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Plenary Lecture

Impact of growth patterns and early diet on obesity and cardiovascular risk factors in young children from developing countries

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Non-communicable chronic diseases are now a worldwide epidemic. Diet and physical activity throughout life are among its main determinants. In countries undergoing the early stages of the nutrition transition weight gain from birth to 2 years of life is related to lean mass gain, while ponderal gain after age 2 years is related to adiposity and later diabetes and CVD risk. Evidence from developing countries undergoing the more advanced stages of the nutrition transition is limited. The early growth patterns of a cohort of Chilean children born in 2002 with normal birth weight who at 4 years had a high prevalence of obesity and CVD risk factors have been assessed. Results indicate that BMI gain in early life, particularly from 6 months to 24 months, is positively associated with adiposity and CVD risk status at 4 years. These results together with existing evidence suggest that actions to prevent obesity and nutrition-related chronic diseases in developing countries should start early in life, possibly after 6 months of age. This approach should consider assessing the effect of mode of feeding and the amount and type of energy fed, as well as the resulting growth patterns. The challenge for researchers addressing the nutrition transition is to define the optimal nutrition in early life, considering not only the short- and long-term health consequences but also taking into account the stage of the nutritional transition for the given population of interest. The latter will probably require redefining optimal postnatal growth based on the context of maternal size and fetal growth.

Early growth: Early diet: Obesity: Cardiovascular risk factors: Developing countries

Global burden of obesity and related chronic diseases: opportunity for prevention based on developmental origins of health and disease

Non-communicable diseases are now the leading causes of death and disability in the world, including transitional and many developing countries[1]. Several risk factors related to nutrition are among the ten leading causes of deaths worldwide. High blood pressure, high cholesterol, elevated BMI and low levels of physical activity as well as low consumption of fruits and vegetables account for approximately two-thirds of all deaths. The causal interactions for early determinants of obesity and related chronic disease are complex and multifaceted; fetal and early-life growth and nutrition interact with current diet and physical activity to determine population prevalence of chronic diseases. The influence of early nutrition on health outcomes in adulthood was initially substantiated by the effects on linear growth, mental development and educational performance[2,3]. Over the past decade it has been demonstrated that early nutrition and patterns of physical activity can also impact on health outcomes that are specifically related to the prevalence of risk factors for chronic diseases. The hypothesis of the 'developmental origins of health and disease' postulates that the early environment programmes metabolism, organ growth and functional development.

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Programming may be explained by structural changes to organs induced during early development or by epigenetic modifications that permanently modify the patterns of expression of various genes that in turn affect organ function at various stages of the life course[4,5]. These changes are associated with permanent changes in physiology and/or structure that will predispose individuals to obesity and other nutrition-related chronic diseases in later life, increasing their susceptibility to chronic diseases directly or by interacting with other risk factors[4]. This hypothesis implicitly suggests that action is needed at all stages of the life course in order to ensure long-term health[6]. Actions to prevent obesity, diabetes, CVD and some forms of cancer should start before conception and continue throughout life.

Rapid growth in early life and consequences for obesity and CVD in countries undergoing the nutrition transition

There is now substantial evidence from industrialized countries on the relationship between low birth weight and later occurrence of central obesity, insulin resistance, type 2 diabetes, hypertension and CVD[7–9]. In Brazil it has also been demonstrated that early malnutrition leading to stunted linear growth is accompanied by an increased risk of obesity in later life, as consumption of energy-dense foods and inactivity during work and leisure have become common[10]. This situation is a matter of concern for developing countries, since low birth weight and stunting and overweight often coexist not only within a given community[11] but also in the same household[12,13], or even in the same individual at different stages of the life course[14,15]. The potential contribution of the developmental origins of health and disease to the conceptualization of preventive care that integrates a programme of actions across all forms of malnutrition, including nutrition-related chronic disease, becomes particularly relevant for these countries. Asia and indigenous populations in the Americas who are of Asian origin represent a special challenge. The particular Asian phenotypic adaptation to malnutrition is associated with increased visceral adiposity and insulin resistance even before the BMI criteria for overweight and obesity based on current Western standards are met. Low-birth-weight infants in India have been found to have increased visceral fat at birth despite being underweight[16,17].

