Does Breastfeeding Protect from Growth Acceleration and Later Obesity?

Atul Singhal

The MRC Childhood Nutrition Research Centre, Institute of Child Health, London, UK

Abstract

Nutrition in infancy has been suggested to have a major influence or program the long-term tendency to obesity. Breastfeeding, in particular, appears to protect against the development of later obesity, a conclusion supported by data from four systematic reviews and evidence that a longer duration of breastfeeding has greater protective effects. The size of the effect (up to a 20% reduction in obesity risk) although modest has important implications for public health. The mechanisms involved, although poorly understood, probably include the benefits of relative undernutrition and slower growth associated with breast rather than formula feeding – the growth acceleration hypothesis. This hypothesis is now supported by data from animal studies and two recent systematic reviews, which suggest an association between faster growth in infancy and later obesity in both richer and low-income countries and for both faster weight and length gain. The present review considers the evidence for a role of early growth and breastfeeding in the programming of obesity and the underlying mechanisms involved.

Introduction

The WHO has described the recent dramatic increase in obesity as the most important public health issue facing both industrialized and developing countries. Globally more than 1 billion adults are already classified as overweight and at least 300 million of them as clinically obese. The rise in obesity has been particularly steep in children. In the USA, for instance, the number of overweight children has doubled since the 1980s, a trend that has immense implications for the prevalence of obesity-related chronic disease and future health care costs.
Ultimately, obesity is a result of a cumulative increase in energy intake above energy expenditure. While genetic factors determine a person’s susceptibility to weight gain, increased consumption of energy-dense foods (with high proportion of fats and sugars) and declining levels of physical activity have been suggested to be the main causes for the rise in obesity prevalence. However, this simple paradigm of an interaction between lifestyle and a genetically determined susceptibility has been challenged by recent research which suggests that factors in fetal and early postnatal life may also have a profound impact on long-term health. By raising the possibility of interventions in early life, this ‘developmental origins’ hypothesis has major implications for primary prevention of noncommunicable chronic disease and hence public health worldwide. The present review considers the evidence for the developmental origins of obesity with particular reference to a possible protective role for breastfeeding.

**Nutritional Programming of Obesity**

The hypothesis that breastfeeding protects against the development of later obesity originates from the more general biological phenomenon of ‘programming’, the influence of a factor or stimulus acting during an early critical window on long-term structure or function of an organism. The specific importance of nutrition in programming first emerged in the 1960s with the pioneering work of McCance [1]. He showed that rats raised in small litters, and therefore overfed in the suckling period, were larger as adults irrespective of nutrient intake after weaning. In contrast, manipulating nutrient intake after weaning produced little effect on final adult size, suggesting that nutrition acted during a critical, early postnatal window to program later body size. Similar effects of early overnutrition were seen in baboons. Lewis et al. [2] found that overfeeding in infancy programmed greater fat mass but not total body weight in adulthood. The effect size was substantial (baboons overfed in infancy had up to \( \times 4 \) greater omental and perirenal fat as adults). The effect also emerged only after adolescence, demonstrating the late manifestation of some programming phenomena [2].

Since these early observations, early postnatal overnutrition has been shown to program adiposity in many animal models. For instance, Ozanne and Hales [3] showed that mice given a higher protein diet during the suckling period (that allowed catch-up growth) were more obese and had a lower lifespan than those given a lower protein diet. Importantly, the adverse effects of higher protein intake postnatally were most marked in rats fed a ‘cafeteria’ or obesity-inducing diet from weaning compared to those given standard laboratory chow [3]. This observation suggested an interaction between nutritional programming and later environment, whereby the adverse effects of a higher nutrient intake prior to weaning were greatest in those given a highly palatable, energy-dense diet after weaning.
In humans, the concept that early nutrition may influence long-term adiposity has focused mainly on the possible protective role of breastfeeding. However, while there is little doubt that breast milk is the best source of nutrition for the newborn, whether breastfeeding has long-term health benefits remains controversial.

