What Is Known? Short-Term and Long-Term Effects of Complementary Feeding

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Introduction

Much is known about the short-term effects of complementary feeding (CF), especially how an optimal diet can prevent poor growth, malnutrition and nutrient deficiencies. The CF period has always been identified as a period during which the infant has a high risk of developing stunting, protein-energy malnutrition and specific nutrient deficiencies such as iron-deficiency anemia and rickets. Furthermore, during this period, the risk of infectious diseases increases dramatically and the mortality from infectious diseases during this age is closely associated with the nutritional status. It has been estimated that malnutrition is a contributing factor in more than half of the deaths of children below 5 years and a considerable part of these deaths happen during the CF period [1]. If resources and good hygiene are available and if the caregiver has the required knowledge, it is not difficult to provide a sufficient CF diet which will prevent poor growth and severe nutrient deficiencies.

However, we are only beginning to understand how feeding during this sensitive period characterized by high growth velocity influences the growth pattern, development and health during later childhood and adulthood. The emerging knowledge about programming or early origin of adult diseases has previously focused on the intrauterine and the early postnatal period, but there is increasing evidence that nutrition and growth velocity during the CF period also has important long-term effects. We know that CF is a determinant of growth velocity and there are some data showing that growth velocity during this period is associated with risk factors for later development of cardiovascular disease and metabolic syndrome [2, 3].
This chapter will discuss some of the existing recommendations on CF from developing and industrialized countries. Furthermore, some aspects of macronutrients (fat, protein) and the use of cow’s milk will be reviewed, ending with a discussion of the research issues that need to be addressed if we want to optimize CF. This will focus on the potential long-term effects of CF.

**Complementary Feeding in Low Income Countries**

In low income countries the feeding period, from 6 to 18 months, is critical for the promotion of optimal growth, development and health. Global statistics have helped to identify this period as the time when malnutrition and stunting develops. In figure 1 the SD scores (Z scores) of weight-for-age and height-for-age are shown for the three regions, Africa, Asia and Latin America, including the Caribbean, compared with the current WHO reference data [4]. For weight-for-age there is a marked decrease from the age of 3–6 months until the age of about 12 months. After that there is no further deterioration indicating that children after the age of 12 months have an average weight gain very close to the reference population. For length-for-age the pattern is almost the same except that the deterioration is slower and lasts longer, until about 24–36 months. The increase at 24 months is an artifact as the reference data are constructed with the children lying down until the age of 24 months after which they are measured standing. Thus, the dramatic deterioration in nutritional status, resulting in a high prevalence of malnutrition and stunting, happens exactly during the CF period. After this period there is no further decrease and also no catch-up. These data support other studies showing that, at least at the population level, it is very difficult to reverse stunting after the age of 2 years [5, 6]. The main causes of this deterioration are an insufficient CF diet, which typically has a low energy density, no or very small amounts of animal foods and a low content of essential micronutrients together with a high prevalence of infectious diseases.

The same pattern of growth deterioration during the CF period is also seen among infants and young children from industrialized countries with failure to thrive caused by an insufficient diet. A very illustrative example is the Dutch study of infants and children who received a macrobiotic diet (fig. 2), which is a diet with no animal products, high in fiber content and low in energy density [7]. The growth pattern of these infants and young children (fig. 2) was close to the pattern seen in many countries in Africa and Asia. These children also had a high prevalence of delayed motor development, rickets, iron and B_{12} deficiencies; all conditions that are common in developing countries [8].

Because of the health problems in low income countries, especially the high mortality in infancy and early childhood caused by low rates of breastfeeding and inadequate CF, the WHO has developed a comprehensive
global strategy on infant and young child feeding [9]. The promotion and protection of breastfeeding have been a high priority for the WHO for many decades, but it is more recently that CF has also been given a high priority. Several expert consultations on CF have been convened. The guiding principles for CF from a WHO global consultation on CF in Geneva in 2001 are...
shown in table 1 [10]. The scientific evidence for most of these guidelines has been summarized in a number of papers published in the same issue of the *Food and Nutrition Bulletin* [10] and in a review of the current scientific knowledge published by the WHO [11]. For some of the guidelines there is no strict scientific evidence. Instead, the guiding principles are based on the best available knowledge. Although these guidelines are mainly directed towards solving the global problems with malnutrition, poor growth and high mortality, most of the guidelines are highly relevant to industrialized countries as well. The guidelines focus on the duration of exclusive breastfeeding and age of introduction of CF, continuation of breastfeeding, amount, energy density, nutrient content and consistency of complementary food, meal frequency, the use of vitamin-mineral supplements and fortified products, safe preparation and storage, and feeding during illness. Furthermore, the guidelines emphasize responsive feeding, giving a set of principles for psychosocial care during feeding.

**Fig. 2.** Weight-for-age and length-for-age in children receiving a macrobiotic diet which is characterized by no animal products, a high fiber content and a low energy density. Reprinted by permission from European Journal of Clinical Nutrition [7], Copyright 1989 by Macmillan Publishers Ltd.

