Early Diet, Insulin-Like Growth Factor-1, Growth and Later Obesity

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Abstract

There is increasing evidence that factors in early life are important for the risk of developing overweight and obesity later in childhood. Among the postnatal factors, breastfeeding and complementary feeding are especially interesting because the pattern of these two factors can be changed. Breastfeeding has been shown to reduce the risk of later obesity, although the effect is not substantial. Complementary feeding also seems to play a role. There is some evidence that a high protein intake is associated with a higher risk of obesity later in childhood, whereas a high fat intake during the complementary feeding period does not seem to be a risk factor for later obesity. Thus, the dietary pattern during this period is different from the pattern seen in older children and adults where a high fat intake is associated with a higher risk of obesity and a high protein intake in some studies seems to protect against obesity. A few studies have also suggested that early introduction of complementary foods (before age 4 months) is associated with an increased risk of later obesity. A high weight gain during early life, especially the first 6 months, is associated with a higher risk of developing obesity. However, some studies suggest that weight gain during the 6- to 12-month age period, when complementary feeding is introduced, is not associated with later obesity. Insulin-like growth factor-1 (IGF-1) values and body composition both play a role in the complex pattern between early diet and later obesity, but our present knowledge about how these factors are influenced by diet during infancy is limited. Future studies should include longitudinal data on IGF-1 and body composition during infancy to improve our understanding of how diet in early life can play a role in prevention of later obesity.

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There is increasing evidence that several aspects of early diet are important risk factors for later obesity. Furthermore, early growth velocity is also closely associated with later obesity, but to what degree this association is causal is not clear. Both insulin-like growth factor-1 (IGF-1) and body composition during the first years of life play important roles in these associations, but with new data suggesting that IGF-1 is not steadily increasing during infancy [1] and that there are significantly different
patterns of body composition during infancy between breastfed and formula fed infants [2], there is still some way to go before we fully understand how these factors in early life interact and which patterns are associated with either a healthy growth pattern or with later obesity. The aim of this short review is to highlight important and new knowledge within this complex area.

**Breastfeeding and Obesity**

Several large meta-analyses have shown that breastfeeding is associated with a decreased risk of obesity later in life. In a meta-analysis including 28 studies and around 300,000 individuals breastfeeding reduced the risk of obesity by 13% [3]. In six of the studies controlling for three major confounders (parental obesity, maternal smoking and social class) the reduction was reduced to 8% but still significant. In a meta-analysis by the same authors the effect of breastfeeding on mean BMI was analyzed [4]. The effect was significant but very small, 0.04 BMI units. In another review, breastfeeding was associated with a 22% reduction in risk of obesity and four of the studies showed a dose-response effect of the duration of breastfeeding [5].

**Age of Introduction of Complementary Feeding and Later Obesity**

The European Food Safety Agency has reviewed the scientific literature regarding health effects of the age of introducing complementary feeding [6]. The working group concluded that when complementary feeding was introduced at age 4–6 months there was no clear impact on the risk of obesity. However, a few studies were found suggesting that introduction before age 4 months could result in increased risk of obesity. A recent study from the US also found that introduction before 4 months was associated with a higher risk of obesity at the age of 3 years when controlled for rapid early growth [7]. In a study of a large cohort born 1959–1961, we found that later introduction of complementary feeding, within the range of 2–6 months was associated with less overweight at age 42 years [8].

**Early Protein Intake and Later Obesity**

There is now convincing evidence that a high protein intake early in life is associated with an increased risk of later obesity. In a multicenter intervention study infants who were not breastfed were randomized to infant formula with high or low protein content. Those receiving the high protein content formula had significantly higher weight-for-height and BMI when the intervention stopped at age 12 months [9]. At a follow-up at the age of 24 months these differences were still significant. In a study
from Iceland those with the highest quartile of protein intake at 9–12 months had a significantly higher BMI at age 6 years [10]. The protein intake in this cohort was quite high with a mean intake at age 9–12 months of 15–16 energy percent. In a study from Sweden, protein intake at age 17–18 months was a significant predictor of BMI at age 4 years [11]. In another observational study from Germany, protein intake both during the complementary feeding period (6 and 12 months) and during the transition to the family diet (18–24 months) were independent predictors of an unfavorable body composition at 7 years of age [12].

**Early Fat Intake and Later Obesity**

While there are several studies showing a positive association between early protein intake and later obesity there seems to be no studies suggesting that a high fat intake during the first years of life increases the risk of later obesity. There were no associations between early fat intake (age 1 and 2 years) and weight and skinfolds at 8 years [13]. Furthermore, there were no associations between fat intake and BMI or body fat in children in cross-sectional studies of 2- to 5-year-old children [14, 15].

