference (19,22) at all target ages. This indicates that the breast-fed group was not more homogeneous than

<table>
<thead>
<tr>
<th>Age (mo)</th>
<th>FB</th>
<th>B</th>
<th>S</th>
<th></th>
<th>AGE</th>
<th>WHO (n = 319)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1</td>
<td>54</td>
<td>74</td>
<td>5</td>
<td></td>
<td>100*</td>
<td>100*</td>
</tr>
<tr>
<td>&gt;2</td>
<td>41</td>
<td>59</td>
<td>24</td>
<td></td>
<td>100*</td>
<td>100*</td>
</tr>
<tr>
<td>&gt;3</td>
<td>32</td>
<td>46</td>
<td>42</td>
<td></td>
<td>100*</td>
<td>100*</td>
</tr>
<tr>
<td>&gt;4</td>
<td>24</td>
<td>38</td>
<td>64</td>
<td></td>
<td>100*</td>
<td>100*</td>
</tr>
<tr>
<td>&gt;5</td>
<td>17</td>
<td>31</td>
<td>85</td>
<td></td>
<td>77</td>
<td>97</td>
</tr>
<tr>
<td>&gt;6</td>
<td>12</td>
<td>25</td>
<td>94</td>
<td></td>
<td>56</td>
<td>87</td>
</tr>
<tr>
<td>&gt;9</td>
<td>5</td>
<td>13</td>
<td>100</td>
<td></td>
<td>29</td>
<td>54</td>
</tr>
<tr>
<td>&gt;12</td>
<td>2</td>
<td>7</td>
<td>100</td>
<td></td>
<td>14</td>
<td>28</td>
</tr>
</tbody>
</table>

From WHO/UNICEF (1) and Forty-Fourth World Health Assembly (2). Numbers are percent fully breast-fed (FB), breast-fed (B), and receiving solids (S). *Exclusive breast-feeding.
**FIG. 1.** Difference in mean weight (g) between the Euro-Growth reference (19) and the Euro-Growth reference for breast-fed boys and girls (22) (0–24 months).

**FIG. 2.** Difference in mean length (mm) between the Euro-Growth reference (19) and the Euro-Growth reference for breast-fed boys and girls (22) (0–24 months).
TABLE 2. Comparison of calculated (50th centile) length differences in boys and girls (selected intervals between 1 and 24 months)

<table>
<thead>
<tr>
<th>Length (cm)</th>
<th>Gender</th>
<th>1–3 mo</th>
<th>1–6 mo</th>
<th>1–12 mo</th>
<th>1–24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euro-Growth ref. for breast-fed children (22)</td>
<td>M</td>
<td>6.4</td>
<td>12.7</td>
<td>21.1</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>6.0</td>
<td>12.3</td>
<td>20.7</td>
<td>33.3</td>
</tr>
<tr>
<td>Euro-Growth ref. (19)</td>
<td>M</td>
<td>6.5</td>
<td>13.5</td>
<td>21.5</td>
<td>33.5</td>
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<tr>
<td></td>
<td>F</td>
<td>6.2</td>
<td>12.9</td>
<td>21.2</td>
<td>33.8</td>
</tr>
<tr>
<td>NCHS ref. (14,15)</td>
<td>M</td>
<td>6.4</td>
<td>12.8</td>
<td>21.4</td>
<td>32.9</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>5.8</td>
<td>11.9</td>
<td>20.6</td>
<td>32.7</td>
</tr>
</tbody>
</table>

NCHS, National Center for Health Statistics.
From Haschke F et al. (19,22), Hamill PVV et al. (14), and World Health Organization (15).

the overall Euro-Growth cohort. This characteristic is crucial to the definition of growth references because it determines the placement of z scores, centile lines, and statistically defined cutoff values. Our study also confirmed earlier reports (10–12) showing that during the first 4–6 months of life, breast-fed infants have higher mean weight and lower weight variance than the NCHS/WHO references (14,15).

Tables 2 and 3 indicate differences in length and weight (50th raw centiles; 1–3, 1–6, 1–12, 1–24 months) of the children from the Euro-Growth reference for breast-fed children (22), the Euro-Growth reference (19), and the NCHS/WHO reference (14,15). Length differences between the three references for boys and girls for the interval 1–12 months did not exceed 0.4 and 0.6 cm. It is of interest that length gains for the interval 1–24 months were lowest for the NCHS/WHO reference (14,15). Weight differences between the three references for boys and girls for the interval 1–12 months did not exceed 0.37 and 0.25 kg.