While the principles for a CF developed by the WHO as part of the infant and young child feeding strategy are global, they focus on preventing malnutrition, growth faltering and a high rate of infectious diseases. The guidelines followed in many industrialized Western countries, where these...
Table 1. Summary of the Guiding Principles for CF of the Breastfed Child [10]

1 Duration of exclusive breastfeeding and age of introduction of complementary foods
   Practice exclusive breastfeeding from birth to 6 months of age, and introduce complementary foods at 6 months of age (180 days) while continuing to breastfeed

2 Maintenance of breastfeeding
   Continue frequent, on-demand breastfeeding until 2 years of age or beyond

3 Responsive feeding
   Practice responsive feeding, applying the principles of psycho-social care. Specifically: (a) feed infants directly and assist older children when they feed themselves, being sensitive to their hunger and satiety cues; (b) feed slowly and patiently, and encourage children to eat, but do not force them; (c) if children refuse many foods, experiment with different food combinations, tastes, textures and methods of encouragement; (e) minimize distractions during meals if the child loses interest easily, and (f) remember that feeding times are periods of learning and love – talk to children during feeding, with eye to eye contact

4 Safe preparation and storage of complementary foods
   Practice good hygiene and proper food handling by (a) washing caregivers’ and children’s hands before food preparation and eating; (b) storing foods safely and serving foods immediately after preparation; (c) using clean utensils to prepare and serve food; (d) using clean cups and bowls when feeding children, and (e) avoiding the use of feeding bottles which are difficult to keep clean

5 Amount of complementary food needed
   Start at 6 months of age with small amounts of food and increase the quantity as the child gets older, while maintaining frequent breastfeeding. The energy needs from complementary foods for infants with ‘average’ breast milk intake in developing countries are approximately 200 kcal/day at 6–8 months of age, 300 kcal/day at 9–11 months of age, and 550 kcal/day at 12–23 months of age. In industrialized countries these estimates differ somewhat (130, 310 and 580 kcal/day at 6–8, 9–11 and 12–23 months, respectively) because of differences in average breast milk intake

6 Food consistency
   Gradually increase food consistency and variety as the infant gets older, adapting to the infant’s requirements and abilities. Infants can eat pureed, mashed and semisolid foods beginning at 6 months. By 8 months most infants can also eat ‘finger foods’ (snacks that can be eaten by children alone). By 12 months, most children can eat the same types of foods as consumed by the rest of the family (keeping in mind the need for nutrient-dense foods, as explained in item 8 below). Avoid foods that may cause choking (i.e., items that have a shape and/or consistency that may cause them to become lodged in the trachea, such as nuts, grapes, raw carrots)

7 Meal frequency and energy density
   Increase the number of times that the child is fed complementary foods as he/she gets older. The appropriate number of feedings depends on the energy density of the local foods and the usual amounts consumed at each feeding. For the average healthy breastfed infant, meals of complementary foods should be provided 2–3 times/day at 6–8 months of age and 3–4 times/day at 9–11 and 12–24 months of age. Additional nutritious snacks (such as a piece of fruit or bread or chapatti with nut paste) may be offered 1–2 times/day, as desired. Snacks are defined as foods eaten between meals – usually self-fed, convenient
problems are not common, focus also on other aspects of CF. Some countries have no official guidelines, while others have guidelines given by the health authorities or by pediatric associations. These recommendations are often based more on tradition and the availability of foods than on science.

The recommendations on CF covers some main issues: (1) duration of breastfeeding – exclusive and partial; (2) when to use infant formula and cow's milk; (3) the order in which different foods should be introduced and the consistency; (4) securing a sufficient energy intake through adequate energy density, fat content, and meal frequency; (5) prevention of iron deficiency; (6) prevention of micronutrient deficiencies, and (7) prevention of allergic diseases in infants with a family history of allergic diseases.

There are a number of issues in which the recommendations differ among the countries. Many countries have followed the WHO recommendation on exclusive breastfeeding for 6 months. However, some countries like Finland have maintained the recommendation that CF should be introduced between the ages of 4 and 6 months. Although the WHO recommends that breastfeeding should continue until the age of 2 years, most countries in Europe recommend that breastfeeding should continue until the age of 12 months or longer, without stating when it should be stopped. While many countries have no recommendations on when eggs could be introduced, some
state eggs could be introduced from the age of 6 months while several countries state that egg whites should not be introduced before the age of 12 months. The reason for this recommendation is to reduce the risk of allergy to eggs, but the advice is not evidence-based [12]. Recommendations on when to introduce cow's milk are mentioned in the section on cow's milk. Most countries recommend vitamin D drops while only some countries recommend vitamin A supplementation, which might be a remnant from the time supplementation with cod-liver oil, which contains both vitamins D and A, was common.

A set of guidelines based on infant and young child feeding and aimed at the WHO European region has been developed [13]. These guidelines are aimed at a group of countries including both highly industrialized countries and low income countries. The EU European region includes, in addition to Europe, all the former Soviet republics including the Central Asian Republics. Thus, it comprises highly industrialized Western countries, low income countries with poverty and high rates of infectious diseases and many countries in transition.

