Human Milk vs. Cow’s Milk and the Evolution of Infant Formulas

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Abstract

Until the early 20th century, a wet nurse was the only safe alternative to breastfeeding, one reason being that each species has a unique composition of its milk. When techniques for chemical analyses of milks and assessment of the energy requirements of infants became available during the 19th century, reasonably safe breast milk substitutes started to be developed. Successively, these were developed into modern infant formulas during the 20th century using human milk composition as reference and cow’s milk as protein source. Even with a composition similar to human milk there are differences in performance between formula-fed and breastfed infants. Novel ingredients and new techniques within the dairy industry will contribute to minimize these differences and so might techniques in molecular biology allowing large scale production of recombinant human milk proteins. This technique may be used for production of bioactive substances present in low concentrations in human milk but absent from bovine milk with proven effect on nutrient utilization or other health benefits. For formulas containing novel ingredients with potent biological activities produced with new techniques it will be extremely important that their safety and efficacy are rigorously evaluated because ‘functional effects’ are not necessarily the same as health benefits.

Introduction

‘A child is to get a sufficient quantity of good nourishment, if it is to thrive well. The best food for it is, no doubt, the mother’s milk. We therefore find that children thrive well suckled by their mother’s milk, tho’ that should not stand all the proofs which are required towards approving that of a nurse’. These words of wisdom are from what is considered the first comprehensive textbook of pediatrics, The Diseases of Children and their Remedies, first
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published in 1764 by the Swedish physician Nils Rosén von Rosenstein, often named the father of pediatrics [1]. At that time, there was no other safe alternative than a wet nurse if the mother could not breastfeed her infant. Rosén von Rosenstein and his colleague David Schulz von Schulzenheim, professor of obstetrics, were well aware of the fact that merely substituting breast milk for milk from other species, including milk from cows, could have fatal consequences. This was clearly expressed by von Schulzenheim in his inaugural speech to The Swedish Royal Academy of Sciences 1760 [2], although the reasons were not fully understood. Rosén von Rosenstein in his textbook suggested that should the wet nurse happen to get her period, it would not be good for the baby to suck her milk: ‘therefore it would be much safer, if some other female should suck the nurse’s milk on those days, and the child in the meantime, to be fed with clear whey, which is to be prepared of coagulated milk and eggs: such whey I mean, as we get in preparing egg cheese’. 250 years ago, that was the best recipe of a breast milk substitute available, which certainly did not meet the standard of today’s infant formulas, which are defined as foodstuffs intended for particular nutritional use by infants during the first months of life and satisfying by themselves the nutritional requirements of such infants until the introduction of appropriate complementary feeding [3].

Principal Differences between Human Milk and Cow’s Milk

The composition of milk is unique to each species. Human milk contains 9 g protein/l to be compared with 34 g/l in cow’s milk and 120 g/l in rat’s milk. The fat content is similar or about 38 g/l in human and cow’s milk but as high as 150 g/l in rat’s milk. With respect to lactose, the content differs less, 70 g/l in human, 48 g/l in cow’s and 30 g/l in rat’s milk [4, 5]. In principle, there is an inverse relationship between these differences in protein and energy content and the time it takes for the offspring to double its birthweight. Bovine milk protein is dominated by the casein fraction, which constitutes 80% of total protein, while the whey protein fraction constitutes 20%. The corresponding figures for human milk are 40 and 60%. Also, within the casein fraction the relative proportion of the various subclasses differ between bovine and human milk. α-S1 caseins constitutes the largest fraction in bovine milk, while β-caseins by far dominate in human milk. With respect to the whey protein fraction, the differences are as striking. The concentration of α-lactalbumin is twice as high in human milk as in bovine milk and the iron-binding protein lactoferrin, which second to α-lactalbumin is the dominating whey protein in human milk, constitutes only a minor fraction in bovine milk. In contrast, β-lactoglobulin, the predominant protein in bovine whey, is completely absent from human whey. IgA is by far the major immunoglobulin fraction in human milk, but in bovine milk IgG is present in 10-fold higher concentration than
IgA, and the total immunoglobulin fraction is much lower than in human milk [4]. The specificity of the secretory IgA antibodies reflects environmental exposure of the mother and confers significant antimicrobial protection on the infant [6]. Goldman [7] suggested that overall the variation of antimicrobial and immune-modulating agents in milk, e.g. immunoglobulins, iron-binding proteins, lysozyme, oligosaccharides, leukocytes, cytokines, etc. (see below), seem to serve to compensate for development delays in early postnatal production of antimicrobial factors among various species, and vary depending on type of placenta, maturity of the offspring, lactation pattern and environment of the species.