Several well-designed studies (3–9) have provided data on length, weight, and indexes of body fatness of infants fed according to WHO recommendations (1,2). The data from these studies were used for the construction of the WHO growth reference (10,11), which shows a slower gain in length (−0.8 cm) and weight (−1.2 kg) in breast-fed infants between 1 and 12 months of age than the NCHS/WHO reference

TABLE 3. Comparison of calculated (50th centile) weight differences in boys and girls (selected intervals between 1 and 24 months)

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Gender</th>
<th>1–3 mo</th>
<th>1–6 mo</th>
<th>1–12 mo</th>
<th>1–24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euro-Growth ref. for breast-fed children (22)</td>
<td>M</td>
<td>1.74</td>
<td>3.34</td>
<td>5.62</td>
<td>8.23</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1.52</td>
<td>3.14</td>
<td>5.35</td>
<td>7.91</td>
</tr>
<tr>
<td>Euro-Growth ref. (19)</td>
<td>M</td>
<td>1.86</td>
<td>3.66</td>
<td>5.88</td>
<td>8.51</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1.58</td>
<td>3.32</td>
<td>5.46</td>
<td>8.20</td>
</tr>
<tr>
<td>NCHS ref. (14,15)</td>
<td>M</td>
<td>1.80</td>
<td>3.61</td>
<td>5.89</td>
<td>8.36</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>1.44</td>
<td>3.23</td>
<td>5.60</td>
<td>8.00</td>
</tr>
</tbody>
</table>

NCHS, National Center for Health Statistics.
From Haschke F et al. (19,22), Hamill PVV et al. (14), and World Health Organization (15).
INFLUENCE OF EARLY NUTRITION ON GROWTH

(14,15). The cohorts used for the construction of the WHO reference were smaller (between 44 and 144 infants) and rather selective [maternal educational levels were generally high (10–12)] in comparison with the Euro-Growth cohort (19). Most infants of the WHO growth reference continued to be breast-fed until 12 months of age, whereas only 57% of the Euro-Growth breast-fed cohort continued breast-feeding between 9 and 12 months of age.

INFLUENCE ON GROWTH OF DURATION OF (ANY) BREAST-FEEDING, MIDPARENTAL HEIGHT, AND TIME OF INTRODUCTION OF SOLIDS

We employed multiple regression analysis to examine the influence on growth of the duration of breast-feeding and of the introduction of solids (22). Dependent variables were increments in length (mm/month) and weight (g/month) and change in BMI (kg/m²/year) during the age intervals 1–4, 1–12, 1–24, and 1–36 months. Duration of breast-feeding, defined as the age (months) at which any breast-feeding ceased, and age at introduction of solids (months) were the independent variables. Interactions between breast-feeding and solids were also considered. Additional independent variables in the model were gender (0 = male; 1 = female), educational level of the mother [levels 1–5 (18,19)], and midparental height.

We found a significant negative correlation between duration of breast-feeding and both gain in length and weight (Table 4) and change in BMI until 24 months of age (22). However, the influence of breast-feeding was small and clinically unimportant. A 1-month difference in the duration of breast-feeding was related to differences in monthly length and weight gains (1–12 months) of 0.12 mm and 8 g. The influence of midparental height on increments in length and weight was much stronger and persisted until 36 months of age. A 10-cm difference in midparental height was related to differences in monthly length and weight gains (1–12 months) of 0.8 mm and 32 g. Between 1 and 36 months of age, the duration of breast-feeding was no longer related to gains in length and weight, but the influence of midparental height remained highly significant (p < 0.001). The Euro-Growth references (18,19) had already confirmed that midparental height was a strong indicator for the genetic growth

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change</th>
<th>1–12 mo (g/mo)</th>
<th>1–24 mo (g/mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast-feeding</td>
<td>+1 mo</td>
<td>−7.9b</td>
<td>−3.3b</td>
</tr>
<tr>
<td>Intro-solids</td>
<td>+1 mo</td>
<td>+4.5c</td>
<td>−1.5</td>
</tr>
<tr>
<td>Gender</td>
<td>M</td>
<td>+31.6b</td>
<td>−7.9c</td>
</tr>
<tr>
<td>Maternal education</td>
<td>+1a</td>
<td>−4.8c</td>
<td>−1.9c</td>
</tr>
<tr>
<td>Midparent height</td>
<td>+10 cm</td>
<td>+33.9a</td>
<td>+21.9a</td>
</tr>
</tbody>
</table>

*a* p < 0.0001 multiple regression analysis.

