Whole Cow’s Milk: Why, What and When?

Kim Fleischer Michaelsen, Camilla Hoppe, Lotte Lauritzen, Christian Mølgaard

Department of Human Nutrition and LMC Centre for Advanced Food Studies, Faculty of Life Sciences, University of Copenhagen, Copenhagen, Denmark

Abstract

There are differences between at what age industrialized countries recommend that cow’s milk can be introduced to infants. Most countries recommend waiting until 12 months of age, but according to recommendations from some countries (e.g. Canada, Sweden and Denmark) cow’s milk can be introduced from 9 or 10 months. The main reason for delaying introduction is to prevent iron deficiency as cow’s milk is a poor iron source. In one study mainly milk intake above 500 ml/day caused iron deficiency. Cow’s milk has a very low content of linoleic acid (LA), but a more favorable LA/α-linolenic ratio, which is likely to be the reason why red blood cell docosahexaenoic acid (DHA) levels seem to be more favorable in infants drinking cow’s milk compared to infants drinking infant formula that is not supplemented with DHA. It has been suggested that cow’s milk intake can affect the later risk of obesity, blood pressure and linear growth, but the evidence is not convincing. There are also considerable differences in recommendations on at what age cow’s milk with reduced fat intake can be introduced. The main consideration is that low-fat milk might limit energy intake and thereby growth, but the potential effects on development of early obesity should also be considered. Recommendations about the age for introduction of cow’s milk should take into consideration traditions and feeding patterns in the population, especially the intake of iron and long-chain polyunsaturated fatty acids and should also give recommendations on the volume of milk.

Introduction

It has for decades been discussed at what age cow’s milk can be introduced to the diet of the infant or young child, at what age milk with reduced fat content can be introduced, and how much the recommended daily intake should be. The discussion is ongoing.
The role of cow’s milk in the complementary feeding diet was also discussed at a joint meeting between ESPGHAN and the International Paediatric Society (IPA) in Casablanca in 1999 [1]. In the proceedings from the meeting some of the main issues on cow’s milk were highlighted and the following research questions were mentioned [2]:

1. What is the appropriate age for the introduction of cow’s milk?
2. What is a reasonable daily amount during ‘late’ lactation, and when the diet has been diversified?
3. Is there a need for special modified formulas for young children (toddlers’ formulas)?
4. Is there an effect of the fatty acid composition of cow’s milk on the risk of developing cardiovascular disease later in life?
5. Do fermented milk products have significant positive effects on morbidity and growth in countries with poor hygiene or in industrialized countries?
6. Does cow’s milk protein have a role in the development of diabetes?

Some of these issues will be discussed in this article in the light of new evidence. The aim is to give an update on the scientific evidence for some of the potential negative and positive effects of giving cow’s milk to infants and young children. The potential effect of a high renal solute load in cow’s milk and the data suggesting that cow’s milk can provoke microscopic intestinal bleeding will only be briefly mentioned as these two topics are discussed in detail in the article in this volume by Ziegler (pp. 185–195). The effects of fermented milk products are discussed in the article by Brunser et al. (pp. 235–247).

This article discusses both short-term and potential long-term effects of using whole cow’s milk in complementary feeding. However, very few randomized studies are available and although there is an increasing literature on the potential programming effect of early diet it is still not known to what degree late infancy and young childhood are also periods sensitive to programming.

**Recommendations on Age of Introduction**

The main reason for delaying the introduction of cow’s milk is to prevent the development of iron deficiency. Recommendations on age of introduction will thus have to take into account the risk of iron deficiency in the population, the iron content of the remaining diet, recommendations on iron supplements, alternatives to cow’s milk, and the amount of milk given.

In most countries it is now recommended that cow’s milk is not introduced before the age of 12 months, whereas some countries recommend that it can be introduced from the age of 9 months [3, 4] or 10 months [5].

The American Academy of Pediatrics Committee on Nutrition published recommendations on the use of whole cow’s milk in 1992 in which the main statement was that whole cow’s milk (and low iron formulas) should not be used
during the first year of life [6]. The main argument was the low iron content and the risk of iron deficiency. In the recommendations it was also noted that infants fed whole cow’s milk have low intakes of linoleic acid (LA) and vitamin E, and excessive intakes of sodium, potassium, and protein.

In Canada the official recommendations for healthy term infant feeding were updated in 2005 [3]. The guidelines are issued by a joint working group including the Canadian Paediatric Society, Dieticians of Canada and Health Canada. The recommendations are that pasteurized whole cow’s milk may be introduced at 9 months. The text reads: ‘Infants weaned from breastfeeding before 9 months of age should receive iron-fortified formula. Non-fortified formula and cow’s milk are unsuitable alternatives as they contain very little natural iron which is poorly absorbed. When milk is combined with other dietary sources of iron, such as iron-fortified infant cereals, puréed liver, meat, fish, legumes and egg yolk, it may be possible to avoid iron deficiency and anemia. However, there are limited data to support or refute this estimation. After 9 months of age, when a wider variety of foods is being ingested, the introduction of cow’s milk is not associated with any risk of iron deficiency.’

