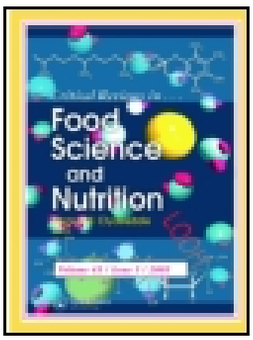

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Evo-Devo of Child Growth: The Role of Weaning in the Transition from Infancy to Childhood

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Short title: Weaning and the infancy - childhood transition

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Abstract

Homo sapiens are unique in having a life history phase of childhood, which follows infancy, as defined by breastfeeding. This review uses evolutionary life-history theory in understanding child growth in a broad evolutionary perspective, using the data and theory of evolutionary predictive adaptive growth-related strategies for transition from infancy to childhood. We have previously shown that a delayed infancy-childhood transition (DICT) has a lifelong impact on stature. Feeding practices during infancy are fundamental elements of nutrition as they program for future growth and body composition. A relationship between the duration of breastfeeding and the nature of weaning has been suggested as a possible cause for later obesity and growth patterns. This review highlights the role that breast milk feeding and variations in the weaning age have on transition to childhood, growth and body composition.

Key words: Evolution; weaning, breastfeeding; nutrition; growth

Introduction

Humans' life history is characterized by early immature birth, a relatively short period of infancy, defined among other by breastfeeding, and we are the only species that have a childhood - a biologically and behaviorally distinct interval of stable growth between infancy and the juvenile period that follows(Hochberg, 2008).

We have previously shown that a delayed infancy-childhood transition, which we refer to as DICT, has a lifelong impact on stature and is responsible for as many as 44-50% of children with idiopathic short stature(Hochberg, 2008;Muller, 2007).

The premise of this review is that the traditional definition of infancy - weaning from mother's milk has physiologic, metabolic and evolutionary correlations with the growth transition from infancy to childhood.

Evo-devo of child growth

Evolutionary developmental biology (evo-devo) addresses the issues of how developmental systems have evolved, and probes the consequences of these historically established systems for organismal evolution (Muller, 2007). We have previously taken evo-devo into the realm of clinical medicine, showing how child growth is best explained in terms of evo-devo principles(Hochberg, 2008;Muller, 2007;Wang and Chard, 1992).

If we consider the lifespan of humans, the period of infancy, as defined by breastfeeding, is markedly shorter than, for example, the 60 month infancy of the chimpanzee, which lives for 25 years in the wild. In humans and other mammals, infancy is characterized by rapid and

decelerating growth, deciduous dentition, and feeding by maternal lactation. While the duration of infancy is shorter in humans than in other mammals, its quality is higher. Greater physical support by the human infant produces more intense social stimulation, and during this period the brain grows rapidly. Evolution of this life history has involved the gradual cumulative selection and development of traits over millions of years. As a major consumer of energy, growth plays a foremost role, and the ability to vary growth patterns and the rate of growth during particular life stages, to shorten or prolong life stages and to add or delete life stages - provides a compelling strategy. Thus, weaning is followed in other social mammals by juvenility – a stage of independence for provision and protection(Hochberg, 2008), occurs in human traditional societies at about 30–36 months of age. The childhood stage is peculiar to humans, and has been defined by stabilization of the growth rate, immature dentition, and weaning (whilst continuing to depend on older people for food), and on behavioral characteristics, including immature motor control. The evolutionary fitness advantage of childhood lays in the mother's freedom to discontinue breastfeeding her 3 year-old infant to initiate a new pregnancy.

Control of infantile and childhood growth

By the age of infancy-childhood transition, those weaned earlier are heavier and longer(Forsyth et al., 1993). Among infants on prolonged and exclusive breastfeeding, weight-for-age *z* scores fell slightly during infancy; length-for-age fell below the reference by 6 months with catch-up to the reference by 12 months.