**Does Breastfeeding Protect against Later Obesity?**

A case-control study by Kramer [4] was one of the first reports to suggest a protective effect of breastfeeding on later obesity. Since then many, but not all, population-based studies have confirmed an association between breastfeeding and lower risk of later adiposity, as summarized recently in four systematic reviews [5–8].

The first review by Arenz et al. [5] confirmed a protective effect of breastfeeding against later obesity (adjusted odds ratio 0.78, 95% CI 0.71–0.85) (table 1). Obesity was defined as a BMI above the 90th, 95th or 97th percentile and the analysis was confined to studies that had adjusted for at least three of several confounding or interacting factors (birth weight, parental overweight, parental smoking, dietary factors, physical activity and socioeconomic status). Age, definition of breastfeeding, or the number of confounding factors adjusted for did not affect these findings and there was no evidence of publication bias. However, there was evidence from four studies of an inverse and dose-dependent effect of duration of breastfeeding on later obesity prevalence.

**Fig. 1.** Fat mass determined by bioelectric impedance at age 6–8 years according to thirds of z score change for length between birth and age 9 months (from lowest to highest) (p = 0.02).
The second report by Owen et al. [6] also defined obesity on the basis of BMI percentiles and again found a protective effect of breastfeeding on later obesity risk (table 1). Interestingly, the effect size in four studies that compared exclusive breastfeeding with exclusive formula feeding was similar to that shown by Arenz et al. [5]. However, the inverse association between breastfeeding and later obesity was stronger in smaller than larger studies.
raising the possibility of publication bias. The effect was also reduced markedly in six studies that adjusted for three potential confounding factors (parental obesity, maternal smoking and social class), with a fall in odds ratio from 0.86 (95% CI 0.81, 0.91) to 0.93 (95% CI 0.88, 0.99). Again, as in the review by Arenz et al. [5], the effect of breastfeeding was not altered by age at outcome and was stronger amongst prolonged breastfeeders.

The third review examined the evidence that breastfeeding reduced average levels of adiposity (i.e. mean values for BMI) rather than obesity per se [7]. This analysis, based on the possibility that breastfeeding moved the upper tail of the BMI distribution to the left but did not shift the whole distribution, found that breastfed infants had a slightly lower mean BMI than those formula-fed (table 1). As with their data on obesity [6], the authors found greater effects of breastfeeding on mean BMI in smaller studies than larger studies. The effects of breastfeeding were also markedly attenuated by adjustment for confounding factors (socioeconomic status, maternal BMI and maternal smoking during pregnancy) [unadjusted mean difference in BMI: \(-0.10\) (95% CI \(-0.14, -0.06\)) kg/m\(^2\) compared to adjusted mean difference: \(-0.01\) (95% CI \(-0.05, 0.03\)) kg/m\(^2\)]. The authors concluded, therefore, that any effect of breastfeeding on later BMI was likely to be influenced by publication bias and confounding factors.

The most recent meta-analysis summarized the evidence that duration of breastfeeding programmed obesity risk [8]. Consistent with previous reviews [5–7], this analysis confirmed that prolonged breastfeeding reduced the tendency to obesity (each month of breastfeeding was associated with a 4% reduction in risk of obesity, 95% CI \(-6\%\), \(-2\%\), independent of the definition of obesity or age at measurement.

Clearly, the above systematic reviews were based on observational studies, and because of marked differences in demographic and socioeconomic characteristics between breast- and formula-fed infants cannot establish causation. Randomized studies comparing breast and formula feeding are unethical, although data from cluster randomized studies of breastfeeding promotion by Kramer et al. [9] could be informative. Nonetheless, although residual confounding by sociodemographic differences between breast- and formula-fed infants could be influential, adjustment for these factors did not reduce the benefit of breastfeeding on obesity risk to zero. Methodological issues such as differences in age at outcome, definition of obesity, and publication bias also did not explain the protective effect of breastfeeding. The definition of breastfeeding, however, could be relevant to interpretation of published data. In reviews by Arenz et al. [5] and Owen et al. [6], for instance, confining the meta-analysis to studies comparing exclusive breastfeeding with exclusive formula feeding found remarkably similar reduction of obesity risk by breastfeeding (odds ratio of approximately 0.77). Exclusivity of breastfeeding may therefore be central to the mechanism by which breastfeeding protects against later obesity.
Overall, therefore, there appears to be some evidence that breastfeeding protects against the development of obesity, a conclusion supported by data from several systematic reviews which showed that a longer duration of breastfeeding had a greater beneficial effect [5–8]. The size of the effect (up to 20% reduction, table 1) has major implications for the health of populations.