**Fat**

During the last decade there have been considerable discussions about the timing of the reduction of the dietary fat content during the CF period. Breast milk has a high fat content, about 50 energy percent (E%) and, in most countries, the recommended fat content of the family diet is 30 E%. The concerns have been that a fast reduction might reduce energy intake and thereby impair growth, and a too slow reduction could have a negative effect on risk factors of cardiovascular disease, especially if the intake of saturated fat is high. Furthermore, there has been concern that a high fat content could increase weight gain and thereby the risk of overweight.

No population-based studies from industrialized countries have shown an association between low fat intake and growth. In the Finnish STRIP study children with the lowest fat intake, which at 13 months was 22 E% from fat (FE%) and at 5 years 26 FE%, had normal growth [14]. However, in this cohort the children were monitored closely and growth faltering is likely to have resulted in some sort of intervention. In reviews considering data from developing countries, Uauy et al. [15] concluded that it was not before the FE% was <22 that there was a risk that growth was impaired. This is in line with the review by Prentice and Paul [16] who concluded that the FE% should be a minimum of 20–25 FE% to prevent growth impairment.

A high fat content will result in high energy density and thereby a theoretical risk of excessive weight gain, which is a concern in populations with a high prevalence of childhood obesity. However, there are several
studies in early childhood showing no association between fat intake and weight gain. In cross-sectional studies of 2- to 5-year-old children there were no associations between FE% and body mass index [17, 18] or body fat percent [19]. Furthermore, there was no difference in energy intake, weight, length or body composition at the age of 2 years in children receiving milk with 2 or 3.5% fat from the age of 12–24 months [20].

If the fat content of a diet is increased by adding oil, butter or margarine, the nutrient density of minerals and most vitamins and also other nutrients will be reduced as the intake of other foods will be reduced. In extreme cases, for example if a teaspoon of oil is added to a 100-gram serving of maize porridge prepared with water, the content of protein and iron will be reduced by more than 50%, when expressed per unit of energy. Therefore, if fat is added to the CF diet to increase energy density and prevent growth faltering it is important that only moderate amounts are added. Just adding 3 teaspoons of oil (15 ml) replaces about 14% of the energy needs of a 1-year-old infant.

A working group under the Danish Nutrition Council reviewed the literature about the possible associations between fat intake during the first 3 years of life and the risk of developing cardiovascular diseases later in life [21]. The working group found that there was a very limited scientific basis for evaluating the importance of fat intake during the first 3 years of life for later development of atherosclerosis. Although young children do develop fatty streaks in the aorta, they are reversible and are probably not influenced, to a major degree, by traditional risk factors for atherosclerosis. The working group found that these risk factors might influence the vascular function in children, but its importance for later development of atherosclerosis is unknown. Furthermore, no investigations have been carried out on whether the amount or quality of fat intake in the first 3 years of life influences the risk of developing atherosclerosis later on. The working group found that there was no risk of reduced growth if the fat content is above 25 E%. To avoid a very low fat E% there is a recommendation in Denmark that a teaspoon of fat or oil, preferably vegetable fat, should be added up to the age of 12 months to each serving of homemade mash and porridge, which otherwise will have a very low fat content, which was supported by the working group. Though a high content of saturated fat and cholesterol in the young child’s diet increases the cholesterol level in the blood, the cholesterol level during childhood is considerably lower than the adult level. As there are no positive effects of a high intake of saturated fat in this age group, the working group found it prudent to reduce the intake of saturated fat from the age of 12 months in order to establish healthy dietary habits. Therefore, it recommended that from the age of 12 months the intake of saturated fat should be reduced to the same level as that recommended for adults, i.e. maximum 10 E%. To reduce the intake of saturated fat it was recommended that from the age of 12 months children are preferably given semi-skimmed

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milk (1.5 fat%) and from the age of 3 years preferably low fat (≤0.5%) milk. The recommendations of the working group were adopted by the National Board of Health as official recommendations.

The dietary recommendations for the Nordic countries have recently been revised [22]. According to these, the FE% should be between 30 and 45 during the 6- to 11-month period, lowered to 30–35 during the 12- to 23-month period and, thereafter be between 25 and 35 with a population goal of 30 E%. This is a reduction compared to the previous recommendation. The reason for this reduction is that it was found that the evidence for a negative effect of a low fat intake on growth is not very strong.

There are many other potential health aspects of fat quality than the effect of saturated fat on cardiovascular risk factors. The effects of long-chain polyunsaturated fatty acids and especially the effects of the relation between n-3 and n-6 fatty acids on cognitive and visual development, growth and the immune systems have been studied in detail in early infancy where the interest has been to identify the optimal fat composition of infant formula. The composition of the fat intake during the CF period could potentially have the same effects and could also be of importance for the development of allergic diseases. However, only very few studies have explored the potential health effects of fat quality during this period. Such studies should be given high priority.