Prenatal weight gain

There have been few cohort studies from developing countries. Recent reports from India[18], Guatemala[19,20] and Brazil[21] demonstrate that birth weight is positively associated with BMI at age 25–30 years[22,23]. However, the association is stronger for lean mass than for fat mass; thus, the link with BMI may represent an association between birth weight and lean mass rather than with adiposity. Additional studies supporting a link between birth weight and later occurrence of central obesity[16,19], insulin resistance[24–26], type 2 diabetes[27], high cholesterol[25,26,28], hypertension[26,29,30] and CVD[31] strengthen the relationship with chronic disease, although the results have been inconsistent. Thus, these older cohorts from populations at earlier stages of the nutrition transition do not permit a full elucidation of the relationships, especially in the case of nutrition-related chronic diseases. However, it is likely that as countries move into the more advanced stages of the nutrition transition mothers and newborns will be increasingly exposed to obesogenic conditions that will influence the direction of these associations. For example, results from the Avon Longitudinal Study of Parents and Children birth cohort show that in contemporary English children birth weight and ponderal index are positively associated with both lean body mass and percentage body fat at 9–10 years[32]. Moreover, there is now increasingly more information on the detrimental impact of maternal adiposity during pregnancy on later health outcomes. The notion of developmental energy overnutrition is being increasingly supported by emerging data[9,33,34], although results are not positive for all studies[35,36]. This premise suggests that mothers who are obese at the time of their pregnancy and during the breast-feeding period maintain higher concentrations of glucose and NEFA, which in turn affect fetal metabolism, tissue growth and hormonal regulation and possibly induce lasting epigenetic changes[37,38]. These changes will define permanent changes in appetite control, neuroendocrine function, fuel metabolism and energy partitioning during early development, leading to greater adiposity and risk of obesity in later life. If this hypothesis is substantiated it would imply that the obesity epidemic will progress through generations irrespective of other changes in both industrialized and developing countries[39].

Postnatal weight gain: first two years of life

The influence of postnatal growth on later development of obesity and nutrition-related chronic diseases has been reviewed based on systematic analysis of studies conducted in developed countries in which catch-up growth has been observed. The evidence indicates that rapid postnatal growth interacts with prenatal growth and birth weight status, so that the association between birth weight and adult disease becomes stronger or only emerges after adjusting for adult body size, which indicates that postnatal weight gain has an independent significant effect in terms of susceptibility to chronic disease[40]. Moreover, there is some evidence that the effect of rapid infant weight gain would persist even after catch-up growth is completed, suggesting that it would have a lasting or programming effect[41,42]. Postnatal growth itself, independent of fetal growth patterns, is also associated with later adult disease, particularly if the excess growth is predominantly in weight with constrained linear gain, thus leading to excess weight-for-length; this feature is common in developing countries as they emerge from undernutrition and extreme poverty[22]. In India, Guatemala, South Africa, Brazil and The Philippines BMI growth failure in early childhood (first 2–3 years of life) is associated with less fat-free mass in adulthood[18,43], impaired glucose tolerance and hyperinsulinism[44,45] and higher blood pressure[46]. In contrast,

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studies from industrialized countries, in which undernutrition is assumed to be low, have shown a consistent positive association between infant size and later body size[47–49] but inconsistent associations with later disease[50,51]. Again, these results suggest that as developing countries move into the more advanced stages of the nutrition transition the direction of these associations may change. For example, a small study conducted in African children born of normal weight has shown that a change in weight-for-age Z-score >0·67 from 0 years to 2 years is associated with greater subcutaneous fat, total body fat and lean tissues at age 9 years[52]. Moreover, other changes in developing countries that are associated with the epidemiological and nutrition transition, such as the increase in the prevalence of smoking and maternal obesity, and the changes in patterns of diet and physical activity may influence the link between infant growth and later risk for obesity and CVD[53,54]. Overall, the size of the effect of rapid infant weight gain in infancy on later development of overweight seems to be relevant. In relatively contemporary cohorts of children in the USA the reported population risk for overweight at 4 years or 7 years, attributable to infant weight gain (from birth to 4–6 months) in the highest quintile, is approximately 20%[55,56]. A study in a non-contemporary cohort of African-Americans has reported that approximately 30% of the risk of overweight at 20 years of age is a result of rapid weight gain (>1 SD) from birth to 4 months of age[57]. Given the actual increase in obesity among children and adults it is likely that these attributable risk percentages may even be higher. This outcome is relevant given that the prevailing notion in most developing countries is that early obesity is not a risk factor for later obesity. Moreover, the present WHO approach defines obesity for children ⩽5 years of age as >+3 SD units in BMI for age and overweight as +2 SD[58]. This position is not only confusing but in conflict with the data indicating that rapid weight gain is linked to later obesity in countries in which childhood obesity is widespread.

Postnatal weight gain: after 2 years of life

Evidence relating to the effect of rapid weight gain in late childhood (after 2–3 years of age) on later health outcomes is consistent even among countries in which undernutrition is still prevalent. Studies from several developing countries indicate that rapid weight gain in late postnatal life is positively associated with the acquisition of fat mass[18,19,21,59], blood pressure[46,60], glucose intolerance and type 2 diabetes in adulthood[24,45]. Thus, the available evidence supports the notion that prevention of obesity and obesity-related diseases in developing countries should consider avoiding excessive weight gain after 2 years of age.