According to the recommendations from the health authorities in Denmark cow’s milk can be gradually introduced as drinking milk from the age of 9 months, but there is no advice against continuing with infant formula until the age of 12 months. The potential negative effect on iron status of an early introduction is solved by a general recommendation in Denmark that any infant that does not receive at least 400 ml of iron-fortified infant formula per day from the age of 6–12 months should have medicinal iron as drops. This recommendation covers also breastfed infants. Thus, there is a choice between using either cow’s milk and iron drops or using infant formula, which in Denmark, as in all European countries, is fortified with iron.

In Sweden it is recommended that cow’s milk can be introduced from the age of 10–12 months. In the paper giving the background for these ages it is argued that it is important to wait until 10–12 months to introduce cow’s milk, because earlier introduction would have a negative effect on iron status [5].

Recommendations on when to use cow’s milk with reduced fat content are discussed in the section on fat quantity.

**Current Intake**

Many studies have presented data on the prevalence of feeding cow’s milk at different ages during infancy. Here a few examples are given.

In the Euro-Growth study 2,245 infants participated from 22 centers in 11 countries during the period of 1990–1996 [7]. At the age of 4, 5, 6, 9 and 12 months 4, 6, 9, 18 and 31%, respectively, were fed cow’s milk as the only milk source. At 6, 9 and 12 months the percentage of children receiving any cow’s milk was 18, 33 and 50%, respectively. Of those receiving cow’s milk the
The percentage receiving low fat cow’s milk at 6, 9, 12, 24 and 36 months were 24, 20, 25, 31 and 33%, respectively.

In a recent study from Canada it was found that 13% of mothers said that they were feeding their infant cow’s milk as the primary source of milk before the age of 9 months [8]. This was mainly the case in families with younger mothers, with lower annual incomes, and families that were less likely to have attended prenatal classes. These families were also more likely to have introduced solid foods or skimmed milk before the recommended ages.

In a study from Iceland 7% of the infants received cow’s milk at the age of 5 months but at the age of 6 months as many as 40% of the infants received cow’s milk [9]. At the time of the study the recommendation was that cow’s milk could be introduced from the age of 6 months. The intake of cow’s milk during the age period from 9 to 12 months was divided into quintiles with a median intake of 289 ml, and the median intake in the two upper quintiles being 412 and 583 ml. At the age of 2 years 16% of the children had an intake above 500 ml.

### Iron

The main reason for delaying the introduction of cow’s milk is a concern about the iron status of the infant and young child. Cow’s milk has a low iron content (table 1) combined with a low availability. Furthermore, several studies have

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**Table 1.** Content of energy and selected nutrients in cow’s milk, infant formula and breast milk (per 100 ml)

<table>
<thead>
<tr>
<th></th>
<th>Breast milk</th>
<th>Formula</th>
<th>Full-fat milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kJ</td>
<td>270–290</td>
<td>280–290</td>
<td>270</td>
</tr>
<tr>
<td>Energy, kcal</td>
<td>65–70</td>
<td>67</td>
<td>65</td>
</tr>
<tr>
<td>Protein, g</td>
<td>0.9</td>
<td>1.2–1.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Carbohydrates, g</td>
<td>6.7</td>
<td>70–80</td>
<td>4.4</td>
</tr>
<tr>
<td>Oligosaccharides, g</td>
<td>1.3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fat, g</td>
<td>3.5</td>
<td>3.8</td>
<td>3.5</td>
</tr>
<tr>
<td>Calcium, mg</td>
<td>20–25</td>
<td>42</td>
<td>116</td>
</tr>
<tr>
<td>Phosphorus, mg</td>
<td>12–14</td>
<td>21</td>
<td>93</td>
</tr>
<tr>
<td>Sodium, mg</td>
<td>12–25</td>
<td>16</td>
<td>45</td>
</tr>
<tr>
<td>Potassium, mg</td>
<td>40–55</td>
<td>55</td>
<td>144</td>
</tr>
<tr>
<td>Iron, mg</td>
<td>0.03–0.09</td>
<td>0.4–0.7</td>
<td>0</td>
</tr>
<tr>
<td>Zinc, mg</td>
<td>0.1–0.3</td>
<td>0.4</td>
<td>0.42</td>
</tr>
<tr>
<td>Vitamin A, µg</td>
<td>30–60</td>
<td>50</td>
<td>29</td>
</tr>
<tr>
<td>Vitamin C, µg</td>
<td>10</td>
<td>7–9</td>
<td>1.2</td>
</tr>
<tr>
<td>Vitamin D, µg</td>
<td>0.03</td>
<td>1.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Vitamin K, µg</td>
<td>0.2–0.5</td>
<td>2.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Folic acid, µg</td>
<td>80–140</td>
<td>6.5</td>
<td>11</td>
</tr>
</tbody>
</table>
shown that feeding cow's milk to infants can cause microscopic bleeding from the gastrointestinal tract, in some cases up to about 9 months of age.