**Protein**

The average protein intake in late infancy is high, above the physiological requirements. Typically, it is 3–4 g/kg body weight, which is 3–4 times above the physiological requirements of about 1 g/kg body weight [23, 24]. However, some infants receive a protein intake which is much higher, i.e. 5 g or more. The short- and long-term effects of such a high intake are not clear.

A high protein intake results in high levels of amino acids in the blood which can have specific metabolic effects. Branched-chain amino acids stimulate insulin secretion that have a growth-stimulating effect during infancy [25] and some amino acids have hormonal effects or effects on neurotransmission. The potential effects of protein on growth is discussed in more detail in the section on cow’s milk intake below.

A high protein intake influences the size of the kidney, most likely through an effect of the glomerular filtration rate. In adults, a 6-month intervention study showed that an 18% increase in protein intake resulted in a 2.5% increase in kidney size [26]. A similar effect of protein intake is most likely the explanation that the kidneys were larger in 3-month-old formula-fed infants compared to breastfed infants [27]. At the age of 18 months when there was no major difference in diet, there was no difference, suggesting that the effect on size was reversible.
It has been suggested that a high protein intake during early life increases the risk of overweight and obesity later in life. Rolland-Cachera et al. [28] suggested that it could be caused by an increase in insulin-like growth factor-1 (IGF-1) stimulated by the high protein intake. This hypothesis is been tested in an ongoing large EU multinational project [29]. In a prospective longitudinal study of term infants we found that the protein intake at 9 months was not associated with any measure of body fat at the age of 10 years [30]. However, the group was small and there were only a few obese children at the age of 10. There was, however, an association between protein intake and weight and height at 10 years which might be explained by a growth-stimulating effect of early protein intake as explained in the following section on cow’s milk.

In a cross-sectional study of 2.5-month-old children we found a significant positive association between protein intake and systolic pressure [31]. The effect was substantial as a 1 SD increase in protein intake corresponded to a decrease in systolic blood pressure of 3 mm Hg. Such associations have also been found in older children [32] and adults [33, 34]. It has been speculated that this could be caused by certain amino acids mediated through the production of nitric oxide. It is unknown if the same effect of protein intake on blood pressure is also seen during the CF period and if such an effect could have long-term effects.

Cow’s Milk

In industrialized countries cow’s milk is an important part of the CF diet. In the WHO guidelines for CF, cow’s milk is not mentioned as it is assumed that the infant/young child continues to be breastfed up to the age of 2 years. In most industrialized countries this is far from the reality and cow’s milk is an important part of the diet, as a supplement to breast milk during late infancy, or as a substitute for infant formula when the child has reached an age where it is recommended to change from infant formula. Recently, a technical background paper commissioned by the WHO on the feeding of the non-breastfed infant was published, together with guiding principles from an informal working group [35]. The need to provide a sufficient diet to non-breastfed infants from HIV-positive mothers was one of the reasons for providing these guidelines. According to these guidelines undiluted cow’s milk could be introduced from the age of 6 months, provided that iron supplements or iron-fortified foods are given and the overall amount of fluid is sufficient.

Recommendations for the intake of cow’s milk in industrialized countries differ considerably among countries. Many countries recommend that cow’s milk is not introduced before the age of 12 months. The most important reason for this recommendation is the iron status. Cow’s milk has a very low iron content and the iron in the milk is poorly absorbed, while infant formula
is iron-fortified. Some countries recommend that cow’s milk be gradually introduced from the age of 9 (Denmark) [36] or 10 months (Sweden) [37]. To solve the iron problem in Denmark it is recommended that infants not getting at least 400 ml of iron-fortified formula between the ages of 6 and 12 months should have medicinal iron. In the WHO/UNICEF guidelines for CF for the European region, which also covers some low income countries, the recommendations are that cow’s milk should not be given before the age of 6 months [13]. In the period from 6 to 9 months only small quantities (e.g. in mashes) should be given. Milk should not be given as a drink before the age of 9 months, after which it can be introduced gradually. Once it is introduced the amount should not be more than 500 ml to secure a diversified diet.

Cow’s milk has both positive and negative effects [38]. It contains high-quality protein, is a good source of important micronutrients and is an important calcium source. Furthermore, it contains peptides and other potential bioactive sources which might have beneficial effects. On the negative side, it is a poor iron source with a low iron content and a poor bioavailability, it may cause gastrointestinal bleeding, especially during the first 6 months of life, it has a high protein and mineral content resulting in a high potential renal solute load and has a high content of saturated fat.