Likewise, it is clear that lactation has evolved to minimize the energy cost to the mother while maximizing the utilization of energy and nutrients by her offspring, thus promoting the chance of survival of both. Recent genome studies comparing the bovine genome with 6 other species including the human lend support to this concept. Milk and mammary genes are more conserved and have evolved more slowly than other genes in the bovine genome despite selective breeding to optimize milk production. The most divergent proteins in the lactome are those with nutritional or immunological attributes, suggesting continuing selection of these genes to meet the nutritional and microbial challenges incurred by diverse environments and reproductive strategies. The most conserved genes were those coding for proteins of the milk fat globule membrane, supporting a key role in milk fat secretion [8]. It is quite clear that these and other differences between human and bovine milk have fundamental consequences reflected not only by protective effects against infections and immune development but also by an amino acid profile in human milk, which is better adapted to the needs of the human infant [9], and a lower potential renal solute load, which is essential because of the not fully developed renal function at birth [10].

Diversity in milk composition does not seem to be explained mainly by diversity of the encoded milk proteins; and although gene duplication may contribute to species variation, this is not a major determinant [11]. Thus, other regulatory mechanisms must be involved because, as mentioned, there are clear differences not only between species but also within a species as well as between milks collected from the same dam – or mother (table 1), which makes it difficult to define what is a human milk or a bovine milk, in turn impacting on using human milk as reference and bovine milk as raw material for formula production.

The History of Infant Formulas

The availability of satisfactory infant formulas is a comparatively recent development. Until the 20th century, there was virtually no safe and reliable alternative to breastfeeding, and few infants not suckled by mothers or wet
nurses survived the first year. It was not until the mid-19th century when chemical techniques were developed allowing analysis of the gross chemical composition of milk from various species that it became clear that every species has a unique composition of its milk. Towards the end of the century, pasteurization was adopted by the dairy industry and several physicians attempted to develop adequate substitutes for breast milk. The first marketed preparation, ‘Soup for infants’ was patented in 1867 by the German chemist Justus von Liebig who modestly termed it ‘the perfect infant food’. It consisted of a mixture of wheat flour, cow’s milk and malt flour, cooked with a little potassium carbonate to reduce acidity [15]. The commercial success of this formula raised the interest of competitors, but most of these early efforts were unsuccessful, and little attention was paid to the nutrient requirements of infants. An important step in the development of infant feeding occurred at the end of the 19th century when Heubner and Rubner published their calorimetric method of feeding, which made it possible to feed infants according to their energy requirements and was the beginning of modern studies of infant metabolism [16].

Eventually, substitutes for human milk were developed from milk of other mammals through numerous modifications into the complex formulas that are available today. Successive improvements in the understanding of the chemical and nutrient composition of milks, particularly of human and cow’s milk were the basis for these developments. The composition of human milk became the ultimate reference. The modern era of single formulas of known composition as complete foods for infants began in 1915 when Gerstenberger and colleagues developed an artificial milk in which the fat content was adapted to simulate human milk. The fluid mixture, which became SMA (synthetic milk adapted), contained about 4.6% fat, 6.5% carbohydrate and 0.9% protein [17]. In 1961, the first whey-dominant formula was launched and a decade later, in 1972, came the first Codex Alimentarius standard for infant formulas.

### Table 1. The composition of milk varies

<table>
<thead>
<tr>
<th>Human milk</th>
<th>Bovine milk</th>
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<tbody>
<tr>
<td>• Between mothers</td>
<td>• Genetic variation (both casein and whey protein polymorphisms), which may affect digestability, nutrient absorption, allergenicity, bioactivity [12]</td>
</tr>
<tr>
<td>• During a feed</td>
<td>• Seasonal variation [13]</td>
</tr>
<tr>
<td>• During the day</td>
<td>• Over time [13]</td>
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<tr>
<td>• With lactational stage</td>
<td>• Lactation stage [14]</td>
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<tr>
<td>• With gestational length</td>
<td>• With type of feed</td>
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<tr>
<td>• With the mother’s diet</td>
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[15] genetic variation (both casein and whey protein polymorphisms), which may affect digestability, nutrient absorption, allergenicity, bioactivity

[16] Seasonal variation

[17] Over time

[14] Lactation stage

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It is fair to say that the major goals have been met; formulas do have a nutrient composition similar to human milk, and in high-income countries they are generally safe, effective and affordable for mothers who are unable to continue breastfeeding. In spite of that, there are still differences between breastfed and formula-fed infants also in high-income countries, both with respect to short-term and long-term outcomes [18–20] (table 2). The gold standard has therefore changed. It is now generally agreed that the performance of the breastfed infant, e.g. physiological (growth pattern and body composition), biochemical (plasma and other tissue markers, including metabolomics) and functional (immune responses, neurodevelopment and morbidity) is a more relevant reference than the composition of human milk [10, 19]. Questions remaining to be answered are what breastfed infants? Exclusively or partially breastfed infants? And for how long and at what age should the comparisons be made [20–22]?