**Mechanisms**

The potential mechanisms by which breastfeeding protects against later obesity have been extensively reviewed elsewhere [10], and so will be considered here briefly. These mechanisms can be broadly categorized as those that influence behavior or those related to the unique nutritional composition of human milk.

The most common explanation for the beneficial effect of breastfeeding on later markers of health is residual confounding by unmeasured attributes of the family and parents. Because parents who choose to breastfeed may have a healthier lifestyle (especially those who breastfeed for longer) cumulative differences in dietary habits and physical activity over many years could affect obesity risk despite statistical adjustment for these factors at a single time point in some studies [11]. Another behavioral explanation is that because breastfed babies control the amount of milk consumed they may learn to better self-regulate their energy intake, although whether this difference persists into adult life is unknown.

Mechanisms for programming of obesity related to the nutritional composition of breast milk include a number of bioactive nutrients in human milk, which are absent from some formulas (e.g. long-chain polyunsaturated fatty acids [12]). Lower protein and energy content in human milk compared to formula could also affect later body composition. For instance, protein intake in infancy (up to 70% greater in formula-fed than breastfed infants [13]) has been associated with adiposity in childhood [14] possibly by mechanisms that involve an earlier age of adiposity rebound [15], a hypothesis now being tested in European clinical trials. A higher protein intake could also promote obesity by stimulation of insulin release. Consistent with this thesis, formula-fed infants were shown to have higher plasma insulin concentrations than those breastfed from as early as 6 days of age [16].

Finally and most recently, we have suggested that the benefits of breastfeeding for long-term obesity and cardiovascular disease may be due to slower growth in breastfed compared to formula-fed infants – the growth acceleration hypothesis [17].

**The Growth Acceleration Hypothesis**

The growth acceleration hypothesis suggests that faster postnatal growth (upward centile crossing – particularly in infancy) programs the major
components of the metabolic syndrome [17]. Consistent with this thesis, faster neonatal weight gain was shown to program insulin resistance in preterm infants randomly assigned to a nutrient-enriched diet (preterm formula) that promoted faster growth compared to the standard diet (banked breast milk or term formula). Faster postnatal weight gain also explained the associations between breastfeeding and lower later insulin resistance, and between low birth weight for gestation and greater insulin resistance later in life [17]. Furthermore, early acceleration in weight programmed higher LDL cholesterol concentration and explained the benefits of breast milk feeding on later cholesterol concentration [17]. Similarly, acceleration in both weight and length in the first 2 weeks of life was associated with later endothelial dysfunction, a measure of the earliest physiological changes associated with the development of atherosclerosis [17].

The effect of early growth on later cardiovascular outcomes was substantial and greater than the adverse effects of both formula feeding or of being born small for gestation [17]. For instance, adolescents with the greatest weight gain in the first 2 weeks had 4% lower flow-mediated dilation of the brachial artery (a measure of endothelial function) than those with the lowest weight gain, an effect similar to that of insulin-dependent diabetes mellitus (4%) and smoking (6%) in adults [17]. Similarly, for cholesterol concentration, slower neonatal weight gain was associated with 20% lower cholesterol concentration compared to 10% lowering of cholesterol concentration associated with breast rather than formula feeding [17].

Programming by postnatal growth acceleration is potentially a unifying hypothesis which can explain, in part, adverse programming effects seen in infants born small for gestation (who show ‘catch-up’ growth immediately after birth) and the long-term cardiovascular advantages of breastfed babies (who are relatively undernourished and have slower growth compared to those given formula). This concept is now extensively supported by studies in infants born at term. For instance, upward centile crossing for weight in infancy is associated with higher later blood pressure independent of birth weight [18]. In fact, the adverse long-term effect of faster early growth appears to be a fundamental biological phenomenon seen across animal species as diverse as insects, fish and mammals [19]. Faster growth as a consequence of a higher nutrient intake prior to weaning appears to be particularly important and, in animal models, has been shown to program the metabolic syndrome, obesity and even reduced lifespan [1–3].