Prenatal and postnatal linear growth

In most of the studies presented here growth has been defined only by weight gain. This approach overlooks the possibility that the effect of weight gain can be different in children who gain weight and height in a balanced manner from those who gain weight and BMI but remain stunted in their length. At a global level stunting is presently the most prevalent undernutrition problem in the majority of developing and transitional regions[61]. Thus, a better understanding of how birth length and linear growth relate to adult diseases is particularly relevant[61]. The results of the review of the effects of birth length show a consistent strong association with adult height and fat-free mass, but to date no associations with later chronic disease have been established[18,19], except the potential increase in some forms of cancer[63]. Associations between stunting[14,15,64,65] or linear growth[18,19,66] and adult body composition have been inconsistent. A review of the evidence linking child growth and chronic diseases in five cohorts from transitional countries (China, India, Guatemala, Brazil and The Philippines) has concluded that there is little evidence that increases in height are associated with increased metabolic risks in transitional countries[23].

Overall, these results suggest that in countries in which undernutrition is still prevalent preventive actions should be directed at ensuring weight and linear growth during the first years of life and avoiding excessive weight gain relative to height thereafter[67]. Effective actions to achieve the first goal have recently been revised[68]; however, better evidence is needed to define effective actions to prevent excess weight gain in childhood in the context of developing countries. The available evidence also highlights the need to continuously monitor the strength of the effect of early growth on later health, particularly considering the rapid nutrition transitions that are presently being experienced in most developing countries in Asia and Latin America.

Results from concurrent Chilean cohort of early growth and indicators of CVD and metabolic risk

Having considered this existing information, in 2006 a cohort was established of 1200 Chilean children of normal birth weight (multiple births and premature babies (<37 weeks) were excluded; national prevalence of low birth weight <5·0%[69]) who were born in 2002 and attended nursery schools that were part of a national welfare programme (the National Nursery School Council Program) in an area in south Santiago. Weight and length at birth and gestational age were obtained from obstetric records (>99% of births took place in healthcare facilities) and weight and height (recumbent length for children <2 years) from birth to 3 years of age were taken from health records. In a representative sample of 314 children from this cohort the following measurements were also undertaken at 4 years of age: weight, height, waist and hip circumference, five skinfolds; fasting blood sample for analysis of glucose, insulin and cholesterol levels. This information was used to assess the associations between BMI changes and BMI, fat mass and fat-free mass (based on a validated anthropometric equation), waist circumference, homeostasis model assessment of insulin resistance and a metabolic score at 4 years of age based on the risk factors specified by the International Diabetes Federation definition of the metabolic syndrome in children[70] (Figs. 1 and 2).

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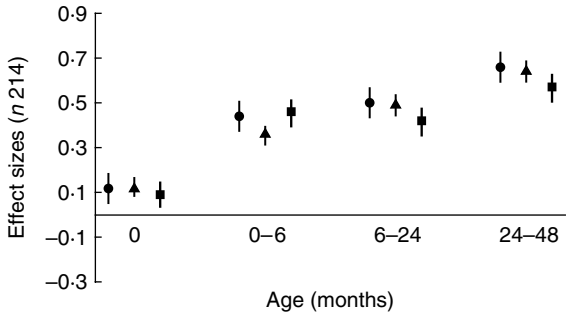

Fig. 1. Standardized regression coefficients for BMI (●), fat mass (fat mass/height^2; ▲) and fat-free mass (fat-free mass/height^2; ■) at 4 years of age per sample-specific 1 SD increments in BMI at birth and changes in BMI from birth to 4 years for a cohort of Chilean children in 2006. Error bars represent 95 % CI. All analyses were adjusted for current age, gender and growth in the previous period. Sample-specific SD were: BMI, 1·70; fat mass, 1·13; fat-free mass, 0·83; BMI at: 0 months, 1·27; 0–6 months, 1·60; 6–24 months, 1·05; 24–48 months, 1·15.