Many studies have shown the association between intake of cow's milk and low iron status. In the large Euro-Growth study including 488 infants from 11 European centers 7.2% had iron deficiency and 2.3% iron deficiency anemia at the age of 12 months. Early introduction of cow's milk was a strong negative determinant of iron status and the use of infant formula a positive determinant [10]. This has also been shown by other studies [11].

In a study from Iceland the association between the daily intake of whole cow's milk and iron status was examined. At the age of 12 months 1 in 5 infants had low serum ferritin and 2.7% were also anemic [9]. Cow's milk intake from 9 to 12 months was negatively associated with iron status, but only significantly, if the intake was above 460 ml/day. At the age of 2 years iron deficiency had declined to 9% with 1.4% having iron deficiency anemia [12]. Of the 11 infants being iron deficient only 1 had a daily milk intake below 500 ml, and among those with an intake above 500 ml, half were iron deficient.

### Protein

Cow's milk has a protein content that is more than 3 times as high as that in breast milk, 3.5 compared to 1% or lower in mature breast milk. The content in infant formula is much closer to the level in breast milk. Calculated as protein energy percent the values are about 5–6, 9–10 and 20–21 for human milk, infant formula and cow's milk, respectively.

When the fat content of milk is reduced, the relative contribution of protein to the energy content (protein energy percentage) is increased. If the intake of low-fat milk is the same as the intake of whole milk, the protein intake from milk will be the same, but if the lower energy intake from low-fat milk is compensated by a higher milk volume, then the protein intake will increase. If an infant drinks 350 ml of whole milk (3.5%) and changes to skimmed milk (0.3%) with the same energy intake, the infant will have to drink 600 ml of skimmed milk and the protein intake will increase from 12 to 20 g.

The potential effects of protein intake on later health are discussed in the sections on overweight and obesity, blood pressure and linear growth.

### Fat Quality

A marked difference between cow's milk, infant formula and breast milk is the fatty acid composition [13–15]. One of the important differences is a high content of saturated fatty acids in cow's milk, about 65–70% of the weight of total fatty acids. For comparison the content of saturated fatty acids is about
40–50% in human milk. It is especially the content of 14:0, 16:0 and 18:0 that are higher in cow's milk.

A high intake of saturated fatty acids from milk increases the cardiovascular risk in adults and it has been discussed whether the early intake of saturated fat also influences cardiovascular risk factors. In a large study from Finland [16] the intervention group was recommended to use skimmed milk from the age of 7 months and to compensate the low fat intake by adding vegetable oil to the diet. However, the intervention group was also advised to continue a diet with a reduced saturated fat intake later in childhood. At the age of 9 years there was still a significant difference in fat intake with a lower intake of total fat and saturated fat in the intervention group compared to the control group [17]. Thus, it is not possible to determine whether the low saturated fat intake during late infancy has also been a determinant of the more advantageous results in the intervention group of insulin sensitivity (HOMA index) at 9 years and endothelial function at 11 years [17, 18]. However, the evidence that there are any adverse long-term effects of a high intake of milk fat in early life is, however, weak [19].

Another main difference in fat quality is that the content of LA (18:2n-6) is considerably lower in cow's milk (about 2%) compared to the content in human milk (8–13%) or infant formula (10–19%). The content of LA (18:2n-3) is also somewhat lower (0.2–1.2%) in cow's milk, but very variable. In human milk it is about 0.7–1.1% and in infant formula 1.2–2.0%. The ratio 18:2n-6/18:3n-3 can therefore vary a lot in cow's milk from values at the same level as infant formula, 8–10, down to around 4, when the level of LA is high. Thus, despite a low level of n-3 fatty acids the n-6/n-3 ratio in cow's milk is quite favorable.

Cow's milk does not contribute to the intake of long-chain polyunsaturated fatty acids (LCPUFA), whereas both docosahexaenoic acid (DHA) and arachidonic acid (AA) are present in human milk. However, the content varies considerably with the diet of the mother. Population mean values of DHA in human milk vary from 0.15 to 1.0% and of AA from 0.4 to 0.8% [13]. Traditionally there was no LCPUFA in infant formula, but now more and more formulas are supplemented with DHA and in some cases also with AA.

The effect of cow's milk intake on LCPUFA status in infants and young children is not well documented. Many infants fed on cow's milk will have a very low intake of DHA as a high fish intake is not common in many populations during the complementary feeding period. On the other hand, it has also been suggested that a high intake of short-chain polyunsaturated fatty acids (PUFA), especially LA (18:2n-6), which is much lower in cow's milk than in human milk and infant formula, can have a negative effect on the LCPUFA status. In one study piglets were randomized to formula with different ratios of LA to α-LA (ALA, 8:3n-3) from 0.5:1 to 10:1 and with LA kept constant at 13% of fat content [20]. The highest incorporation of DHA in brain and other tissues was seen at ratios of 4:1 and 2:1. In rats fed oils with a different content of ALA it was the
oil with the lowest ALA content that resulted in the highest DHA levels in the heart tissue and plasma. The explanation suggested for this was that the low ALA intake resulted in a decreased competition for delta-6-desaturase [21]. In one study comparing breastfeeding, formula feeding and a group fed evaporated cow's milk, the red blood cell DHA level at 3 and 6 months was highest in the breastfed group, but higher in the cow's milk group than the formula group [22]. Thus, regarding DHA status in the infant it is likely that cow's milk with its favorable n-6/n-3 ratio and low PUFA content can result in DHA tissue values at the same level as formula that is not supplemented with DHA.