New data suggest that cow’s milk can stimulate linear growth in young children, even in those who are already receiving an adequate diet with high protein content. In a cross-sectional study of 2.5-year-old children we found a significant positive association between milk intake and height and IGF-1 levels [39]. These data were supported by an intervention study we performed in 8-year-old boys [40]. A very high intake of skimmed milk (1.5 liters/day) for a week resulted in a 20% increase in IGF-1 levels while an intake with the same amount of protein from meat had no effect on IGF-1 levels. Surprisingly, the milk also resulted in a 100% increase in fasting insulin levels, while there were no effects on fasting glucose levels [41]. The meat intake had no effect on insulin levels. The stimulation of insulin levels by intake of cow’s milk is supported by meal studies of the effect of different foods on the insulin index. It was shown that the insulin levels after intake of milk was considerably higher than after other foods, while the glycemic index of milk was lower than the glycemic index of several other foods [42]. In an evolutionary perspective it is not surprising that milk and not meat stimulates growth. Milk has evolved as a diet to support the newborn during a period of high growth velocity, which is not the case with meat. Thus, the traditional concept that growth is optimal if there are no deficiencies may be too simplistic.

It has not been shown that cow’s milk given during the CF period can stimulate growth and IGF-1 levels, but we find it likely that it is also the case during this period. It is well established that infants receiving infant formula based on cow’s milk have a higher linear growth velocity and a higher weight gain than breastfed infants [43], which could be caused by a growth-stimulating factor in cow’s milk not present in breast milk.
If cow's milk intake has an effect on growth velocity during the CF period it is not known if this has a lasting effect or if it will be compensated later during childhood and if it has any positive or negative effects on health.

**Research Recommendations**

The current interest in CF has resulted in two sets of research recommendations. The many research issues and questions that need to be addressed to improve the understanding and practice of CF were discussed in a workshop arranged by the International Paediatric Association (IPA) and the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in Casablanca 1999 [44]. The proceedings include a number of short papers, many of which have included research recommendations. The workshop also agreed on a number of more general recommendations that are given in table 2.

The global expert consultation on CF held by WHO/UNICEF in Geneva 2001 recognized that although the evidence for the guiding principles decided on (table 1) were sound, further research was needed to broaden and refine

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**Table 2.** Recommendations on research issues that need to be addressed, identified by the IPA/ESPGHAN workshop in Casablanca 1999 [44]

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<th>Research Question</th>
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<tr>
<td>How should ‘optimal’ growth and body composition be defined and appraised?</td>
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<td>Long-term studies of functional outcomes related to growth and body composition during the period of CF and to CF itself are needed</td>
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<td>How does CF influence the development of taste and smell and appetite control?</td>
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<td>What impact does CF have on the development of immunotolerance, enteropathies, and atopic disease?</td>
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<td>Does CF affect metabolic imprinting or programming?</td>
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<td>Is health in later life influenced by CF?</td>
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<td>Does the timing of introduction or amount of complementary foods affect breast milk frequency and intake, and the duration of breastfeeding?</td>
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<td>How does CF interact with and influence the physiologic maturation and metabolic competence of infants to digest, absorb, and metabolize non-breast milk and non-formula-based foods?</td>
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<td>What are the accurate nutrient requirements during infancy?</td>
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<td>What strategies would improve nutrient supply and bioavailability in complementary foods?</td>
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<td>Should complementary foods be different for breastfed and formula-fed infants?</td>
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<td>What are the potentially modifiable constraints to adoption of parenting practices that are geared to children's developmental and nutritional needs, and to the maintenance of food safety?</td>
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The consultation identified the research priorities shown in Table 3. The strategies and interventions [10]. The consultation identified the research priorities shown in Table 3.

**Future Directions**

We know how to feed the infant and young child during the CF period to avoid malnutrition, growth retardation and micronutrient deficiencies. The challenge in developing countries is to implement strategies that secure the infants an optimal feeding during this critical period. Both the WHO and UNICEF have given this a high priority through the Global Strategy for Infant and Young Child Feeding. This strategy also identifies the difficult situations that require special attention. These include infants and young children that

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<th>Table 3. Research priorities identified by the WHO global expert consultation on CF in Geneva 2001</th>
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<td>Estimating energy and nutrient requirements of children living in especially vulnerable circumstances, such as infants of HIV-positive mothers who choose to breastfeed, preterm infants, and low-birth weight infants</td>
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<td>Assessing the effects of variations in energy density, feeding frequency, food quantity, and food variety on total energy intake, including the intake of breast milk</td>
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<td>Identifying factors affecting children's appetite and appropriate treatment of anorexia</td>
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<td>Determining the optimal amount and type of lipid and fiber intake by children</td>
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<td>Examining the use of linear programming for developing context-specific CF guidelines</td>
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<td>Identifying alternative approaches to create demand for affordable and effective processed food products</td>
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<td>Assessing the efficacy and effectiveness of fortified complementary foods, sprinkles and spreads in addressing dietary gaps, including optimal levels of formulation and ration sizes to improve nutrient intakes</td>
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<td>Determining the bioavailability of iron and zinc in locally available foods</td>
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<td>Determining methods and criteria for characterizing the responsiveness of feeding styles in various settings and identifying effective methods for promoting responsive feeding</td>
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<td>Determining the impact of improved responsive feeding on child growth and developmental outcomes</td>
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<tr>
<td>Developing and testing appropriate and effective strategies to ensure the safe storage, preparation, and feeding of complementary foods to infants and young children</td>
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<td>Developing strategies for maintaining and sustaining breastfeeding as complementary foods are introduced and the young child progresses to the family diet</td>
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<tr>
<td>Developing and testing indicators and tools for designing, implementing, and evaluating programs promoting appropriate infant and young child feeding</td>
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are already malnourished, low birth weight infants, infants of HIV-infected mothers, and infants and young children that are victims of natural or human-induced emergencies.