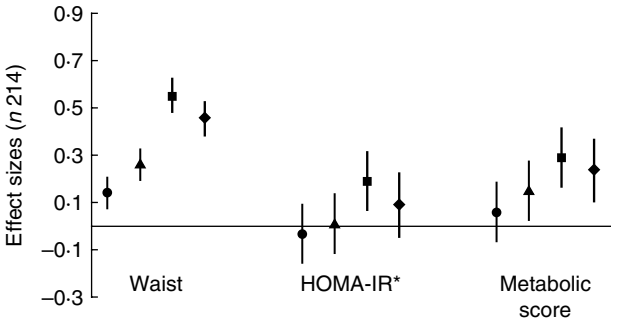

Fig. 2. Standardized regression coefficients for waist circumference, homeostasis model assessment of insulin resistance (HOMA-IR) and metabolic score ((waist-to-height + glucose + insulin + TAG − HDL-cholesterol Z-scores)/5) at 4 years of age per sample-specific 1 SD increments in BMI at birth (●) and changes of BMI from birth to 4 years (0–6 months, ▲; 6–24 months, ■; 24–48 months, ◆) for a cohort of Chilean children in 2006. All analyses were adjusted for current age, gender and growth in the previous period. Error bars represent 95% CI. *Log-transformed variables. Sample-specific SD were: waist circumference, 3·90; HOMA-IR, 0·27; metabolic score, 0·47; BMI at: 0 months, 1·27; 0–6 months, 1·60; 6–24 months, 1·05; 24–48 months, 1·15.

At birth the participants when compared with children in the WHO reference population[71] were found to be slightly taller, heavier and fatter and from 6 months to 4 years they were slightly shorter while becoming increasingly heavier and fatter (C Corvalan, R Uauy, AD Stein, J Kain and R Martorell, unpublished results). By the age of 4 years a prevalence of obesity of 13%, central obesity of 10% and altered plasma lipoprotein-cholesterol fractions of 30% high LDL-cholesterol, 42% low HDL-cholesterol, 15% high total cholesterol and 5% high TAG were observed[72]. These data indicate that Chilean children from low-income families are presently facing risks associated with the double burden of malnutrition, but particularly have an increased risk of developing nutrition-related chronic diseases in the future. In relation to body composition, BMI changes from birth to 6 months were found to be similarly or even more strongly related to fat-free mass than to fat mass, while changes in BMI after the age of 6 months were progressively associated with greater fat mass (Fig. 1). In relation to CVD risk status, changes in BMI, particularly from 6 months to 24 months, were found to be associated with greater waist circumference, homeostasis model assessment of insulin resistance and metabolic score (Fig. 2; C Corvalan, R Uauy, AD Stein, J Kain and R Martorell, unpublished results).

These results suggest that the nutritional status, diet and physical activity of the population might be relevant for assessing the impact of growth on short-term obesity and CVD risk. They also provide some support for the notion that higher weight gain in relation to height after 6 months may be a marker for increased adiposity and abnormal biochemical indices of CVD risk at 4 years of age in countries in which childhood obesity is prevalent.

Effect of mode of feeding on growth, obesity and CVD risk

Recent meta-analyses of published observational studies have suggested that breast-feeding is associated with a lower prevalence of obesity[73] and BMI later in life[74] in a dose-dependent manner (i.e. a longer duration of breast-feeding is associated with a lower risk of overweight)[75]. It has been also proposed that in particular groups breast-feeding could also offset the effect of prenatal obesity risk factors such as maternal overweight[76]. Nonetheless, after adjustment for confounding factors the association between breast-feeding and obesity markedly decreases[73] while the association with BMI becomes non-significant[73]. A protective role of breast-feeding for later development of CVD risks has been suggested in some studies[77–79] but not all studies[80]. Based on these findings an analysis was undertaken of the impact of mode of early feeding on BMI and CVD risks (homeostasis model assessment of insulin resistance, total cholesterol:HDL-cholesterol and metabolic score) at 4 years of age in the Chilean cohort of preschool children (C Corvalan, R Uauy, AD Stein, J Kain and R Martorell, unpublished results). The mothers of 295 children provided information relating to infant feeding and the children were allocated to three categories based on the type of feeding they received at 4 months: exclusive breast-feeding (i.e. only breast milk; *n* 97); predominant breast-feeding (i.e. breast milk and other liquids; *n* 95); partial or no breast-feeding (i.e. breast milk and infant formula; *n* 48) or only infant formula (*n* 55). Assuming 80% power and a significance level of $P<0{\cdot}05$ (two-tailed), this sample size was sufficient to detect small to moderate effect sizes (i.e. f^2 0·10)[81]. The analyses were not found to demonstrate a significant association between mode of infant feeding and BMI or CVD risk status at 4 years of age after controlling for maternal prepregnancy BMI and socio-economic conditions; however, because of the limited sample size it was not possible to test for any gender difference in the lack of effect (C Corvalan, R Uauy, AD Stein, J Kain and R Martorell, unpublished results). These results are in contrast to those of other studies[74,75,77–79] but are consistent with the only available randomized