Based on analysis of growth parameters, the infancy-childhood-juvenility-adolescence growth model divided human growth into these successive and partly superimposed phases that reflect the endocrine control mechanisms of the growth process(Forsyth et al., 1993;Hochberg, 2009). The infancy phase begins at mid-gestation and tails off at approximately 2–3 years of age, representing the postnatal extension of fetal growth, and is regarded as being nutrition dependent and closely linked to the action of insulin-like growth factors (IGFs)(Leger et al., 1996;Wang and Chard, 1992). The stable linear childhood growth phase is growth hormone (GH)-dependent; it starts in affluent Western countries between 6 and 12 months of age(Karlberg et al., 1987;Liu et al., 1999), and continues through juvenility, when growth decelerates(Hochberg, 2010). Thus, the model proposes a period of transition, whereby the initiation of the childhood growth phase overlaps with the infancy growth phase and the infantile life history stage, as defined by weaning at 2–3 years of age(Hochberg and bertsson-Wikland, 2008).

The infancy childhood growth transition represents the age at which growth hormone (GH) begins to regulate growth significantly, and reflects the control of growth by the GH–IGF-I endocrine axis and target cell responsiveness(Karlberg and bertsson-Wikland, 1988;Wit and van, 1992). This growth transition occurs in parallel with a rise in serum levels of GH-dependent IGF-I and IGF-binding protein-3 during the second half of the first year of life, and children with a delayed infancy childhood transition (DICT) show a delay in the 6 to 12 month rise of IGF-I levels(Hochberg and bertsson-Wikland, 2008;Hochberg, 2008;Liu et al., 1999). Moreover, this

transition is absent in children with GH deficiency who receive no hormonal therapy(Karlberg and bertsson-Wikland, 1988).

The course of weaning

Intrauterine and infantile nutrition play a major role in lifetime health. They program for future growth and body composition(Gluckman and Hanson M.A., 2005). Feeding practices are fundamental elements of nutrition, and are influenced by many factors, including personal and familial habits, maternal education, socioeconomic status, and cultural environment(Hochberg, 2008).

Mothers in nonindustrial traditional societies breastfeed their infants for 19-39 months(Sellen, 2001) and the definition of infancy and transition to childhood has been linked to weaning from breastfeeding, as previously reviewed(Hochberg, 2009). They add non-breast milk liquids at a mean age of 4.5 mo (Sellen, 2001). Trends of breastfeeding in developed countries have changed, and currently mother breastfeed, if at all, from as briefly as 3 months (early infancy) to two years - well into the childhood growth phase.

It has been suggested that children who are exclusively or predominantly breastfed for the first 4 months of life have a different growth pattern as compared to children who consume alternative energy sources in the first 4 months of life (1995;2002;Burdette et al., 2006;Cole et al.,

2002;Dewey et al., 1995). Likewise, infants following the WHO recommendations for prolonged and exclusive breast-feeding, and who lived under conditions favoring the achievement of genetic growth potentials, appeared to show a decrease of growth progression in the first year compared with predominantly formula-fed infants (Hamill et al., 1979). This observation of better growth with early weaning has also been noted in beef calves (Meyer et al., 2005;Odhiambo et al., 2009).

Supplements added

The timely introduction of complementary foods during infancy is necessary for both nutritional and developmental reasons, and to enable the transition from maternal milk feeding to family foods (Agostoni et al., 2008). Complementary feeding is associated with major changes in both macronutrient and micronutrient intake.

A relationship between the duration of breastfeeding and the nature of weaning has been suggested as a possible cause for later obesity (Burdette et al., 2006). Factors that relate to the duration of breastfeeding in developed countries, such as maternal education, also influence the age when solid foods are introduced (Bolling K et al., 2007) and the types of solid foods fed during weaning (Bolling K et al., 2007;Noble and Emmett, 2006;Robinson et al., 2007). Both breast milk feeding and variations in the weaning diet should therefore be considered when examining the influence of infant diet on growth, transition to childhood and body composition (Robinson et al., 2009).

Chemical changes at weaning/supplements added

Lipid metabolism

Mammalian development has a prenatal, a suckling, and a weaning stage, distinguished by the mode of food intake and its composition (Little and Hahn, 1990). The gradual transition into the weaning period is marked by an adjustment in fatty acid (FA) metabolism, which is directly associated with the change in diet. This period characteristically reveals a decrease in plasma FA and ketones, a decrease in FA oxidation, ketogenesis, gluconeogenesis, and a rise in FA synthesis (Little and Hahn, 1990).