In industrialized countries the challenge is to understand the potential long-term effects of CF. There is increasing evidence that postnatal nutrition and growth play an important role in the early origins of adult disease hypothesis [45] and that CF is likely to program long-term effects. Breastfeeding has many positive long-term effects and it is plausible that other foods given during infancy and early childhood can also have long-term effects. However, the evidence for such effects is not strong at present.

With the alarming increase in overweight, obesity and allergic diseases during childhood, it is of special importance to explore if the risk of developing these conditions could be reduced by optimizing CF. Regarding this there are a number of areas that are of special interest.

**Gastrointestinal Microbiota**
How is it influenced by the composition of CF?
What are the effects of pre- and probiotics?
Is there a long-lasting effect of the timing of the introduction of CF?
What is the influence of non-digestible carbohydrates?

**Gastrointestinal Barrier**
There seems to be a marked effect when CF is introduced to the exclusively breastfed infant and the function of the gastrointestinal barrier seems to be important for the development of allergic diseases.
What are the mechanisms?
How does the introduction of different foods influence the gastrointestinal barrier?

**Maturation and Polarization of the Immune System**
What is the need for n-3 fatty acid content of the CF diet? How does the n-3/n-6 balance affect immune function?
Is there a long-term effect?
How does the gastrointestinal microbiota influence the immune system?

**Obesity**
Is there an effect of protein intake on later development of obesity?
Does the composition of the CF diet, especially the fat quality, have an influence on body composition on the short- and the long-term?
Do the changes in body fat content during the CF period influence body composition on the long-term of the early n-3/n-6 intake?
Does the gastrointestinal microbiota have an influence on the risk of obesity?
Food Preferences and Appetite

How does the composition of the CF diet and the diversity affect later food preferences?

How is appetite regulated during the CF period?

How is the CF diet influencing leptin levels?

References

Short- and Long-Term Effects of Complementary Feeding


**Discussion**

Dr. Vaarala: You showed that drinking milk causes high production or release of insulin. Have you any evidence that insulin resistance is induced by drinking milk?

Dr. Michaelsen: Strictly speaking these children had some degree of insulin resistance because they had normal fasting glucose and increased insulin levels compared to baseline [1]. However, the intervention lasted for only 1 week and we examined the effect of a milk intake (1.5 liters/day) much above the recommended intake, so based on our data we cannot say that milk causes insulin resistance. I know that there are studies by Nilsson et al. [2] from Sweden showing that milk is especially effective in stimulating insulin secretion after a meal and it seems as though specifically whey stimulates insulin, but they only studied the acute effect after a meal and after some hours the insulin values were down to starting values.

Dr. Vaarala: I only wanted to say that there are two studies, one from Australia [3] and one from Finland [4], in which a high intake of milk during childhood has been associated with the risk of type-1 diabetes. It could be that an increase in insulin and insulin resistance enhances the presentation of insulin to the immune system, which may be the factor. This is really a fascinating study.

Dr. Michaelsen: Do you know how high the milk intake was? What were the levels?

Dr. Vaarala: It was more than 3 glasses/day, so more than 600 ml/day.

Dr. Michaelsen: I think it is important that children don't get much more than 500 ml milk as recommended in some countries in order to keep the diet diversified. I think milk is an important part of the diet, providing important micronutrients. Furthermore, it seems that milk stimulates linear growth, which is important in developing countries where stunting is common. The long-term effects of such a growth stimulation in industrialized countries is not known.

Dr. H. Hoekstra: What is the actual recommendation concerning cis and trans fatty acids for the young child?

Dr. Michaelsen: I don't know. Perhaps Dr. Hernell could answer. He participated in the EU working group on infant formula under the Scientific Committee on Food.

Dr. Hernell: In infant formula I think the most recent recommendation, which is the European Union revised infant formula directive of 2003 (5) is to keep trans fatty acids as low as possible and a maximum level was set to 3% of total fatty acids.

Dr. Michaelsen: But the discussion about trans fatty acids is whether cow's milk trans fatty acids count as much as hydrogenated.

Dr. Hernell: In that recommendation we didn't discuss the potential difference between different sources of trans fatty acids.

Dr. El-Din Amry: What do you mean by cow's milk? Is it raw milk?

Dr. Michaelsen: Here I mean pasteurized cow's milk with a normal fat content or a low fat content. It is not cow's milk-based infant formula.

Dr. El-Din Amry: But in developing countries excessive consumption of cow's milk could lead to rickets because of the calcium phosphorus ratio.