Cow's Milk with Reduced Fat Content

When is it appropriate to introduce cow's milk with a reduced fat content? In several countries the recommendation is that fat-reduced milk should not be introduced during the first 2–3 years of life, while others recommend that semi-skimmed milk can be introduced earlier. The main concern is that reducing the fat content might also reduce total energy intake because the infant might not be able to compensate the lower energy intake by eating more. In an analysis of fat intake and growth in 19 countries from Central and South America it was concluded that it was only when the dietary fat content was below 22% that there was a problem with growth [23]. Other concerns have been that low-fat milk might result in an increased protein intake as explained in the section on protein. Furthermore, it has been suggested that the high intake of saturated fatty acid from whole milk might increase the cardiovascular risk in later life as discussed in the section on fat quality.

The ESPGHAN nutrition committee has made recommendations on fat intake during the first years of life. It was concluded that fat intake should not be reduced before the age of 3 years [19].

In the WHO guiding principles for feeding nonbreastfed children 6–24 months of age [24] it is stated that whole milk is a good source of fat during the first 2 years of life, that semi-skimmed milk may be acceptable after 12 months of life, but skimmed milk is not recommended as a major food source during the first 2 years of life.

In the United Kingdom it is recommended that semi-skimmed milk (1.5–1.8% fat) should not be introduced before 2 years and skimmed milk (<0.3%) not before the age of 5 years [25]. On the official website (www.eatwell.gov.uk/ageandstages/baby/weaning) it is argued that full-fat milk should not be used before 12 months as it does not have the right balance of nutrients and that semi-skimmed milk can be introduced from 2 years, if the child is a good eater and has a varied diet.

According to the Canadian recommendations [3] partly skimmed milk (1 and 2%) is not routinely recommended in the first 2 years, and skim milk is found inappropriate in the first 2 years. The arguments are that skim milk provides
no essential fatty acids and has a very low energy density. With high intakes, protein and solute intake would be significantly higher than the infant needs. It is stated that approximately 15% of Canadian infants are on 2% milk around 1 year of age and although there is no clear indication of negative consequences, there is no medical or nutritional indication to recommend the routine use of partially skimmed milk. Although whole cow's milk is recommended for the second year of life, it is also stated that 2% milk may be an acceptable alternative provided that the child is eating a variety of foods and growing at an acceptable rate.

In Denmark it is recommended that if cow's milk is used it should be full-fat milk up to the age of 12 months, but after that age it is recommended that milk should preferably be semi-skimmed, which in Denmark has a fat content of 1.5% [4]. The background for recommending a reduced fat content, already from the age of 12 months was (1) that this reduction in fat intake in an amount of milk that was not supposed to be more than 500 ml was not likely to bring the fat content of the total diet down to a level that would affect energy intake, (2) that in this age group there was no documented positive effects of a high saturated fat intake and (3) that is was important to get young children used to drinking low-fat milk.

**Milk Volume**

Not many recommendations on milk intake during infancy include recommendations on the preferred volume or give an upper limit.

In the WHO guiding principles for feeding nonbreastfed children 6–24 months of age [24] there are recommendations on the volume of intake. Using linear programming analysis it was calculated that if the diet was not fortified or supplemented 200–400 ml were needed per day if there were other animal source foods in the diet and 300–500 ml if there were no other animal source foods.

One of the problems with a large milk intake is that it can take up a considerable part of the energy intake, leaving only limited space for other foods and thereby a diversified diet. In table 2 the energy content of 350 and 500 ml of cow’s milk with different fat contents has been calculated as a percentage of the recommended energy intake of a 12-, 24- or 36-month-old child. If a 12-month-old child drinks 500 ml of whole cow’s milk daily, it takes up about 36% of the recommended energy intake, and thus leaves 64% of the energy intake for other foods. An intake of 1,000 ml a day will thus take up as much as 72% of the energy intake, leaving only 28% for other foods. No one will recommend such a high intake, but there are children who drink very large amounts of milk, so called milkaholics. It is not known how common this is, but these young children are known at pediatric departments where they are occasionally admitted with severe iron anemia.
In a 2-year-old child 500 ml of whole cow’s milk provides 29% of the recommended energy intake, but if the volume is reduced to 350 ml and the fat content to 1.5% (semi-skimmed milk), milk will only cover 16% of the recommended energy intake. This can be less than optimal if the remaining diet is of poor quality and with little food of animal origin. But if the diet is diverse with a fat content above 25 energy percent, there should be no problem.