**Growth Acceleration and Later Obesity**

The growth acceleration concept may be particularly important for programming of obesity as shown in two recent systematic reviews [20, 21]. Monteiro and Victora [20] showed that upward centile crossing for weight and length in infancy was associated with later obesity in 13 studies, while Baird et al. [21] found similar findings in 10 studies (odds ratios for obesity risk ranging from 1.2 to 5.7 in infants with rapid growth).
Although these systematic reviews were based on observational studies and so cannot establish causality, they provide compelling evidence for an effect of faster growth in infancy on later adiposity. This effect has been seen for both faster weight and length gain (Singhal, unpubl. data, fig. 1), irrespective of the definition of faster growth, in both high and low income countries, and over time (i.e. for people born between 1927 and 1994) [21, 22]. The effect has also been seen in healthy term infants with normal birth weight and is not confined to infants born small [17, 18, 20, 21] who often show ‘catch-up’ growth. Catch-up growth, defined as the nutritional recovery and acceleration in growth seen after a restriction to growth is removed, is common in infants born small for gestation as a consequence of intrauterine growth retardation. Catch-up growth is widely associated with cardiovascular disease and obesity later in life. However, randomized intervention studies have shown that growth acceleration as a consequence of a high postnatal nutrient intake has programming effects independent of birth weight for gestation [17], which suggests that rapid growth, and not the closely related phenomenon of ‘catch-up growth’, is central to underlying mechanisms.

The effects of growth acceleration on later obesity are also not confined to infants fed formula. For instance, breastfed infants with a vigorous feeding style at age 2 and 4 weeks, suggestive of a greater breast milk intake, had greater adiposity at age 3 years [22] and upward centile crossing for length and weight has been associated with later adiposity in breastfed infants with birth weight <10th centile (Singhal, unpubl. data). Similarly, faster weight gain in the first 2 months was associated with higher BMI at 10 years in a large, prospectively followed, and predominantly breastfed cohort from the UK (The Avon Longitudinal Study of Pregnancy and Childhood) [mean, SD BMI of lowest compared to highest quartile of weight change in the first 2 months: 18.1, 0.1 versus 18.6, 0.2 kg/m²; p = 0.01; Charakida, pers. commun.]. Programming effects of faster early growth therefore appear to be applicable to diverse populations.

The size of the effect of early growth rate on later obesity is substantial. For instance, Stettler estimated that 20% of the risk of obesity at age 7 years is attributed to having a rate of weight gain in the highest quintile in the first 4 months of life [23], an effect size important for public health. However, the relative contribution of different growth periods to programming of adiposity is uncertain. Growth is fastest in the first few weeks after birth, which may therefore be a key window for adverse programming. Consistent with this hypothesis, greater weight gain in the first week of life was shown to program obesity in adulthood [24], a finding analogous to programming of insulin resistance and endothelial function by faster early growth in preterm infants [17]. Again the size of the effect was substantial; each 100-gram increase in absolute weight gain during this period was associated with a 28% increase in the risk of becoming overweight (95% CI 8%, 52%) [24]. Emerging evidence therefore supports the first few postnatal weeks as a critical window for programming long-term health in both humans and animals.
The growth acceleration hypothesis could also explain programming of obesity by other factors in infancy. For instance, an earlier age of adiposity rebound, suggested to be a key risk factor for later adiposity [15], may simply identify children whose BMI centile is high and/or crossing upwards (i.e. children with a faster growth rate) [25]. Similarly, previous associations between an earlier age at weaning (complementary feeding) and a greater risk of later obesity [26] may reflect the influence of greater nutrient (and particularly protein) intake with weaning, on growth rate in infancy. Nevertheless, in both humans and animals, it is not possible to separate programming effects of nutrition from growth, as clearly, these factors are interdependent.