*b* p < 0.001 multiple regression analysis.

*c* p < 0.01 multiple regression analysis.

*d* Five-point scale for maternal education.
potential of the entire study cohort (Table 5). Two studies (10,12) compared infants who were breast-fed for at least 9–12 months with infants who were breast-fed for 6–8 months. Longer duration of breast-feeding was associated with lower z scores for weight, length, and weight for length at 12 months of age. Our regression model now indicates that the effect of full breast-feeding on growth was transient in that it was no longer detectable after 24 months of age.

Of specific interest for Euro-Growth was the group that was fully breast-fed to at least 4–5 months of age but in whom solids were introduced before 4 months. In comparison with the infants who were fed according to the WHO recommendations, these infants tended to be longer but to have a lower body weight, which resulted in a lower BMI between 1 and 36 months of age (Fig. 3). Differences in mean BMI as large as

![Diagram](attachment:diagram.png)

**FIG. 3.** Mean z scores of body mass index by feeding group. For definition of groups, see the text.
0.3 z scores from 2 to 6 months of age indicated that early introduction of solids was associated with greater leanness (22). It has been shown that infants given solids at 4–5 months weighed less before 4 months than infants given solids at 6 months or later (10). Low weight for age and leanness may prompt parents to introduce solids earlier. Late introduction of solids was associated with higher weight gain and higher BMI only until 12 months of age. Multiple regression analysis indicated that age at introduction of solids was positively correlated with length gain between 1 and 24 months of age and with weight gain between 1 and 12 months of age (Table 4) (22). The age at introduction of solids was positively correlated with change in BMI between 1 and 12 months of age, but this was no longer the case between 1 and 24 or 1 and 36 months of age. In the multiple regression model, the time of introduction of solids had only a transient influence on growth, which was no longer apparent at 24 and 36 months of age.

INFLUENCE OF EARLY NUTRITION AND GENETIC FACTORS ON OBESITY

The likelihood that obesity present in early childhood will persist and induce morbidity and mortality has important implications for the cutoff point used to assess obesity in children, for how aggressive the treatment directed at obesity should be, and for public health policymaking (25; see also the chapter by Martorell et al. in this book). Guo et al. (26) have published a longitudinal study that examined the odds ratios across childhood for the risk of adult obesity. At 2 years of age, the odds ratios for boys and girls are 2.4 (95% confidence interval 1.08–5.37) and 2.1 (0.93–4.75), respectively. Corresponding odds ratios at 4 years of age are 2.7 (1.33–5.46) and 2.3 (1.08–4.84). The results described by Guo et al. (26) are concordant with other studies that indicate that obesity will persist in a substantial proportion of obese children and adolescents (27–29). The Euro-Growth cohort allowed us to study factors with influence on obesity at 1, 2, and 3 years of age. Early nutrition (duration of exclusive breast-feeding, any breast-feeding, time of introduction of solids), genetic factors [gender, BMI at birth and at 1 month of age, midparental height], and socioeconomic and lifestyle factors (age and education of parents, number of siblings, urban or rural environment, smoking in the household, and so on (18,19)] were considered as the independent variables. We used logistic regression analysis to identify the factors predicting obesity at 1, 2, and 3 years of age. “Obesity” was defined as having a BMI above the 90th or 95th centiles of the respective Euro-Growth references (20). An independent variable was considered to be a significant predictor for the outcome variable (BMI) if the 95% confidence interval for the odds ratio did not include 1. Interactions between the independent variables were also considered. We used BMI at 1 month of age rather than BMI at birth because it was a stronger predictor, and anthropometric measurements at 1 month of age were done according to a standardized protocol (18).