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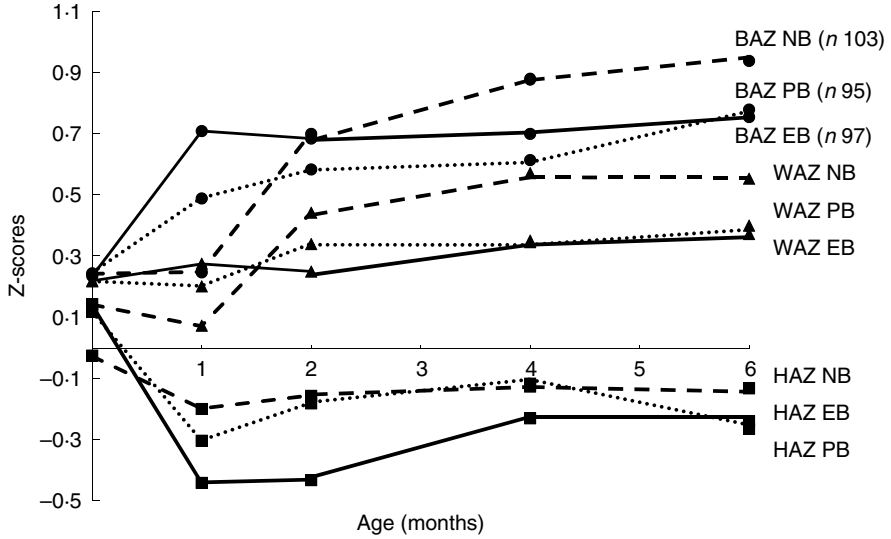

Fig. 3. Z-scores from birth to 6 months of age based on 2006 WHO child growth standards[103] for a cohort of Chilean children by mode of infant feeding at 4 months in 2001–2. BAZ, BMI-for-age Z-score (●); WAZ, weight-for-age Z-score (▲); HAZ, height-for-age Z-score (■); EB, exclusive breast-feeding (only breast milk, *n* 97; –), PB, predominant breast-feeding (breast milk and other liquids, *n* 95; - - -), NB, partial or no breast-feeding (breast milk and infant formula, *n* 48) or only infant formula (*n* 55; · · · · · · ·).

controlled trial, which shows that increasing the duration and exclusivity of breast-feeding does not reduce adiposity or blood pressure at age 6·5 years[82]. Well-conducted cohort studies that take into account all known potential confounders of the association between breast-feeding, obesity and CVD risk are clearly needed to clarify this point[51,83]. Nevertheless, breast-feeding has so many well-demonstrated positive effects on several health and well-being outcomes that exclusive breast-feeding for 6 months should be encouraged irrespective of the final conclusion in relation to its effects on obesity and CVD risk.

The plausibility of biological mechanisms to explain the putative effects of breast-feeding on obesity and CVD risk are a topic of increasing interest. Breast milk contains some unique components such as leptin, insulin and thyroid hormones[84–86]. It is also known that formula-fed children have a 70 % greater protein intake than breast-fed infants[87], which has been associated with an earlier adiposity rebound. These factors may indeed play a role in the programming of adiposity and the later development of obesity and CVD. An alternative explanation for the protective role of breast-feeding is based on the 'growth acceleration hypothesis'; in this case the benefits of breast-feeding for long-term obesity and CVD risk might be explained by the slower pattern of growth in breast-fed children compared with formula-fed children[88,89]. In the Chilean cohort of preschool children it was observed that infants who are exclusively breast-fed at 4 months gain weight faster than predominantly- or partially-breast-fed babies or those not breast-fed from birth to 1 month, but grow slower than or similarly to the other groups after 4 months (Fig. 3). Finally, other less-explored potential explanations for the protective role of breast-feeding in obesity relate to the difference in feeding behaviour induced by breast-feeding. It has been hypothesized that breast-fed babies control the amount of milk they consume and therefore learn better than formula-fed babies to self-regulate their energy intake. For example, one study has shown that among breast-fed babies energy intake is unrelated to later weight gain while among formula-fed babies there is a positive relationship, suggesting that breast-fed babies may adjust or control their energy intake to achieve optimal growth[90]. It has been suggested also that breast-feeding is more common in families that have a healthier diet and lifestyle. Thus, it is very difficult to differentiate whether the effect of breast-feeding is a result of a home environment that promotes a healthier diet and greater physical activity or whether it is related to the intrinsic properties of breast-feeding.