**Early Growth and Later Obesity**

In a recent large review by the Scientific Advisory Committee on Nutrition (SACN) from the UK, it was concluded that there is strong evidence for a positive association between early growth and later BMI, obesity and body fat mass [16]. Interestingly, three studies comparing weight gain during infancy and fat mass or obesity during childhood and adolescence (9, 11 and 17 years) found positive associations between weight gain from birth to six months and no significant associations for weight gain between 6 and 12 months when complementary foods are introduced [17–19].

**Role of IGF-1**

IGF-1 is considerably lower in breastfed infants compared to infants who are formula fed. Most studies have focused on the first 6 months of life [20–22] where the values for breastfed infants are typically considerably lower than the values for infants fed on infant formula. But also in late infancy when infants are getting considerable amounts of complementary foods, there is still a highly significant dose response effect with lower values of IGF-1 the more times the infant is breastfed per day [23]. Two studies have compared IGF-1 values in infants randomized to infant formula with high or low protein content and compared it with a control group of breastfed infants [22, 24]; the studies found a dose response effect with the highest values of IGF-1 in infants.
getting a high protein formula and the lowest IGF-1 values in breastfed infants, which suggests that the low protein content in breast milk is the main explanation of the lower IGF-1 values in breastfed infants. However, other characteristics of breast milk, could also play a role.

Several studies with reference values for IGF-1 during childhood have suggested a steady increase from birth until puberty [25, 26]. However, some new studies have suggested that the pattern is more complex [1]. It would seem that there is an increase during the first months after birth and then from age 2–3 months, a decrease with a nadir around age 7–9 months and thereafter an increase again. This pattern was especially clear in a study from China comparing measurements of IGF-1 during infancy [27]. It is remarkable that the nadir in IGF-1 is at about the same age as the maximum in BMI, which increases from birth up to about 9 months and then decreases again. There is no obvious explanation for the mechanism behind this pattern in IGF-1 values with a nadir around the age of 7–9 months. It could be that this is the age when growth hormone starts to have a stronger effect on IGF-1 as suggested in the infancy-childhood-puberty (ICP) growth model by Karlberg [28], but this is speculative. As protein intake, at least at some ages, has a strong influence on IGF-1 values and early protein intake seems to be a risk factor for later obesity, it is important to achieve a better understanding of which factors regulate IGF-1 concentrations in the blood during infancy and how IGF-1 values during infancy are related to later obesity.

The role of IGF-1 values early in life for development of later obesity is further complicated as there seems to be a programming of the IGF-1 axis. Breastfed infants in the ALSPAC cohort had higher IGF-1 values at 7–8 years than formula-fed infants [29] and we found that IGF-1 values at 9 months of age were negatively correlated with IGF-1 values at 17 years in a cohort of healthy children [30].

**Early Body Composition and Later Obesity**

A recent systematic review has compiled body composition data during infancy from 15 studies comparing body composition in breastfed and formula-fed infants [2]. The studies used many different methods including total body potassium, TOBEC, Pea-Pod, DEXA and isotope dilution. There was a significant pattern showing that breastfed infants during the first 6 months of life had a higher fat accumulation than formula-fed infants. From 6 to 12 months the pattern was opposite with breastfed infants accumulating more lean body mass than those fed infant formula. There are no firm data on the long-term effects of body composition during the first year of life, but with breastfeeding regarded as the optimal feeding during infancy and associated with less obesity later in life, it is likely that a high degree of fat accumulation during the first half of infancy is an optimal pattern associated with a lower risk of obesity later in life.
**Conclusions**

Breastfeeding is associated with a lower risk of later obesity. Although the effect is only moderate the evidence is convincing. Breast milk is characterized by high fat and low protein content compared to complementary foods and the family diet. It is therefore interesting that studies of the effects of composition of the diet during the first years of life also show that a low protein intake and a high fat intake seem to protect against later obesity. There is not convincing evidence that the age of introduction of complementary feeding has an effect on later obesity. However, it would seem that introduction before the age of 4 months increases the risk, but not all studies have controlled for early weight gain, which is important, since infants with a high weight gain during the first months after birth are likely to be introduced to complementary feeding earlier [7].

Both IGF-1 and body composition during infancy are likely to play important roles in programming of the risk of later obesity, but the pattern is complex and at present not well understood. It is likely that we will obtain a better understanding of how early diet influences the risk of later obesity if future studies will include data on IGF-1 levels and body composition.

**References**