In terms of the transition into the GH-dependent childhood growth, adipose tissue exerts a regulatory effect on the GH/IGF-I axis mostly by modifying free fatty acids (FFA) and leptin. FFA and GH integrate a classical feedback loop: a rise in FFA blocks GH secretion(Cordido et al., 1996). This action is rapid, dose-related and exerted at the pituitary level with some evidence for hypothalamic participation.

Transition from a high-fat to a high-carbohydrate diet

Table 1 and figure 1 present the typical food composition according to age and type of feeding. During infancy the infant feeds on maternal milk-based, providing relatively high protein, low carbohydrate diet characterized by a greater dependency on hepatic gluconeogenesis as the source of glucose for brain growth, development and function. Gradual weaning, which ultimately increases the proportion of carbohydrate to protein and fat in the child's diet, requires

the emergence of an increased sensitivity to insulin action, enabling the utilization of carbohydrates and sugars, rather than protein and fat as metabolic fuel. The hormonal and metabolic changes that occur in response to the increase in plasma levels of glucose and insulin result in adaptation of digestive hormones and function. The parallel change in the nature and solidity of the ingested foods, affect the rate of activity of gut enzymes and the rate of maturation and activity of gut hormones (Agostoni et al., 2008;Girard et al., 1993;Girard et al., 1994). Thus, to a large degree GI maturation is driven by the foods ingested (Agostoni et al., 2008).

Gut changes at weaning and added supplements

The weaning process and its consequences have been extensively studied in piglets (Boudry et al., 2002;Boudry et al., 2004;Montagne et al., 2007). Similarly to humans, the process is marked by significant social, environmental and nutritional changes. These changes generally result in a critical period of low voluntary feed intake, during which the pig is adapting to the starter diet (Montagne et al., 2007). Immediate post-weaning anorexia results in the alteration of gut integrity, characterized by shortened villous length, disturbed absorptive-secretory electrolyte and fluid balances, increased mucosal permeability, decreased enzymatic activities, stimulation of proinflammatory cytokine gene expression, activation of heat shock proteins in the mucosa, as well as lowered level of mucins and goblet cell density. A 1–2-week adaptive phase to solid diet based on plant ingredients is then observed (Boudry et al., 2002;Boudry et al., 2004;Montagne et al., 2007). Montagne et al. showed the temporal changes induced by weaning on the GI structure and function that can be divided in two: an acute and short time-period, observed from day one

to five after weaning, followed by a more progressive adaptive and maturational phase, from day 5 - 15(Montagne et al., 2007).

Changes in gut histology at weaning

At birth, the human neonatal gut has predominantly narrow finger-like villi and small crypts. Breastfed infants have smaller villi and crypts than bottle fed infants, suggesting that crypt binary fission (duplication), associated with cylindrical growth of the small intestine, may be the predominant mechanism of epithelial growth during milk feeding, whereas crypt hyperplasia predominates later during weaning (Cummins and Thompson, 2002). Presumably, growth factors in breast milk or those produced endogenously, such as corticosteroids, thyroxin, GH, glucagon like polypeptide-2, insulin, IGF-1, epidermal growth factor, erythropoietin, fibroblast basic growth factor, hepatocyte growth factor, keratinocyte growth factor, prostaglandin E2 polyamines and transforming growth factor beta interact with specific mucosal growth factor receptors in the neonatal gut, as reviewed by Cummins et al. (Cummins and Thompson, 2002).

It has been suggested that breast milk may contain inhibitory growth factors for crypt hyperplasia (1995). At weaning, epithelial crypt hyperplasia may be promoted by physiological inflammation of the gut-associated lymphoid tissue from antigenic stimulation. Indeed, immune suppression with cyclosporine A or with antibody blockade of interleukin 2 receptor retards intestinal growth at weaning(Thompson et al., 1996). Expansion of the intestinal surface area during weaning accommodates the new nutrient load(Cummins and Thompson, 2002).

The Immune system at weaning

During infancy the immune system faces extensive antigenic load either by food as new allergens or infections, thus the mucosal immune system undergoes extensive changes in early childhood in response to environmental stimuli.