BMI at 1 month of age turned out to be the strongest predictor for having a BMI above the 90th and 95th centiles at 1, 2, and 3 years of age (Table 6). Later
TABLE 6. Factors that are significantly associated with body mass index (BMI) >90th and >95th centiles at 1, 2, and 3 years of age

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>n</th>
<th>Centile</th>
<th>BMI at 1 mo (kg/m²)</th>
<th>Education of mother (levels 1–5)</th>
<th>Exclusive breast-feeding (duration, mo)</th>
<th>Introduction of solids (age, mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,849</td>
<td>90th</td>
<td>1.91 (1.16–2.26)</td>
<td>0.85 (0.73–0.97)</td>
<td>0.84 (0.77–0.92)</td>
<td>1.19 (1.06–1.34)</td>
</tr>
<tr>
<td>2</td>
<td>1,481</td>
<td>90th</td>
<td>1.73 (1.44–2.07)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>957</td>
<td>90th</td>
<td>1.81 (1.44–2.27)</td>
<td>0.72 (0.59–0.88)</td>
<td>—</td>
<td>1.17 (1.03–1.33)</td>
</tr>
<tr>
<td>1</td>
<td>1,849</td>
<td>95th</td>
<td>2.18 (1.75–2.72)</td>
<td>—</td>
<td>0.82 (0.72–0.91)</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>1,481</td>
<td>95th</td>
<td>1.83 (1.44–2.32)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>957</td>
<td>95th</td>
<td>2.15 (1.59–2.90)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Values are odd ratio (95% confidence interval).

The introduction of solids was positively and higher maternal educational level negatively associated with a BMI above the 90th centile at 1 and 3 years of age. Duration of exclusive breast-feeding was negatively associated with BMI above the 90th and 95th centiles only at 1 year of age. Our data therefore do not show that the duration of exclusive or any breast-feeding protects against having a BMI of >90th and >95th centiles at 3 years of age. A recent study in Germany (30) suggested that a history of having been breast-fed, after adjusting for potential confounders, remained associated with reduced obesity (defined as BMI of >97th centile; odds ratio 0.75) and reduced overweight (defined as BMI of >90th centile; odds ratio 0.79) in 5- to 6-year-old Bavarian children. In that study, data on breast-feeding were collected retrospectively. However, it is unlikely that 9% of the children in that study were exclusively breast-fed between 6 and 12 months of age because in the Euro-Growth study with two participating German study centers, 3 and 0% of the infants were exclusively breast-fed beyond 6 and 9 months of age.

CONCLUSIONS

The Euro-Growth references (19) may be used to monitor growth of breast-fed infants and children if the limitations of the weight reference during the first 2 months of life are understood. The additional Euro-Growth references for breast-fed boys and girls (22) are based on data from children who were fed according to WHO recommendations and who lived in environments that favored the achievement of their full genetic growth potential. WHO has published criteria for data suitable for the development of international references (16,31). The Euro-Growth study followed the set criteria for anthropometric data, and all the suggested demographic variables are being collected (e.g., smoking in the mother). Comparison with data presently being collected at seven geographic sites around the world (25) will help to determine whether a single growth reference can be used for all the world’s children if they are fed according to health recommendations and if their mothers did not smoke during pregnancy or lactation.
Low weight for age and leanness during the first 6 months of life may prompt parents to introduce solids earlier. Further studies on breast-fed infants are necessary, examining weight gain, length gain, and breast-feeding practices immediately before and after the introduction of solids. The finding that later introduction of solids is associated with a BMI above the 90th centile beyond the period of infancy needs to be confirmed in a prospective study following children at least until school age.

Our studies have further shown that the influence of breast-feeding on growth is transient and no longer apparent after 24 months of age. The influence of genetic factors such as midparental height and of the child’s BMI at 1 month of age on subsequent “obesity” is much stronger and persists until 3 years of age.

REFERENCES

DISCUSSION

Dr. Haschke: These differences between breast- and formula-fed babies have already been described by Dr. Frongillo. However, a retrospective questionnaire-based study where mothers were asked about the duration of breast-feeding 5 or 6 years later may produce a different result from a prospective study. This is the reason why prospective studies must always be done to confirm data from retrospective studies. I have discussed the Multicenter Allergy Study (MAS) results with the authors, and they think that educational level has a substantial influence as a confounder on the prevalence of obesity. It would also be very interesting to look at the available data on BMI in early life and put them into the model.

Dr. Koletzko: That would be very appropriate. In fact, in the MAS cohort, the most important predictor of obesity at 5 or 6 years is maternal BMI. We know that genetics are important in predicting obesity risk. We also looked at other confounding factors such as sociodemographic characteristics and education of the parents, and the relation remained significant in the MAS cohort, which, as I said, is a prospective study.