It is difficult to recommend what is a reasonable energy intake from milk and when the intake is so high that it will interfere with a varied intake of other healthy foods. It depends on the composition of the remaining diet. A daily intake of about 500 ml of cow’s milk seems to be a reasonable upper limit, although the evidence for such a limit is not strong. The data from Iceland on milk intake and iron status [9, 12] support that it is only if the volume is above 400–500 ml that there is a problem with iron deficiency, in a society with no recommendations on routine iron supplementation. As 500 ml whole cow’s milk is covering about one third of the energy requirements during the second year of life, there is a reasonable amount of space left for a diversified diet.

### Table 2. Percentage of energy requirements covered by an intake of 500 or 350 ml of cow’s milk with different fat content

<table>
<thead>
<tr>
<th></th>
<th>Whole cow’s milk (3.5% fat)</th>
<th>Semi-skimmed milk (1.5% fat)</th>
<th>Skimmed milk (0.3% fat)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>500 ml</td>
<td>350 ml</td>
<td>500 ml</td>
</tr>
<tr>
<td>12 months</td>
<td>36</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>2 years</td>
<td>29</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>3 years</td>
<td>26</td>
<td>18</td>
<td>20</td>
</tr>
</tbody>
</table>

The energy requirement was calculated as the energy requirement per kilogram body weight (Nordic Nutrient Recommendations) multiplied by the median weight of Danish children. The values are averages for boys and girls.

Overweight and Obesity

It has been suggested that a high protein intake early in life could result in an increased risk of developing overweight or obesity later in life. The proposed mechanism is that a high protein intake stimulates secretion of insulin-like growth factor-1 (IGF-1) and thereby triggers precocous cell multiplication and accelerates maturation. The increased IGF-1 levels may then accelerate growth and increase muscle mass and adipose tissue, and thus induce an early adiposity rebound, the time point at which the BMI increases after its nadir in childhood.
An early adiposity rebound is then associated with a higher risk of obesity later in childhood and possibly also in adulthood [26]. In a longitudinal study from France it was found that the protein energy percentage at the age of 2 years was positively correlated with BMI and subscapular skinfold thickness at 8 years after adjustment for energy intake at 2 years and parental BMI [24]. The protein-adiposity hypothesis was supported by an Italian study, in which Scaglioni et al. [27] examined the influence of the intake of macronutrients in early life on the development of overweight at 5 years. Those with a BMI above the 90th percentile at age 5 years had a significantly higher protein intake at 1 year of age than children with a lower BMI. In this population, the protein intake was very high, 22 protein energy percent (PE%) in the overweight group against 20 PE% in the nonoverweight group. Also, the proportion of overweight was very high. However, a study from the United Kingdom of factors affecting timing of adiposity rebound, in which almost 900 children were followed from birth to 5 years of age, there was no evidence of associations between protein intake and timing of adiposity rebound [28]. The average PE% at 18 months was about 14.5. Also, in our study of 105 Danish children, analyzing whether diet at 9 months of age was associated with adiposity at 10 years of age, there were no significant associations between protein intake at 9 months and body fat percentage (DEXA scan) or BMI at 10 years [29]. The average PE% at 9 months of age was 14 in this study. Thus, the data on the relationship between protein intake and adiposity is inconclusive. In a recent review Agostoni et al. [30] suggested that it was only when the protein intake was above 15 energy percent that there was a significant association between protein intake and development of adiposity.

The protein hypothesis is at present being tested in a large multicenter randomized controlled trial where nonbreastfed infants are randomized to infant formula with different protein contents (www.danoneinstitute.org/EUchildhoodobesity). This study tests whether moderate differences in protein content of infant formula will have an effect in formula-fed infants and if this is the case whether it is possible that the differences in protein content between human milk and infant formula could be an explanation for the lower prevalence of childhood overweight and obesity in breastfed infants seen in some studies. As the intervention will have its main effect during the first part of infancy, the results from this study will not be able to determine directly whether differences in protein intake during late infancy and young childhood have an effect on later development of overweight.

In relation to the potential effect of protein and milk intake on the risk of developing obesity later in life the recent paper by Moore et al. [31] is of interest. They found that low dairy intake in early childhood predicts excess body fat gain. Dietary intakes recorded during the 3- to 5-year age period with BMI and skinfolds measured from 10 to 13 years were compared. They found that those in the lowest tertile of dairy intake had a BMI that was approximately two units higher and had an extra 25 mm of subcutaneous fat in the sum of 4 skinfolds. The effects were stronger after controlling for intake of energy.
and saturated fat, suggesting that there was a protective effect in the nonfat part of the dairy products. An effect of calcium has been suggested by several authors [32, 33], mainly based on findings from studies in adults, but in the study by Moore et al. adding calcium to the multivariate analysis strengthened the results, suggesting that the effect did not come from calcium.