SOCS proteins have important roles, not only in macrophages, but also in dentritic cells (DC) activation(Yoshimura et al., 2007) as a link between innate and adaptive immunity. As the infant transits into childhood, higher cell densities are found at the ventral tracheal site, indicating that the increasing population of mucosal DC across infancy-childhood transition reflects immunological maturation(Tschernig et al., 2006). During DC maturation, the expression of SOCS2 mRNA and protein is dramatically up-regulated (Hu et al., 2009). It appears that in order to build an effective immunological protection for a post-weaning diet, the DC network of SOCS2 is up regulated, and inhibits the JAK-STAT signaling cascade of the GH, as it takes over growth control at IC-transition.

Endocrine changes at weaning/supplements added

Circulating leptin concentration increases markedly after 34 weeks gestation and bears a close temporal relation with the exponential accumulation of body fat mass during that period (Ng et al., 2001).

Breastfeeding influences leptin, ghrelin and IGF-I in infancy, mainly during the first 4 months of life. During the first 4 moonths of life, formula-fed infants compared to breast-fed

show higher ghrelin levels, higher IGF-I levels and lower leptin levels. A multiple regression analysis showed an inverse correlation between ghrelin and leptin values and between IGF-I and leptin levels(Savino et al., 2005).

The GH/IGF1 axis

GH circulating levels are high in the fetus and newborn compared with those in later childhood and in adults (Adcock et al., 1997;Adrian et al., 1983;de et al., 1990;Gluckman et al., 1981;ynsley-Green et al., 1977) and IGF-I levels are low, resembling a GH insensitivity state. During infancy, growth is regulated mostly by nutrition, insulin, and IGF-I. The transition between infantile growth and childhood growth is associated with the activation of the GH axis, evading the GH insensitivity pattern, as evident from increasing serum IGF-1 and IGFBP3 at age 9 months(Milsom et al., 2008) during normal ICT. Indeed, children with DICT have also a delay in their IGF1 rise (Xu et al., 2002). A negative association between IGF-I at 9 month of age and at 17 years supports the hypothesis that the IGF-1 axis is programmed at ICT(Larnkjaer et al., 2009).

During infancy, GH is constantly secreted. As the infant matures, the frequency of total arousals, cortical arousals, and subcortical activations decrease affecting GH-inhibitory REM sleep and GH-stimulatory NREM sleep(Montemitro et al., 2008). This maturation process was found to be similar in breastfed and bottle-fed infants across the different ages and sleep pattern changes(Montemitro et al., 2008).

Hormones in breast milk

Human milk is a source of various hormones and growth factors that are obviously missing in any formula. Adiponectin found in human milk is primarily of the active high-molecular-weight octadecamer (18mer) form. Median adiponectin concentrations were >40 times those of leptin concentrations. Given the importance of adiponectin in inflammation, insulin sensitivity, and fatty acid metabolism, milk adiponectin may influence infant development. **Adiponectin decreases through lactation/infancy phase**, each month of lactation is followed by decrease of 5-10% in milk adiponectin concentration(Woo et al., 2009). Adiponectin receptor 1 is expressed in fetal small intestine and may directly affect intestinal maturation. Adiponectin has been shown to increase insulin sensitivity, and may augment insulin's action in the gut(Martin et al., 2006).

Comparison of ghrelin values for lactating women showed lower concentrations in colostrum, transitional milk and mature milk than in the corresponding plasma samples. Obestatin, which is derived from the same gene as ghrelin, is higher in colostrum and mature milk than the corresponding blood levels of the mother. In contrast, leptin levels in colostrum and mature milk are more than five-fold higher than the corresponding blood levels (Woo et al., 2009).

Breast milk contains IGF-I, IGF-II, IGFBP-1, IGFBP-2, and IGFBP-3. IGFBP-3 levels are high from day 4 to day 6 and then decrease by days 10-12. In contrast, IGF-I and IGF-II and IGFBP-1 and IGFBP-2 show little change over the first 2 weeks after birth. Subsequently, all the IGF

components show a moderate decline over approximately the first 1-3 months and then stable levels up to transition to childhood at 9 months(Milsom et al., 2008), when levels increase substantially(Leger et al., 1996).