Mechanisms

Animal studies have helped shed light on the mechanisms that link early growth and nutrition with long-term obesity. Of particular interest is the role of the appetite-regulating hormone, leptin, which in the first few days after birth programs hypothalamic neuronal projections related to long-term regulation of appetite and energy expenditure [27]. For instance, rats overfed before weaning have been shown to be overweight, hyperleptinemic, and show hypothalamic leptin resistance later in life [28]. Similar mechanisms may apply in humans in whom leptin resistance in early infancy could be advantageous by allowing infants born small for gestation to increase their appetite and so facilitate catch-up growth. However this programmed increase in appetite could contribute to long-term obesity. In support of this hypothesis, breast milk feeding has been associated with lower leptin resistance in adolescents [29] raising the possibility that relative undernutrition and slower growth associated with breastfeeding in the first few weeks permanently programs a lower appetite. In contrast, formula-fed infants may have upregulated appetite leading to obesity when faced with a highly palatable, energy-dense western diet (analogous to greater obesity in rats growing fast before weaning and fed a highly palatable ‘cafeteria’ diet after weaning [3]).

Does Breastfeeding Protect against Growth Acceleration?

Central to the hypothesis that relative undernutrition associated with breastfeeding protects against later obesity is evidence that breastfed infants grow more slowly than those formula-fed [9]. Over the first 3 months, however, the rate of weight gain in breastfed infants may be greater than those formula-fed as suggested by the new WHO breastfed reference charts [30]. However, these charts were based on data from highly selected populations from six centers worldwide (Brazil, Ghana, India, United States, Norway, Oman) with those from poorer countries represented by subjects from affluent communities [30]. Faster growth in breastfed infants may therefore reflect postnatal catch-up growth following a period of in utero restraint,
an effect that is most marked in affluent communities (both in richer and developing countries) where parents from a higher socioeconomic group tend to both breastfeed and be taller. In contrast, data from large epidemiological studies have confirmed the growth-accelerating effects of formula throughout infancy [9]. In fact differences in growth rate between breast- and formula-fed infants may be greatest in the first few postnatal weeks, a time when breastfed infants often lose weight, while those formula-fed tend to put on weight. As suggested by studies in animals [1–3] and humans [17, 24] this difference may be critical for programming of obesity.

**Conclusion**

There is now strong evidence to support a benefit of breastfeeding for long-term risk of obesity, an effect possibly related to the slower growth and relative undernutrition associated with breast compared to formula feeding. Breastfeeding is therefore a preventative strategy, which is both evidence based and has large potential benefits for public health.

**References**

Does Breastfeeding Protect from Growth Acceleration


Discussion

Dr. De Curtis: In preterm infants, especially in very low birth weight infants, it is suggested that aggressive nutrition should be started as soon as possible in order to avoid catabolism, allow rapid growth and obtain catch-up growth. What is your opinion on the catch-up growth of preterm infants? A lot of people don't think that the Barker hypothesis is true. Do you think that sometimes there is no correspondence between the statistical evidence and clinical importance, especially when the effect is seen in a large population?

Dr. Singhal: I couldn’t agree with that more. There is a big difference between epidemiology and clinical care. As a neonatologist I would try to make any preterm infant grow because the most important thing is survival. Most preterm infants fall off their weight centile despite us trying to give them a high nutrient intake. So in preterm infants the situation is incredibly simple, promote growth to help them get off the ventilator and make them anabolic. We know that this will also benefit their long-term cognitive function and possibly their bone health.
Dr. Pazvakavambwa: In terms of your theories on insulin, what is the risk for the infant of a diabetic mother, and what is the outcome in terms of cardiovascular risk compared to the normal infant?

Dr. Singhal: This is a very active area of research. I don’t know about cardiovascular risk, but the infants of diabetic mothers are at higher risk of later obesity, although the mechanisms involved are uncertain [1].

Dr. Fisberg: Could you possibly comment more on the influence of birth weight on the further development of obesity? In our experience we have seen that the odds ratio for low birth weight is exactly the same for children with a birth weight of over 4 kg.