Dr. Michaelsen: I didn't know that. I know that, in developing countries where milk is not part of the diet, if there is a very low calcium intake this could cause rickets.

Dr. El-Din Amry: It is not because of the calcium intake but because of the calcium phosphorus ratio in the milk. The calcium absorption from the intestine could lead to rickets and it is advised that vitamin D supplementation is given in this case.

Dr. Michalesen: Many countries recommend universal vitamin D supplementation, and in countries where rickets is prevalent this should be considered. At this meeting we also heard that vitamin D could be important for diabetes prevention.

Dr. Steenhout: A recent article published in Pediatrics [6] showed that multivitamin supplementation increases the risk of atopy and asthma in certain sub-classes of the
population. The authors were speaking about a whole range of vitamins but also more specifically about the risks of vitamin D supplementation. What is your opinion on that?

Dr. Michaelsen: I don't think I have any further comments. We are faced with a lot of research data that are difficult to draw public health conclusions from. Also some of the data I gave on cow's milk are difficult to transform into simple advice. So there is still a lot to do in complementary feeding research.

Dr. Schmitz: One comment that can be made from the workshop and from what you said is that the pros and cons for every nutrient must be taken into account, and this is difficult for cow's milk for example. In your talk you did not comment on solids and the number of solids. In my talk, I stressed the fact that the introduction of too many solids too early was dangerous. In the European document you showed us, are there data concerning the number and the timing of solids?

Dr. Michaelsen: No, we didn't make a recommendation on that. I know that several countries recommend that one food at the time be introduced in order to be able to know if there are allergic reactions, but as far as I know this is not evidence-based. I think it makes it too complicated and too disease-oriented.

Dr. Schmitz: I agree with you completely.

Dr. Caroli: Thank you very much for your absolutely wonderful presentation. As you said, in Italy we have a very high intake of protein during weaning, even during the first year of life between 6 and 12 months of age, we even have an intake of 5 g protein/kg. The reason for this is that pediatricians use this to increase iron intake, which is really a silly thing because in meat baby food in Italy the iron content is not labeled. There is not enough advice given to pediatricians on the use of fortified supplemented iron or cereals. There is a WHO declaration saying that it is impossible to reach the recommended iron level if you don't use unrealistic and unbelievably high amounts of meat. I think that this should be stressed for teaching mothers how to wean because otherwise we will still have this problem of protein intake and obesity and so on. What do you suggest?

Dr. Michaelsen: I think that iron-fortified complementary foods have a place in some situations, but I don't think we should restrict meat intake because of the fear of protein intake. In any case infants and young children don't eat large beef steaks; they eat small amounts of minced meat. If we address the issue of iron supplementation, we are not addressing the zinc issue. Meat is a good source of zinc and also other nutrients. I think it is important to introduce meat as part of the complementary feeding diet. Most countries recommend its introduction at about 6 months. Last week in Milan there was a discussion on meat introduction and I was very surprised to see that there was such a lot of reluctance among Italian pediatricians to introduce meat early. They talked about the histidine content of meat; they talked about mad cow's disease; they talked about other diseases in chickens. So people are very afraid and I don't think these issues are appropriate. I think meat is an important part of the complementary feeding diet.

Dr. Moreno Villares: When you recommend less than 0.5 liters of milk, does this also apply to the dairy products or only milk?

Dr. Michaelsen: I think in some countries dairy products are included. This is not a very sharp limit but I think for the diversity of foods we shouldn't feed our children too much milk. Once in a while in Denmark we see children being admitted with severe iron-deficiency anemia. They drink 1.5 liters of milk (so-called milkaholics) because the child and the mother think that it is a very easy way to cover the needs. So I think we should be active in keeping milk intake at a reasonable level.

Dr. Wei Cai: During your talk you mentioned that a high protein intake could induce a high prevalence of obesity. A couple of papers published recently recommend 4 g amino acids/kg/day. Is there a long-term effect in children?

Dr. Michaelsen: I mentioned the hypothesis that a high protein intake could induce obesity but I don't think it has been proven. There have been a few studies...
showing an association and a few studies showing no association. There is a large ongoing multinational study in Europe addressing this. So I don’t think we should cut down on protein for obesity, we don’t have the evidence.

**Dr. Mexitalia:** You mentioned the high protein intake, but in most developing countries the animal source protein intake is very low and the problem is the low protein intake. What is the recommended protein energy ratio?

**Dr. Michaelsen:** A protein intake at 10–15 energy percent would be adequate. In developing countries protein intake can be a problem, especially if there are no animal sources and only few vegetable protein sources. If there is a mix of vegetable protein the situation is better, and many studies have shown that if it is possible to add a little animal protein, not only because of protein quality but also because of the minerals and other micronutrients to be gained from animal food, then there might be a considerable stimulation of growth and thereby improved health. So I think if a little animal food can be given with a mixed vegetable diet, then protein problems would be very rare.