Gut hormones

The GI tract is the largest endocrine organ in the body and an important source of regulatory peptide hormones. Beside their major role in regulation of GI function, gut hormones have an important role in energy homeostasis. They respond briskly to breastfeeding. At the 9-months transition to childhood, postprandial breastfed infants have lower insulin, insulin-glucagon ratio, gastric inhibitory polypeptide, pancreatic polypeptide, and cholecystokinin than formula-fed infants. A difference in the opposite direction was observed for plasma gastrin levels. No significant differences appeared between postprandial breastfed and formula milk fed infants in blood glucose, plasma glucagon, vasoactive intestinal polypeptide, motilin, enteroglucagon, secretin, or neurotensin concentrations after feeding(Salmenpera et al., 1988).

Ghrelin

Ghrelin is a 28 amino acid peptide originally isolated from rat stomach as an endogenous ligand for the GH secretagogue receptor (Kojima et al., 1999). It is mainly produced by endocrine cells in the oxyntic mucosa of the stomach. Intraduodenal infusion of long-chain fatty acids

suppresses circulating ghrelin levels, although not in the presence of a lipase inhibitor, suggesting that fat digestion is required to influence ghrelin release (Feinle-Bisset et al., 2005). The fact that 25% of the saturated fatty acids in milk are long-chain SFA and long chain and Oleic, linoleic and α-linolenic acid (ALA) are 31·26, 17·73 and 1·03 %, respectively may have an important role in ghrelin secretion(Wan et al., 2010).

In addition to the somatotropic effects of ghrelin, the peptide stimulates food intake and increases adiposity(Fak et al., 2007). In the developing rat, gastric density of ghrelin cells is low on suckling and greatly expanded after weaning (Bjorkqvist et al., 2002;Hayashida et al., 2002). Similar observations have been made in humans (Bjorkqvist et al., 2002;Wierup et al., 2002). Fak et al(Fak et al., 2007) showed that gastric ghrelin expression and plasma ghrelin concentration are maintained at a lower level by delayed weaning. They also found that the relation between gastric ghrelin expression and body weight was altered by delayed weaning. Thus, timely weaned rats displayed a positive correlation between ghrelin expression and body weight, while no such correlation was evident in animals with delayed weaning. They concluded that delayed weaning exerts a negative influence on ghrelin expression, and that commencement of solid food intake may trigger normal ghrelin expression. Thus, the GH secretagogue ghrelin may constitute a hormonal link between weaning, the GH-IGF1 axis and growth.

Weaning and growth in a malnourished environment

Protein-energy malnutrition is a syndrome resulting from interaction between poor diets and diseases, leading to anthropometric deficits and generally with deficits in micronutrients

(Faruque et al., 2008). Three anthropometric indices are commonly-used indicators of malnutrition: weight-for-age (underweight), height-for-age (stunting), and weight-for height (wasting). A deficit in any one of these indices reflects malnutrition, and a z-score below -3 reflects a severe form of that condition (Faruque et al., 2008). In developing countries, an estimated 50.6 million children aged less than five years are malnourished, and those who are severely malnourished with a severe illness leading to hospitalization face a case-fatality rate exceeding 20% (Faruque et al., 2008). Based on earlier studies demonstrating that exclusive breastfeeding reduces morbidity and deaths from common infectious diseases, the WHO estimated that promotion of exclusive breastfeeding for the first six months could avert the deaths of 1.3 million infants globally each year (Black et al., 2003). In non-industrious tribal societies, the duration of breastfeeding has been reported to be 29.0 ± 10.0 months among a sample of 113 such populations, concord with those at which key weaning transitions are biologically optimal for most normal healthy children (Sellen, 2001). In developing countries, the situation is by far less optimal. Although the prevalence of breastfeeding is very high in Bangladesh, appropriate breastfeeding is rarely practiced. Despite universal (97%) breastfeeding and a median duration of breastfeeding of over two years, the proportion with exclusive breastfeeding remains as low as 1.8 months. This short duration of exclusive breastfeeding is related to early introduction of plain water and breast milk substitutes. To meet their physiological requirements, infants aged above six months require high-quality complementary foods in addition to breast milk (Brown et al., 1995). Children in Bangladesh stunt their growth when they start to take complementary foods. In developing countries, weight gain of children commonly falters during infancy, between 3 and 15 months of age. Their transition to childhood

at age 15 months onward reflects the unfavorable energetic cue, leading to adult relative short stature(11), whereas after transition to childhood, no further deterioration has been observed (Shrimpton et al., 2001).