Several other studies have suggested that milk intake is inversely associated with body weight and obesity. However, it is unknown which components in milk possess the bioactivity associated with weight loss. As mentioned, the milk minerals, such as calcium, might play a role in the regulation of body weight [32, 34], through decreased absorption of fat from the intestine or through regulating the fat metabolism by influencing lipolysis, fat oxidation and lipogenesis. Other components in milk, such as milk peptides, might also be of importance in the regulation of body weight. Protein diets are popular for reducing obesity, because they seem to increase satiety [35]. Protein digestion leads to stimulation of many physiological and metabolic responses known to be involved in the regulation of food intake, and effects are found to be dependent on the protein source. Mechanisms by which peptides from protein digestion exert their effect on food intake via the gut include slowing stomach emptying, perhaps via opioid receptors and direct or indirect stimulation of gut hormone receptors. Milk protein hydrolysis products of relevance to regulation of food intake include casomorphins and caseinomacropeptide. Casomorphins are peptides released upon the digestion of casein and are known to interact with gastric opioid receptors thus slowing gastrointestinal motility [36]. Casomorphins may play a role in regulating food intake because the opioid antagonist was found to prevent reduction in food intake after a casein preload was given to rats [37].

The data supporting the protein-obesity hypothesis are still not convincing and it is above all not clear to what degree this hypothesis is relevant for the intake of cow’s milk at the age from 9 to 18 months. Likewise, the data suggesting that low-fat dairy products have a beneficial effect on the development of obesity should still be considered as a hypothesis and if it is confirmed, there are at present no data to elucidate whether such an effect is relevant for the 9- to 18-month age period.

**Blood Pressure**

The type of milk intake at 3 months has been associated with blood pressure as young adults. The Barry Caerphilly Growth study cohort, involving infants born between 1972 and 1974, was followed up at the age of 23–27 years [38]. In the 1970s infants that were not breastfed were given formulas based on dried whole cow’s milk, which consequently had a high protein and sodium content. In this study there was a significant positive association between the amount of whole cow’s milk given at the age of 3 months and
systolic blood pressure as young adults. As it is an observational study it is not known if this effect is caused by a programming effect of a high protein intake, a high sodium intake or other factors in milk or if it is caused by a bioactive effect of human milk, as also pointed out by the authors. Giving unmodified cow's milk at 3 months of age is very 'unphysiological' and infants at this early age are likely to be much more sensitive to a programming effect than during late infancy.

We have examined the effect of dietary intake in young children at age 2½ years on blood pressure measured at the same age. We found that protein intake measured as protein energy percentage was significantly negatively associated with both systolic and diastolic blood pressure. The average protein intake in this group was about 42 g/day or 12 energy percent and milk intake about 400 ml/day [39]. Thus, approximately one third of the protein intake came from cow's milk. This effect of protein intake on blood pressure has also been shown in older children and in adults [39].

These data suggest that a very early high protein intake might have a programming effect on blood pressure and at the same time that a high protein intake in young children could be associated with a reduction in current blood pressure. As with many other issues about programming the sensitive age window is not known and it is in particular not known whether the age period from 9 to 18 months is a sensitive period for this kind of programming.

**Linear Growth**

In a recent review summarizing epidemiological and intervention studies it was concluded that cow's milk seems to have a positive effect on linear growth [40]. The strongest evidence that cow's milk stimulates linear growth comes from observational studies in both infants and preschool children, and from intervention studies in developing countries that show considerable effects. Additionally, observational studies from well-nourished populations also show an association between milk intake and growth [41]. These results suggest that milk has a growth-stimulating effect even in situations where the nutrient intake is adequate. This effect is supported by intervention studies that show that milk intake stimulates circulating levels of the growth factors insulin [42] and IGF-1 [43], which suggests that the growth-stimulating effects of cow's milk are at least partly due to the stimulation of the IGFs. We speculate that this stimulating effect is the reason why at least three studies have shown that formula-fed infants have higher levels of IGF-1 than breastfed infants [44–46]. This is in accordance with studies showing that formula-fed infants have a linear growth velocity which is slightly, but significantly, higher than breast-fed infants [47, 48]. We are not aware of studies comparing the IGF-1 levels of infants fed formula and cow's milk. Although we do not know which compounds in milk stimulate IGF-1 levels, we speculate that the effect
of cow’s milk is stronger than that of formula because of its high content of protein and minerals.

There are emerging data suggesting that the IGF axis can be programmed by early diet, and it is possible that the type of milk intake during early life also has a role in this programming [48, 50]. Despite the lower IGF-1 levels in breastfed compared to formula-fed infants, studies have suggested that breastfed infants have both higher IGF-1 levels during childhood [51] and are taller as adults [52, 53].

We speculate that cow’s milk intake compared to infant formula intake, also during late infancy and early childhood, will increase IGF-1 levels and thereby perhaps also increase linear growth velocity. However, it is not known whether this has positive or negative effects in the long-term and whether this age period is also sensitive to programming of the IGF-1 axis. In adults high levels of IGF-1 are associated with an increased risk of several cancers [54, 55], whereas low levels of IGF-1 are associated with an increased risk of cardiovascular disease [56].