Dr. Haschke: Interestingly, in the Euro-Growth data, maternal BMI does not play a role. We know from several studies that maternal BMI is influenced by age, and it is usually measured in a very imprecise way. For example, when should the mother be weighed? She is often weighed immediately after birth, when she is enrolled for study, at a time when body weight is definitely not normal. Indeed, we found that both midparental BMI and maternal BMI were much poorer predictors than midparental height.

Dr. Gasser: I just would like to make a few comments on the construction of centiles. To achieve a reasonable sensitivity and specificity of centiles for practical use, we need extreme values, which makes for statistical problems. There has been a good deal of progress in the statistical literature in the last decade in constructing centiles.
I would like to make the point that conditional centiles could offer further progress. Conditional centiles would take into account the height of mother and father, in the form of midparental height. I would also like to make the point that in the future, we should replace conventional growth charts by computer programs, which means providing them on CD-ROM or over the Internet; in this way, they can readily be updated and are also amenable to correction for ethnic subgroups. However, my main point is that we should use more refined centiles, which incorporate knowledge of midparental height. This results in gains in both sensitivity and specificity.

Dr. Ulijaszek: I would like to ask Dr. Koletzko a question in relation to what Dr. Gasser has just said. Dr. Gasser mentioned that growth charts should be made available to pediatricians as computer programs. I know that in Germany at least, this has been available from the human growth hormone program since 1998. I wonder if this has had a wide uptake and what influence it has had on the pediatric community in Germany, if not elsewhere in Europe.

Dr. Koletzko: I can only give you my subjective judgment on this. My impression is that it is really only used in outpatient departments in hospitals, particularly by physicians concerned with growth and endocrinology. I doubt whether the average pediatric office uses this reference source as a general rule.

Dr. Haschke: Access to these programs depends on how complicated they are. The first versions were much too complicated for day-to-day use in pediatric offices. With the Euro-Growth data, which will shortly be on the Internet, it takes exactly 30 seconds to download everything on the growth charts, so day-to-day use would be a practical proposition. Furthermore, you won't need to do any calculations because the Internet program derives BMI immediately and also does conversion from centimeters/kilograms to inches/pounds. So, we have been thinking about making it more user-friendly.

Dr. Martorell: I have a comment and a question for Dr. Haschke. I think your analysis again underscores the point that the WHO interim reference for breast-fed infants may exaggerate the difference between breast-fed and bottle-fed infants, but your study also confirms that the shapes of the growth curves are different. One caveat I would make is that you were very successful in finding a relatively large group of children who followed the WHO breast-feeding recommendations and could do this analysis. However, you are comparing that group with the total group. So, breast-fed infants are included in both comparison groups, which would tend to attenuate the differences.

Dr. Haschke: I only made the comparison in that way for this presentation. In our article on these data, the breast-fed cohort is compared with all infants who were not breast-fed or who were breast-fed only for a very short time. However, the differences are not much greater than when the breast-fed cohort is included. In this presentation, I thought it important to show that an overall reference that included many breast-fed infants could be very close to a subcohort that is fed according to the WHO breast-feeding recommendations.

Dr. Martorell: I also have a comment about Dr. Koletzko's presentation. I was interested that the differences in the prevalence of obesity began to emerge at age 5 or 6. I wonder if this has something to do with "adiposity rebound," which has been found to be important for predicting later obesity. In other words, this is a sensitive period: Children who begin to put on weight at this early age may be at higher risk. Breast-feeding may delay the adiposity rebound.
Dr. Koletzko: It is certainly a natural thought that obesity rebound could explain the deviation of mean BMIs at this age. We have already been reminded by Dr. Rääihä that protein intake at 10 months and at 2 years was related to age at obesity rebound in a small cohort (1,2). Whether it is really the protein that is responsible or whether protein is a proxy for other aspects of feeding is an open question. I don’t think the association proves cause and effect, but it raises a number of hypotheses that need to be followed up in properly designed prospective studies.

Dr. Adair: Regardless of which growth reference we adopt, we are still faced with the tricky problem of how to establish a cutoff point that defines risk, whether for clinicians or for people who are working in public health. It seems that we have done a good job in defining the lower cutoff points after many years of research on undernutrition and its functional outcome. But it seems that we are still floundering around—regardless of whether we use the NCHS or the new IOTF obesity references—in terms of where the risk is for the heavier children. I would be interested to hear ideas about what we could incorporate along with our growth studies to try to identify what cutoff points might be relevant and what risks we could begin to look at in children, so that we know how to use these references at the upper centiles.