Evolutionary perspective

Trends in human evolution were precipitated by large-scale ecosystem changes, and research on bioenergetics is a central component of ecosystem ecology. Life history trade-offs result from limitations in the availability of critical resources such as energy or nutrients, necessitating decisions on the differential allocation of resources to costly traits.

Body size is intertwined with life history because it is critical to energy budget. At any given body size, a species that extracts higher quality foods from the environment has increased life history options for evolutionary fitness. On the other hand, while requiring more total energy, increasing body size improves heat retention and lessens the relative energy needed per gram of tissue(Schmidt-Nielsen, 1975). For the infancy-childhood transition to occur, the child must have a positive energy balance. Thus, the age when this transition occurs is influenced and delayed by disease(Karlberg et al., 1994), when energy consumption increases rapidly, and by undernutrition, GI infection and socioeconomic impediments (Liu et al., 2000;Liu et al., 1998), with insufficient energy supplies.

DICT is the main mechanism resulting in short stature in children living in poor areas of developing countries. In a community-based longitudinal study in Lahore, Pakistan, the median

ages of the transitions were at 15, 13, 10 and 9 months in the suburban village, urban, and Swedish control groups, respectively(Liu et al., 1998). Among the poorest suburban children of Lahore, who suffer frequent infections and undernutrition, 35% have DICT, and among the poor children of Malawi, Africa, as many as 60% have a delayed IC growth transition(Liu et al., 1998). Many of them have growth transition that occurs at 3–4 years of age, which compromises their prepubertal height by 15–20 cm, culminating in mean adult male and female heights of 162.5 and 155 cm, respectively(Zverev and Chisi, 2004). It has been suggested that relative length of breast- and transitional feeding is inversely related to adult diet quality(Sellen, 2009): programming for smaller size that is appropriate for low adult diet quality requires later infancy-childhood transition and longer breast- and transitional feed.

We have proposed that the transition period from infancy to childhood growth phases corresponds to a period of plasticity in growth that has evolved to adjust an individual's growth to environmental circumstances, such as limited energy resources (Hochberg and bertsson-Wikland, 2008). The ability of the genotype to produce different phenotypes in response to environmental circumstances, and plasticity (the ability of the individual to modify phenotypic response to altered environmental conditions) of the timing of life history transitions, such as the infancy childhood growth transition, is evolutionary strategy and the basis for this adaptability (Kuzawa, 2005). Whereas the evolutionary origin of the switch and control mechanisms for onset of the childhood growth phase is genetic, we speculate that the plasticity of the transition switch responds to the environment, and more specifically to weaning from breastfeeding.

Weaning age is plastic and sensitive to ecological factors that constrain maternal ability to meet the increasing energy needs of growing offspring and the ability of infants to survive without mother's milk(Sellen, 2007).

Sellen suggested coevolution of human life history and lactation biology (Sellen, 2007). As compared to other mammals, primates' milk is lower in volume, more dilute, lower in energy, fat, and protein, and higher in lactose than would be predicted by body size. From a nutritional perspective, nonhuman primate postnatal life has been divided into phases of exclusive suckling, transitional feeding, and weaning, separated by two key life history markers - first consumption of solid food and weaning (Sellen, 2007).

Cross-species comparisons have generated several models to predict ages at which primates are adapted to terminate lactation, which include: five times the length of gestation, tripling or quadrupling of birth weight and attainment of one third adult weight (Sellen, 2007). When applied to humans, each model yields a wide range of predicted values. Hominids wean their babies significantly earlier than most other apes do, and all evidence suggests that the basic composition of human milk, its basic functions in the infant, and its mechanism of secretion and delivery remained unchanged during seven million years of human evolution(Sellen, 2009). The most remarkable change is the human use of complementary foods, which is unique among mammals (Sellen, 2007) and results in a pattern of transitional feeding that appears to be fundamentally different from that of other primates. In contemporary human societies, breastfeeding is even shorter.