Conclusions

There is no doubt that the most important implication of giving cow’s milk in late infancy and early childhood, compared to infant formula, is the potential negative effect on iron status. If cow’s milk is given instead of infant formula, a sufficient iron intake should be secured either through a diet with sufficient meat or iron-fortified foods or through iron supplements. The age at which cow’s milk can be introduced depends on to what degree the iron needs of the infant or young child can be met by other iron sources.

One of the problems mentioned in giving cow’s milk is the low level of LA [6]. However, cow’s milk has a favorable n-6/n-3 ratio and it is likely that feeding cow’s milk will results in DHA tissue concentrations at the same level as feeding infant formula which is not fortified with DHA. Late infancy and young childhood represent a period during which the brain still develops and a sufficient DHA intake is, therefore, important. However, there are insufficient data on how diet affects LCPUFA status and functional outcomes during this age period. There is a need to know more about the relative impact of cow’s milk versus infant formula, the effect of infant formula fortified with DHA and the effect of fish intake.

Important nutrients during the complementary feeding period are iron and fatty acids. To what degree the intake of these nutrients should rely on a diversified diet or should be covered by formula will be different in different populations, depending on economic status, infant feeding habits and tradition.

When cow’s milk is given to infants and young children, it is important to make sure that cow’s milk intake does not compete with breast milk intake, as is also the case with infant formula.
The complementary feeding period is a period when the infant should be accustomed to a diversified diet. If the intake of cow's milk is very high, there is less space for a diversified diet. A maximum intake of about 500 ml seems a prudent recommendation. A reasonable intake will also reduce the risk of too high a protein intake.

Cow's milk with reduced fat intake should not be introduced too early as it will have a negative impact on the energy density of the diet, which might affect growth. On the other hand, in view of the current obesity epidemic, young children should be accustomed to a low fat diet at an early age.

There are some data suggesting that cow's milk intake during the complementary feeding period, perhaps through the high protein intake, has long-term effects on risk factors for noncommunicable diseases. However, the available data point in many directions and at present it is not possible to draw any firm conclusions. Data on the long-term implications of diet during the complementary feeding period are scarce and should be studied more in the future. There has been a shift in focus of research in programming from the intrauterine to the postnatal period. Much data is available on the long-term implications of feeding and growth during early infancy, but very little about the effects of diet and growth during the complementary feeding period.

References

4 The National Board of Health (Denmark): Recommendations for the Nutrition of Infants; Recommendations for Health Personnel (in Danish). Copenhagen, The National Board of Health (Denmark), 2005.
Discussion

Dr. Ziegler: You showed us the fatty acid composition of cow’s milk but you did not mention that this fat is very poorly absorbed by normal infants. Butter fat is the fat of cow’s milk. If you do a fat-balance study you find that about 60% is absorbed. Compared to fat absorption from breast milk which is 95%, there is a substantial
amount of fat loss in the stool of an infant who is fed cow's milk. About introducing cow's milk at 9 months, to which I do not object, I showed you that blood loss disappears toward the end of the first year of life. And most importantly, the dehydration concern diminishes as children acquire the ability to express and communicate thirst, which protects them against dehydration.

**Dr. Simell:** I have an experimental comment from real life from the STRIP study where children were introduced to the study at the age of 6 months and randomized to an intervention and a control group [1]. In the intervention group the children received regular dietary and lifestyle counseling at half-year intervals from 6 months of age, and they are now between 16 and 17 years of age. We have been looking at obesity development in these children because part of the counseling in the early years was that they be switched to fat-free skimmed milk at the age of 1 year, from formula or breast milk to skimmed milk. We have found no difference in the proportions of obesity and overweight in boys, but in girls there is a very significant difference between the proportions: much fewer obese girls in the intervention group through the years. In the counseling we actually have not concentrated on the amount of fat but on the quality of fat; we have been supporting the higher intake of polyunsaturated and monounsaturated fat as compared to saturated fat. The goal has never really been to focus on the total intake, and surprisingly it has been very effective, actually much better than any other obesity prevention programs we have seen.

**Dr. Ribeiro:** Regarding your comments that the possible use of these milk sources could be beneficial in countries where stunting is prevalent: we have seen some publications showing that people with stunting are potentially more vulnerable to become obese later in life than the rest of the population. Perhaps this is one of the reasons for the paradox in Brazil now where the proportions of children with malnutrition and obesity are the same. We see in this recommendation just the opposite; we are very concerned about the use of cow's milk or other sources of high energy and high protein in the stunting population.

**Dr. Michaelsen:** If you are talking about obesity I think it is a question of reducing the fat intake at an early age using fat-reduced milk, and there are some data suggesting that this might have a beneficial effect on the development of obesity later on. So from the available data, it is difficult to say exactly when and how fast the fat content of the milk should be reduced. But if semi-skimmed milk is introduced at an early age and then later skimmed milk, I think the milk will not promote later obesity.

**Dr. Ribeiro:** But the IGF impact is one of the concerns. The possible recovery from stunting needs to be considered as a potential because of the later compensation growth, but the same effect is also a response here.