**Dr. Mexitalia:** If we want to increase the energy density we can add oil, but it would lower the protein energy.

**Dr. Michaelsen:** That is right. But again breast milk, which is the food with the highest growth velocity, contains only 5 energy percent of protein, but it is of high quality. So for a composite diet 10–15 would be appropriate.

**Dr. Lafeber:** During the ESPGAN meeting in Paris in July 2004, Dr. Rey told me that the European Committee, which advises on normal formulas, is no longer recommending follow-on formulas. Looking at the continuity of protein in formulas, just regarding normal infants, not special formulas, and the introduction of cow’s milk, some attempts have been made to lower the amount of protein in formula milk. There is now a formula available with I think 1.8 g of protein/100 kg/cal. That is alright, but it is advised that the formula be given for 6 months and then changed over to a follow-on formula, particularly with iron in it. But if there is now a new European recommendation that no longer advises the use of follow-on formulas, then the only way out is to introduce cow’s milk with a high protein content at 6 months.

**Dr. Michaelsen:** In the report with suggestions for a new EU directive on infant formula, it is recommended that follow-on formula has the same protein content as infant formula [7].

**Dr. Lafeber:** Also the continuity of a low protein formula. Of course if you have that and then at 6 months change to a protein-fortified follow-on formula, that doesn’t make sense either.

**Dr. Michaelsen:** My personal idea is that we don’t need a follow-on formula. We can stay with the starter formula throughout. With the low protein content we might then, at least for the first 6 months, get a lower growth velocity, as Dr. Singhal also stated, which might then result in a lower growth velocity with potentially beneficial effects. What the optimal growth velocity from 9 to 12 months is, and what the protein content should be, I don’t think we really know.

**Dr. Bee Wah Lee:** Is there any negative effect of using a soy formula in place of a cow’s milk-based infant formula?

**Dr. Michaelsen:** The report from the Scientific Committee on Foods on Infant Formula concludes that there are no nutritional advantages to using a formula with soy as the protein source [7]. Furthermore, they mentioned some potentially negative effects that have not been fully evaluated, and advocate that the effects of soy-based infant formula needs to be better evaluated.

**Dr. Caroli:** As far as I know, in Italy at least, the high protein intake is always associated with a very low fat intake because, when looking at some old nutrients used in the traditional way of weaning in Italy, it is found that even at 8 months of age or 11 or 12 there is only 30% of the fat calorie intake.
Dr. Michaelsen: What kind of protein is given to the infants when there is no fat in it? It is my impression that much of the protein is from milk, from cheese, and from meat. Of course some of the meats given will be pretty lean, but is it because a lot of meat is given that there is not so much fat?

Dr. Caroli: In Italy pediatricians use a meat baby food which is very low in fat. When a baby eats 80 g of baby food, he cannot eat many other things. If the nutrients in the traditional Italian way of weaning are counted, then it is found that the fat intake is very low. I am worried about brain growth in the first 2 years of life. What is your opinion? Are there any data on that?

Dr. Michaelsen: I think brain growth is not so much a question of total fat content, but fat composition might have an effect. There must be a reasonable balance between n-3 and n-6 and, if that is not the case, it might influence brain and psychomotor development. As I said, in most children a fat content of about 30% would not cause growth retardation. If a low fat content is found in combination with a mother who is not very responsive to the hunger and satiety clues of the infant, an infant who eats only a few meals a day and perhaps has many infections, a low fat content might be a limiting problem. For some years I was more worried about a low fat intake but as long as it is about 30 fat energy percent, it is not very likely that fat intake will have a negative effect on growth.

Dr. Lafeber: You showed us Dr. Singhal's slide which also provokes the question: what is optimal growth? One of the observations made by Dr. Singhal and Dr. Lucas is that there is a period of in utero growth restriction resulting in intrauterine growth retardation, and there is growth restriction shortly after birth because, in the case of low birth weight, it takes a while before proper nutrition can be given, and often there are signs of malnourishment. If you do not react to this with an adapted diet and give a low protein diet, it has been demonstrated that the brain will not develop properly, so we are very much in favor of at least giving enough protein to spare the brain. But then comes the question of how long we should continue that protein gain. Regarding the Barker hypothesis, it is always said that if there is an insufficiency before birth and an insufficiency after birth, then there is no problem, there will be no disease, there will be no heart disease, there will be no type-2 diabetes. But if you are supplying very rich formulas after birth then the problems start. I think it is the same in these preterm infants, they must be given more protein for brain development at a certain time, but then there is a risk if the diet is continued for too long a period. What are your thoughts on this?

Dr. Michaelsen: Neonatologists often ask about the optimal growth rate of preterm infants. It is a very difficult question for which I have no clear answer. There are studies showing both positive and negative effects of a high growth velocity, depending on the outcome. The long-term effects of growth velocity are likely to be different for term and preterm infants, and depend on a time window. The first 6 months could be very different from the effects of growth velocity during the last part of infancy, when complementary feeding influences growth velocity.

Dr. Lafeber: There is still a lot to be studied regarding insulin growth factor insensitivity and sensitivity.

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