Perspective:

We have suggested that an evolutionary perspective is useful in understanding various components of human growth patterns. Humans are a species with relatively short infancy and a unique life history stage of childhood. Childhood, as an essence of humanity, has made possible our long life, and evolution has geared us toward emphasis on brain development, which requires a high parental investment in a few progeny with a high probability of surviving. The transition from infancy to childhood is marked by weaning and growth acceleration. This strategy evolved to allow a period of nutritional deprivation during that crucial transition stunts growth to lower adult stature. This provides an evolutionary basis for the strong epidemiological evidence that early weaning is associated with greater adult stature and obesity. This perspective argues for reevaluation of the current recommendations issued by the leading health authorities on the preferred weaning age. Such recommendations should also take into consideration the evolutionary development aspect of the infant/toddler.

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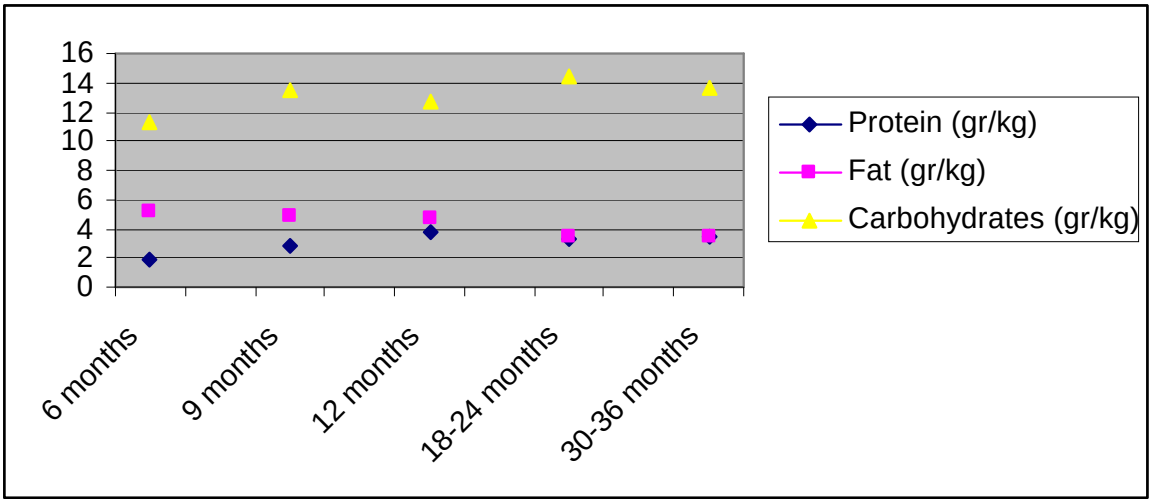

Figure 1: Food composition according to age and type of feeding

For the age of 6 months food composition is based on exclusive breast feeding. For later ages food composition is based on breast feeding or formula plus complementary feeding according to age.

Table 1: Typical food composition according to age and type of feeding

Age Type of feeding	Kcal (Kcal/kg)	Protein grams (gr/kg)	Fat grams (gr/kg)	Carbohydrates grams (gr/kg)
6 months **Average weight 8kg**				
Breast milk	800 (100)	15 (1.87)	42 (5.25)	90 (11.25)
Formula	780 (97.5)	19 (2.37)	38 (4.75)	90 (11.25)
Formula plus complementary feedings	890 (111)	20 (2.5)	38 (4.75)	115 (14.3)
9 months **Average weight 9.2kg**				
Breast milk	920 (100)	23 (2.5)	47 (5.1)	102 (11.08)
Formula	920 (100)	26 (2.82)	45 (4.9)	102 (11.08)
Formula plus complementary feedings	1000 ((108.7)	26 (2.82)	45 (4.9)	124 (13.47)

12 months **Average weight** **10.2kg**				
Breast milk	1050 (103)	35 (3.43)	50 (4.9)	115 (11.3)
Formula	1040 (102)	38 (3.72)	48 (4.7)	115 (11.3)
Formula plus complementary feedings	1100 (107.8)	38 (3.72)	48 (4.7)	130 (12.74)
18 months **Average weight** **11.8kg**	1200 (102)	38-40 (3.3)	40 (3.39)	170 (14.4)
24 months **Average weight** **12.7kg**	1300 (102)	40-42 (3.3)	45 (3.54)	182 (14.3)
30 months **Average weight** **13.5kg**	1350 (100)	47-48 (3.5)	47 (3.48)	185 (13.7)

36 months **Average weight** **14.5kg**	1450 (100)	50-51 (3.5)	50 (3.44)	200 (13.8)