**Dr. Michaelsen:** I think the data that IGF-1 is involved in obesity development is not the response, that was part of the original hypothesis. Obese children will have normal or increased IGF-1 levels, but the increased IGF-1 level is because they eat more. They are also taller up to the age of puberty, then they are not taller, and that is because they get a lot of fuel and that also increases IGF-1 and linear growth. But I don't think it because of the increase in IGF-1.

**Dr. Solomons:** I think in the dialogue between you and Dr. Ribeiro, your response was that taller people were obese and had more IGF. Meanwhile, Dr. Ribeiro's question was about stunting and the risk of obesity. But I think the difference – or the missing piece of dialogue – is the constraint that makes the stunting in countries like Brazil or Guatemala. In these settings, for reasons other than diet, one may not grow, therefore you are forcing more body mass onto a non-elongated frame. Then you get a kind of obesity that is certainly not IGF-driven, and may not even be IGF-associated. It would be interesting to study.
Dr. Michaelsen: So if you give milk you can increase the frame?

Dr. Solomons: No, because the constraint would be running against even giving milk. A lot of stunting is related to the same mechanism why animals don’t grow in an infected environment, that there is a constant immuno-stimulation which is essentially catabolic and anti-growth. No matter how much you pour into them they are not going to grow because the mechanisms for forward growth are disrupted by the environment. That is the reality for the countries in the world with more than 20% stunting, it is a massive number of countries in the world.

Dr. Michaelsen: But there are still some intervention studies showing increased growth after animal foods. Then there is the question of what is the effect of meat and what is the effect of milk.

Dr. Solomons: There are more dietary intervention trial studies that are failures with regard to achieving growth than there are successes. Moreover, if one pushes a nutrient-rich diet on children who are already of established short stature, obesity may be the obvious result.

Dr. Shahkhalilli: Can you please comment on what the contribution of fat is in the total energy content of the diet (percent of fat energy) in developed and developing countries? Does the present level of fat in complementary diets need to be modified?

Dr. Michaelsen: In our society we recommend that the family diet should be below 30%, perhaps it should be 25–30%, and breast milk has 52%. So there should be a gradual decline, and there is much debate as to how fast that should go. Some reviews say that in developing countries caution should be taken not to get below 20–25%. In Denmark and in some other countries we have seen that there was a tendency to go from the 52% to very low levels down to 20%. Most families will have a diet with about 30 or 35 or even 40%. So we saw a surprising pattern where at 12 months the children actually had a lower fat energy percentage than the family diet, and I think it is important not to have that. But again at 2 years the energy fat level should be down to 25%–30% in developed countries, and in developing countries where the concern is that it is getting too low and it should be increased to at least 20–25%.

Dr. Biasucci: As a pediatrician, what would you suggest with regard to the time of introduction of cow’s milk in the case of infants who do not easily accept meat during the weaning process? Would you still suggest introducing cow’s milk at 9 months or would you suggest it later on?

Dr. Michaelsen: If you think about introducing cow’s milk at 9 months then you should be sure that there is sufficient iron intake, and this is a problem when they won’t eat any meat. You could use infant formula. I am not saying that cow’s milk is better from the age of 9 months, I am just saying that I think it is a possibility. I also have a conflict of interest because I am from a country where this is recommended, but we give the mothers a choice to shift to cow’s milk at 9 months and then give iron drops or continue with infant formula, and we are not really saying that one is better than the other. In that situation you want to be sure that the iron needs are covered which could be done with infant formula, fortified cereals, or iron drops.

Dr. Haschke: One thing is really missing in the data set and probably the data are not available. If you consider that the breastfed infant should be the reference, at least until 12 months of age and even beyond, we don’t have the data on their metabolic outcome, IgF1, and so on, to really compare what would be the pattern of an infant who is exclusively breastfed until 6 months of age and then a weaning diet is introduced. So if we consider this as the reference, as far as I am aware there are not enough data to really compare with another milk, such as cow’s milk, which is substantially different in protein content. Would you agree?

Dr. Michaelsen: I do agree that we know very little about the whole programming concept from 9 to 18 months, so we don’t know the long-term consequences. I showed some potentially positive and some negative effects.
**Dr. Giovannini:** When we speak about whole cow's milk, 9 months is the age at which it is introduced in Denmark whereas the Italian Society of Pediatric Nutrition recommends not using it in the first year of life. But the biggest problem is compliance in Western countries. When mothers taste the formula and also taste cow's milk, they find that cow's milk tastes better because of the saturated fatty acids. For this reason I think we have a big problem regarding education. This is a reality and we should not forget that the mothers taste all the formulas and they think that their children will have the same taste which is a big mistake. Moreover, the problem is also to check later between the early introduction of cow's milk and later nutrition with too much sweets and cakes. I think that the mothers should receive nutritional education before delivery, during pregnancy.

**Dr. Michaelsen:** It is interesting that the mothers taste the infant formula. That could be the reason why in southern Europe or in some European countries there are some formulas with sugar instead of lactose. I don’t know if they are still on the market, but previously there were some formulas with sugar.

**Reference**