Breast milk contains different concentrations and composition of fats, especially long-chain PUFA, which can affect patterns of growth, body composition and CVD development[84–86]. In terms of plasma lipoproteins, breast-feeding has been described to have a transient detrimental impact by increasing total cholesterol: HDL-cholesterol; however, these changes disappear over time. Moreover, over the long term the early effect of breast-feeding is reversed so that total cholesterol : HDL-cholesterol of adolescents and adults who were breast-fed as infants is lower than that of those who were formula-fed as infants, and thus breast feeding is protective[79,91]. It is now well established that the fat content of human milk is dependent on the quantity and quality of the mother's fat intake, which raises the concern of the potential adverse effect of maternal consumption of *trans*-fatty acids, which is known to be high, especially in developing countries, and can be transferred to human milk. Moreover, the amount of *n*-6 PUFA intake consumed by women is also known to affect

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the composition of human milk[92,93]. Overall, the role that compositional differences in maternal dietary fat play on the fatty acid profiles of mother's milk and the corresponding effect on the lipid profile of the offspring requires further examination. Controlled studies have also assessed the effect of feeding a specified fatty acid and cholesterol diet on plasma total cholesterol and lipoprotein-cholesterol fractions. In one study a group of infants randomized to controlled lipid diets and compared with a matched breast-fed group from birth to age 12 months followed by *ad libitum* diets from age 12 months to 24 months was studied prospectively[94]. The experimental approach was based on the comparison of oleic acid-predominant *v*. linoleic acid-predominant diets (both low in cholesterol) as compared with human milk (oleic acid-predominant and high in cholesterol). The human-milk group was weaned at a mean age of 6·2 (range 4·0–8·5) months and after weaning received a mixed diet resembling human milk in its cholesterol content. As a result of weaning the percentage energy delivered as fat decreased in all groups from 50% (up to age 4 months) to 35% (from age 4 months to 12 months). This study shows significant ($P<0·05$) effects of exclusive human milk feeding on lipoprotein-cholesterol concentrations at 4 months of age. However, at 9 and 12 months of age cholesterol concentrations for the human-milk group were not found to differ from those in the high-oleic acid low-cholesterol diet group. The high-linoleic acid low-cholesterol diet group were found to have lower total cholesterol and LDL-cholesterol throughout the study. These data suggest that the specific fatty acid intake rather than dietary cholesterol plays a predominant role in determining total cholesterol and LDL-cholesterol. More recently, the association between the quantity and quality of dietary fat intake from 6 months to 12 months of age and serum lipids at 12 months has been assessed in 300 healthy term Swedish infants recruited to a longitudinal prospective study at the age of 6 months, of whom 276 remained in the study at 12 months[95]. This study reveals that a higher PUFA intake is associated with lower serum total cholesterol, LDL-cholesterol and apoB independent of total fat consumed. The results provide added support to the notion that the quality of the dietary fat has a greater impact on serum lipoprotein-cholesterol levels than the quantity of fat, with the conclusion that higher PUFA and lower SFA intakes may reduce total cholesterol and LDL-cholesterol early in life. Parallel observations from the cohort of 317 Chilean children indicate that total cholesterol : HDL-cholesterol at 4 years of age is positively associated with BMI increases from birth to 6 months in children who were exclusively breast-fed to 4 months of age (β_{std} 0·24 (95% CI −0·02, 0·50)), while for children who were partially breast-fed or not breast-fed BMI increases from birth to 6 months are negatively related to total cholesterol : HDL-cholesterol at 4 years (β_{std} −0·30 (95% CI −0·52, −0·08)) after adjusting for current age, gender and growth in the previous period (C Corvalan, R Uauy, AD Stein, J Kain and R Martorell, unpublished results). The possibility that early diet conditions the total cholesterol–HDL-cholesterol relationship should be contemplated, although the direction of the associations may be reversed in the long term[79,91]. The authors are presently conducting a follow-up of the cohort to establish these associations at 7 years of age.

How to define 'normal' growth in the first years of life?