Dr. Singhal: The association between birth weight and later obesity is complex because most studies don’t separate fat and lean mass. There is an association between birth weight and later BMI, but for lean rather than fat mass [2]. There is also evidence of increased risk of obesity in babies with a high birth weight but there are few studies that use two-component models of body composition to show that this is fat and not lean tissue. There is also evidence that low birth weight increases abdominal fat mass later in life [3].

Dr. Ziegler: Thank you for this very comprehensive review of the existing information and the association between breastfeeding and later adiposity. You probably know that I am a skeptic. The simple fact that the obesity epidemic among children has coincided with a sharp increase in breastfeeding in the United States makes me wonder whether I should believe in causality, that is, breastfeeding causes children to be less obese. So could you please review for us the arguments in favor of causality?

Dr. Singhal: I think that researchers in the developmental origins field must not overplay their hand. The developmental origins hypothesis gives you a tendency, but does not directly lead to obesity. Even if you are programmed to eat more, or programmed for an increased risk of obesity, by far the strongest influence on obesity is your environment later in life, and you will never become fat unless you have a positive energy balance, despite your programming. I completely agree that the environment is the main reason that the obesity epidemic in children has occurred, but that is not to say that programming factors are not important. They are important given the current lifetime environment. In fact there may be an interaction between programming and environment probably mediated via appetite regulation.

Dr. Giovannini: I would like to ask about protein intake. The first point is not only the low protein but also the quality of amino acids. The second point is the quality of intrauterine development and complementary feeding.

Dr. Singhal: There are a lot of issues here. We don’t even know what total protein intake does for later obesity. To my knowledge, the trial of Koletzko et al. [4] is the only randomized trial looking at the effects of differences in protein intake on obesity later in life. When you know that protein intake matters in an intervention study, only then can you investigate particular amino acids. It is early days in terms of identifying the nutritional window that influences long-term outcome, but we can see evidence of that process both in animals and humans. There is no doubt that there is an association between birth weight and long-term obesity risk. The question is how much of that is antenatal nutrition, how much due to genetic factors, such as imprinted genetic factors, and how much is due to postnatal growth. I think with the current level of knowledge, all we can say is that there is an association – at least until the results of intervention studies now taking place (e.g. in India) are available.

Dr. Cardoso: Why didn’t you put discipline in the list of mechanisms to control obesity? I think that it is very important that the medical team make some comments about discipline during routine examinations for every child. Many things about behavior in their homes, in school and with friends contribute a lot to the weight of the child.
Dr. Singhal: I think that is the next stage. At the moment in the UK there is no such thing as an ‘overgrowing’ baby for mothers or pediatricians. If a baby is growing fast everybody is happy. We still have the attitude that fatter is better. One of the commonest things I see is a breastfed baby who has been supplemented with formula (often by health professionals) to make him grow faster. The baby was born on the 10th centile, is growing on the 10th centile, but nobody is happy because he is not on the 50th centile.

Dr. Cabus: In clinical practice we have seen children who are exclusively breastfed and they are too fat. Are there any studies that have investigated this kind of growth in normal children who were exclusively breastfed as babies?

Dr. Singhal: The data show that the mechanism is more fundamental than breastfeeding versus bottle feeding. The mechanism for early growth having adverse long-term effects occurs in yeast [5] and may not have anything to do with the type of feeding. A breastfed baby is less likely to accelerate centile upwards than a formula-fed baby, but there are a lot of data to show that the same phenomena occur in breastfed babies [6, 7]. There is no public health message for breastfed babies, suffice it to say that breastfed babies shouldn’t be supplemented with formula just to make them grow faster.

Dr. Jongpiputvanich: You mentioned the critical window period of nutrition. But there are two hypotheses: one by Dr. Barker in the prenatal period, and you and Dr. Lucas mentioned the postnatal period. Could you comment further about this?

Dr. Singhal: I think at the end of the day there are going to be different critical windows for different outcomes. Dr. Barker and his team are quite rightly very interested in the antenatal period. Our team believe that postnatal factors are more important because you can more easily intervene postnatally and the effect sizes for postnatal growth (in our own work and that of others) appear to be much larger than the effects of birth weight, e.g. blood pressure. I don’t think you can say that this is an antenatal or a postnatal hypothesis. I think that we should be focusing on what interventions we need, what public health policy is needed and what experiments we need to test the hypothesis, rather than saying it is all postnatal or antenatal.