Dr. Guesry: I would like to relay the point of view of our task force for childhood obesity at the European level in the International Life Science Institute. We have addressed this question, and it was felt by the group that we have abandoned adiposity index in favor of BMI a little too rapidly. Of course, BMI is easier to measure than adiposity, and we all know that skinfold thickness is difficult to measure in infants and children. But BMI can be misleading—for example, if muscle mass is decreasing and fatness is increasing, BMI may decrease. So, it is probably important, if we want to be more intelligent, to combine BMI and some index of adiposity.

Dr. Uauy: I think we should probably follow the same pattern that was suggested for the adult obesity—namely, to obtain a measure not only of adiposity or BMI but also of the metabolic consequences. In the case of children, insulin resistance and dyslipidemia might be adequate indicators, because at a given level of BMI or even of adiposity, metabolic complications may be related to a whole range of factors such as population background or ethnicity. In fact, in terms of metabolic complications in the adults, the findings from Asian studies suggest that a BMI of 25 is not an appropriate cutoff; it may be closer to 23. So, we may need to follow the same approach in children, measuring metabolic complications early on to validate what cutoff is reasonable.

Dr. Gibson: I just have a question about Dr. Haschke’s talk. I was wondering whether in the Euro-Growth study, they collected data on the type of complementary feeding that was given to the infants and whether they plan to look at a relation between growth and the type of complementary feeding that was being used.

Dr. Haschke: We have indeed collected data on the type and time of introduction of complementary foods, and we have grouped the complementary foods so that they are internationally comparable. We haven’t yet analyzed whether the type of solids influences growth, so I cannot answer your question at present.

Dr. Brunser: Do the parents who participate with their children in the Euro-Growth program know the aims of the program or not?
Dr. Haschke: The parents know that it is a growth study, and all of them have volunteered to be included in the program. As with all longitudinal studies, it needs a lot of cooperation by the parents to follow the study protocol, so the parents are indeed familiar with the study and are given sufficient information when the children are enrolled.

Dr. Brunser: My comment is that when you have this kind of study, you don’t have a purely observational situation. The parents react in very subtle ways to your requirements. That is something that you cannot control, but it may influence your results to some extent.

Dr. Haschke: We cannot exclude that. However, we took measures to ensure as much distance from the parents as possible in that the nutritional recommendations and day-to-day advice on nutrition, as well as the measurements, were done by the local pediatricians and not by the study centers. We also did a nonparticipation study, and in those areas where we collected random samples, we looked at the nonparticipating population initially to see whether the Euro-Growth sample was representative.

Dr. Grummer-Strawn: When I think about the WHO effort and how it might be accepted in the USA, I think this is less an issue of the breast-fed child than it is an issue of a standard versus a reference. People in the USA currently talk about this as the “WHO breast-fed curve,” and I don’t think it is not going to sell very well; most clinicians there will be dealing with formula-fed children, so their attitude will probably be that they don’t need such a chart. On the other hand, many of the other things that were done—making sure that the data were obtained in a highly select socioeconomic stratum, that the children were healthy, that they followed immunization guidelines, and so on—are going to be very important in getting across the view that this is a standard of the way children ought to grow.

Dr. Haschke: This might be not an issue in the USA, but it is certainly an issue in Europe that there should be standards indicating the growth of breast-fed infants. I think it is very important that we collect this kind of data.

Dr. Frongillo: I hesitate to disagree with Dr. Grummer-Strawn, but I think it is important to point out that the WHO growth reference study is seen by WHO, and, I think, by most of us involved with it, as producing a reference and not a standard. The standard part of it is that a judgment has been made, that we know how infants should be fed—what is optimal for how infants should be fed—so, the “should” part is how infants should be fed. The reference that results from this will be a description of the growth that occurs when infants are fed as we think they should be fed. The distinction between prescriptive and descriptive is important, and the distinction between reference and standard is important; but they are not synonymous. I think we should be careful to recognize that once WHO produces the new growth charts, WHO will not be saying: This is how children should grow. It will be saying: This is how children grow who are fed as they should be fed. Those are not quite the same things.

REFERENCES