Historically, good health and nutrition have been defined by the capacity to support normal growth. Existing national and international standards have defined normal growth based on the weight and length gain observed in apparently 'healthy' children. This approach has led in practice to support for the notion that 'bigger is better'. This proposition is reasonable if the objective is to enhance survival in infancy and early childhood in areas in which malnutrition and infection in synergy claim the lives of infants and young children. However, it is certainly not the case in countries in which deaths of young children are rare and the concern has shifted to the prevention of obesity and the related burden of chronic disease[96]. Moreover, as has been discussed earlier there is also mounting evidence that exposure to undernutrition during early life (i.e. fetal life and the first 2 years of life) may have long-term consequences for adult body composition and health if there is a mismatch between early nutritional deprivation and later nutritional conditions that may support rapid weight gain in childhood[97–99]. Conversely, the relationship between early growth and later health can have a different direction once undernutrition is replaced or compounded by overnutrition problems. Thus, the definition of 'normal' growth is of paramount importance to secure normal health and nutrition of both individuals and populations in developing countries and presents the challenge of arriving at a definition that takes into account the nutritional background of the population as well as both short-term and long-term health. Ideally, normative information on body composition (lean body mass and fat stores) according to gender and age should be available. However, given the difficulties of collecting these data current reference values are based on anthropometric measurements (weight and length) that serve as proxy markers for increased or reduced adipose tissue energy stores. Until 2006 most of the available growth charts[100,101] were based on the observed growth for a normal reference population rather than recommended growth based on health outcomes throughout the life course. These reference values had major flaws because they were derived from a non-representative sample of the population and the infants included were predominantly formula-fed and received energy-dense complementary foods. In fact, infants fed according to current WHO recommendations[102] and living in conditions that favour the achievement of genetic growth potential will grow in weight less rapidly than indicated by the WHO/National Center for Health Statistics reference values[100], particularly after 4–6 months. Thus, WHO/National Center for Health Statistics distributions for normal weight-for-age and weight-for-length are skewed towards higher values, relative to those observed in predominantly-breast-fed infants.

Aware of these limitations, in 2006 the WHO launched the new multicountry (Brazil, Norway, India, Ghana, USA and Oman) growth reference standards[103]. The release of

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the multicountry growth reference standards has provided a good opportunity for countries to critically assess the need to modify both existing norms to assess growth and to redefine early nutritional practices[104,105]. The multicountry growth reference standards provide a descriptor of physiological growth across human population groups because their development was based on the observed growth of representative samples of healthy infants from six countries across all races and continents. Moreover, they had a similar dietary regimen (predominantly breast-fed from birth to 4–6 months and fed appropriate complementary foods after 6 months)[106]. In order to avoid environmental factors that restrict infant growth they were selected from non-smoking mothers living in clean environments and with good access to health care and immunizations. Given these characteristics it is reasonable to advocate that the 2006 WHO growth standards[103] should be used as the gold standard for defining normal growth and good health. However, the issue of whether this standard should be applied to all children from birth to 5 years of age requires adequate discussion and testing in consideration of both short-term and long-term outcomes. In the past two decades Chile has experienced a series of social and economic improvements that ensure that even children from low-income families are exposed to a safe environment during early life with decreased rates of infections and undernutrition. However, nutritional improvements have not been reflected in terms of adult stature, with mean maternal height remaining at approximately 1·53 m. The growth (BMI, weight, and height) from birth to 6 months of age has been assessed, based on the multicountry growth reference standards, for ninety-seven children of the Chilean cohort who were exclusively breast-fed for 4 months (Fig. 3). It was observed that although weight and height at birth are within the normal range, thereafter weight gain is slightly above the standard while linear growth is slightly below the standard, resulting in increasing BMI gain. It is considered that these results highlight the need to take into account trans-generational effects when defining optimal growth as well as underlining the need to focus on improving height and avoiding excessive weight gain relative to height. Other authors have already emphasized the need to improve adult stature in order to improve productivity and that gains in BMI beyond the ideal range will increase mortality risks associated with low stature[107,108].

In addition, there is now an added dimension to this policy, since the prescription for energy intake of normal children has also been redefined. Historically, energy recommendations for infants and children published by FAO/WHO/UNU in 1985[109] were estimated from observed energy intakes of children from industrialized countries who were growing optimally according to the Harvard growth standard[110] (the best available at the time). To this intake an additional 5% was added to support growth in conditions prevailing in developing countries in which infection was more prevalent and diets might have a lower digestibility. The need to consider actual expenditure rather than intake was recognized at the time, but there were insufficient data on energy expenditure of young children, except for neonates and young infants. Thus, the energy expenditure approach to estimating energy needs was only used in children >13 years of age, based on the sum of estimated basal energy expenditure + the energy required for normal growth and a defined level of physical activity. The increasing use of the doubly-labelled-water methodology to assess total energy expenditure over the past decades and the development of methods to assess activity levels applicable to young children have permitted measurements of daily energy expenditure in children from different parts of the world and the definition of recommendations based on actual expenditure[111]. The actual measurements of daily total energy expenditure were obtained either by the doubly-labelled-water method or estimated from heart-rate monitoring during active periods coupled with individual calibrations of O_2 consumption. The energy needs for tissue deposition in relation to growth in the case of infants, children and adolescents were added to the estimate of daily total energy expenditure. The new recommendations are about 20% lower than the older values for the first 24 months of life; the differences increase with age, especially after the first 6 months of age. Fig. 4 shows a comparison of the 2004 and 1985 recommended daily energy intakes, considering both the new estimates of energy needs (based on expenditure) and the new normative data on growth for the corresponding age. The sum of these two factors explains the differences observed. These differences between the two sets of energy recommendations expressed per d and as a percentage of total intake are shown in Fig. 5. The predicted daily energy gains if a typical infant of average weight and length consumes the recommended intake is also shown as the time (d) needed to accumulate +25 104 kJ (6000 kcal), which would imply approximately 1 kg body weight gain if composition of gain is that of the corresponding age (about 60 d for a 7-month-old infant and 20 d for an 18-month-old infant).