Dr. Haschke: The question regarding the critical prenatal or postnatal window might not be an either/or, it could also be an and. I refer to the study recently presented by Dr. Bergmann in which they looked at two cohorts of mothers with breastfed infants in Germany; one cohort was supplemented with DHA from 32 weeks of gestation onwards and during the lactation period, and the offspring were followed until 21 months of age, and both cohorts were fully breastfed until 6 months of age. At 21 months of age the cohort whose mothers had received DHA had a lower body mass index, the difference being highly significant. So there are mechanisms which we still don’t understand and the critical window for programming, whatever it is, might be before and after birth.

Dr. Singhal: I completely agree. In fact at a recent meeting in Sweden we agreed that programming is a life course event. The biology has to be continuous from antenatal to postnatal. That is not the same thing as saying that there cannot exclusively be a postnatal effect. The analogy I would make here is with an antihypertensive drug which has an effect by reducing your blood pressure but doesn’t tell you anything about the biology of the high blood pressure in the first place. So breastfeeding can have an effect postnatally but the critical window for biology has to be continuous. So we don’t need to make the dichotomy between antenatal and postnatal windows.

Dr. Brunser: We had a peculiar experience in Chile because at one time there was a very high incidence of infant malnutrition. To solve this situation these severely malnourished children, between 3 and 6 months of age, were placed in special centers where they were intensively fed to regain weight. Most of them were subsequently lost
from control, but about 30 have been followed now for close to 30 years and they tend to be obese, they are short and tend to have lower intellectual development. So probably, as some people think, there is a window in which, if you increase the growth rate very rapidly, obesity tends to occur. The dilemma is that at that time, 30 years ago, we had to decide whether to run the risk of either the children dying of malnutrition or becoming obese 30 years later, and we decided then that it was probably better to be obese later in life than dead at an early age.

*Dr. Agostoni:* My question concerns your randomized trial on term SGA infants, there was also a nonrandomized control group taking human milk in this trial. Was the unfavorable association between early weight gain and later blood pressure still working in this group?

*Dr. Singhal:* Infants who showed upward centile crossing for weight between birth and age 8 months had a higher blood pressure [7] and body fat mass [Singhal, unpublished] whether they were breastfed or formula fed.

*Dr. Agostoni:* So in this case you take human milk, but it does not protect you?

*Dr. Singhal:* No, the mechanism is more fundamental than formula versus breast milk [5].

*Dr. Agostoni:* And with breastfed babies, those who have a rapid growth?

*Dr. Singhal:* They seem to be showing the same effect.

*Dr. Solomons:* 30 years ago when I went to work in Guatemala, we had the notion that developing an appropriate weight was important to develop optimal height. I am wondering if your epidemiological and clinical experience in Europe now suggests any kind of causal or dependency relationship between gaining weight and gaining height? This, because for Europeans, height seems to be an important thing. Is there any kind of a floor issue where this could explain why people grow in weight as best as they can as a mechanism to protect their height? Thereafter, they can lose the additional weight, but in the meanwhile one will have achieved the correct height. What is the science relating to this kind of reasoning?

*Dr. Singhal:* I can only speak about our two intervention studies. In preterm babies, who are incredibly malnourished, infants who received a low nutrient formula showed no differences in long-term height compared to babies who received the high nutrient formula [8], despite big differences in nutrient intake and short-term growth. Similarly, in our trial of infants born small for gestational age, there were no long-term differences in height between groups randomized to different nutrition in infancy [7]. So I don’t know if there is any evidence from randomized studies that early nutrition makes any difference to final height.

*Dr. Leone:* Don’t you think that preterm babies depend on the level of immaturity at birth, and is there a causality or a relationship between these? Is there bigger or lesser sensitivity to these factors?

*Dr. Singhal:* There may be other factors that affect growth. I have focused on nutritional intervention, but obviously morbidity, prematurity, maternal size, genetic, many other factors may contribute to growth.

**References**