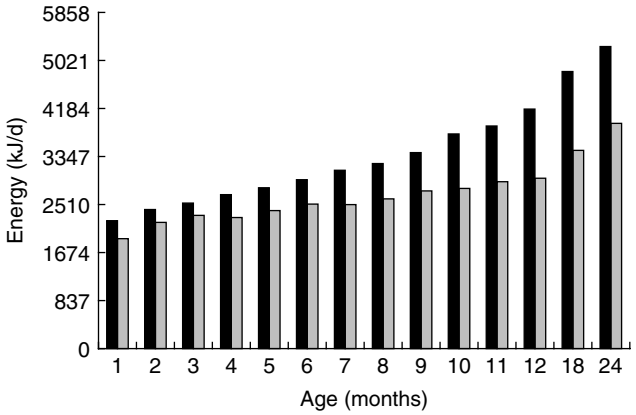

Fig. 4. A comparison of recommended absolute daily energy intake (kJ) for the first 24 months of life using the 1985 FAO/WHO recommendations based on historic data for energy intake[109] (■) and the 2004 FAO/WHO recommendations based on energy expenditure[111] (▨). The data are intakes for the corresponding body weight based on normative reference values: 1977 WHO/National Center for Health Statistics[100] and the 2006 WHO multicountry growth reference standards[103] respectively.

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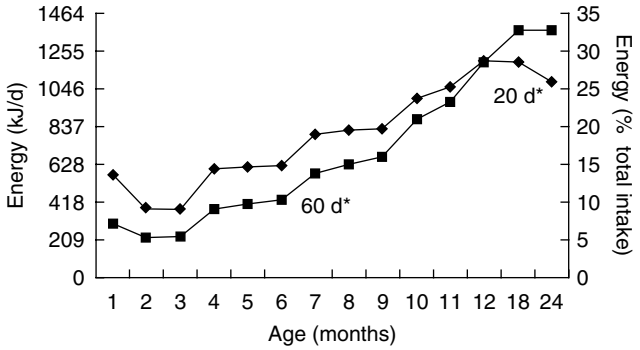

Fig. 5. Differences between the two sets of energy recommendations (the 1985 FAO/WHO recommendations based on historic data for energy intake[109] and the 2004 FAO/WHO recommendations based on energy expenditure[111]) shown in Fig. 4 are expressed on a per d basis (■) and as percentage total energy intake using the 2004 FAO/WHO recommendations as a base (◆). The excess energy consumed if a child is fed using 1985 FAO/WHO recommendations is maximal during the second 6 months of life. *Time period (d) required to accumulate 25 104 kJ (6000 kcal) excess (which corresponds to 1 kg body weight gain assuming an age-appropriate body composition).

These two examples demonstrate that normative data should be periodically re-examined and redefined based on the best available scientific evidence and the nutritional status of the population. In the context of the existing double burden of malnutrition, it is considered that optimal nutrition should be defined based on growth in weight and length associated with the lowest risk of early undernutrition, but also considering the long-term consequences in terms of obesity and the related burden of death and disability.

Conclusion

The present study adds to the existing evidence that suggest that actions to prevent obesity and nutrition-related chronic diseases in developing countries should start early in life, possibly after 6 months of age. Potential actions to be considered and evaluated in prospective trials are the effect of mode of feeding and the amount and type of energy fed, as well as the resulting growth patterns assessed by anthropometry and completed measurement of body composition. The challenge now for researchers addressing the nutrition transition is to define the 'optimal nutrition' in early life in terms of early prevention of obesity and related co-morbidities, going beyond compliance with the most recent WHO growth reference standard[103]. This task is daunting because there is a need to consider not only the short- and long-term health consequences but also take into account the stage of the nutritional transition for the given population of interest. It has been assumed that all children must comply with the reference standard for weight and height independent of birth weight (if born within the normal range) and maternal height (if born of mothers with normal BMI before and during gestation). However, this assumption is unlikely to be the case in developing countries and even in industrialized countries; therefore, it is possible that optimal postnatal growth will need to be redefined with consideration of the context of fetal growth and maternal size. The challenge of matching optimal postnatal growth with the critical maternal and fetal growth information must be faced by all researchers.

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