### Recent Modifications of Infant Formulas

The difference in performance between breastfed and formula-fed infants with respect to susceptibility for infections, immune responses, blood pressure, the risk to develop obesity and certain diseases, including health effects far beyond infancy [18, 22] (table 2) has put into focus the many ‘biologically active’ compounds in milk with proven or potential ‘functional’ effects. To add such components to formulas to achieve a performance more similar to breastfed infants has led to recent modifications; e.g. addition of bovine α-lactalbumin improving protein quality and thus allowing reduced protein concentration and a growth pattern more similar to breastfed infants [9, 23], certain bovine milk proteins with antimicrobial and immune-modulating properties such as lactoferrin [24, 25], nucleotides to improve immune function [10, 25, 26], long-chain polyunsaturated fatty acids affecting

<table>
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<th>Table 2. Differences in performance between breastfed and formula-fed infants [18]</th>
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<tr>
<td>Compared to formula-fed infants breastfed infants have</td>
</tr>
<tr>
<td>• Different growth pattern</td>
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<tr>
<td>• Fewer infections (gastrointestinal infections, acute otitis media)</td>
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<td>• Reduced risk for celiac disease</td>
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<td>• Reduced risk for obesity</td>
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<td>• Reduced risk for type 2 diabetes</td>
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<td>• Reduced risk for type 1 diabetes</td>
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<tr>
<td>• Lower blood pressure?</td>
</tr>
<tr>
<td>• Lower total and LDL cholesterol?</td>
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<tr>
<td>• Better cognitive achievements?</td>
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neurodevelopment and immune function [20, 27] and oligosaccharides as prebiotics [10, 28, 29]. Formulas based on hydrolyzed protein are not targeting the composition of human milk but an allergy-preventing effect similar to breastfed infants, or are used for treatment of cow’s milk protein allergy [30, 31]. Whether addition of probiotic bacteria targets the composition of human milk or merely a gut microbiota, stool composition and immune functions similar to breastfed infants is under debate [29, 32]. There is no consensus on the true health benefits of most of these modifications, which is illustrated by the fact the there is as yet no recommendation on their inclusion in infant formulas, although should the manufacturer choose to do so, the amounts allowed are regulated for long-chain polyunsaturated fatty acids, nucleotides and oligosaccharides [3].

Even with these most recent modifications, differences in performance between breastfed and formula-fed infants still remain [18]. Hence, with new knowledge novel ingredients will be identified and new technology within the dairy industry developed to produce them, and both scientific and market interests will drive further modification of formulas. It seems likely that the next step in modification will focus further on the so called ‘functional’ compounds in human milk, i.e. compounds that are not considered nutrients themselves but with the potential to affect nutrient utilization or confer additional ‘functional effects’ on breastfed infants, making formula-fed infants perform more similar to breastfed infants. Such compounds may be lipids, e.g. sphingomyelin, which is a constituent of the milk fat globule membrane and the major phospholipid in human milk with potential effects on gut maturation and signal transduction [30], and gangliosides affecting gut microbiota and neurodevelopment, the latter possibly via their carbohydrate moiety sialic acid, important for neurodevelopment reflected in effects on learning and memory [34]. There will most likely be further development of oligosaccharides added to formulas since those available today, even if they affect gut microbiota composition and stool consistency, are of much less complexity and variety than those in human milk. Interestingly, the oligosaccharides may exert their function as decoy receptors for pathogens both as free and protein bound. For instance, breastfeeding-associated protection against calicivirus diarrhea is associated with high levels of 2-linked fucosylated oligosaccharides in the milk, and human calicivirus strains, including Norwalk virus, use gut 2-linked fucosylated glycans as receptors. Recently, it was shown that milk of mothers who are non-secretors, and thereby lack 2-fucosylated oligosaccharides in their milk, had little inhibitory activity against binding to mucosal biopsies. Interestingly, the same was true for free oligosaccharides from milk of secretor mothers, having 2-linked fucosylated glycans, while the milk proteins bile salt-stimulated lipase (BSSL) and mucins MUC1 and MUC4 accounted for virtually all the inhibitory activity. These proteins have in common that they have O-glycosylated tandem repeat sequences offering multiple binding sites [35], which these viruses obviously need. Thus, also the
backbone to which the decoy receptors are attached is important. In analogy, we recently showed that BSSL is the main, or the only glycoprotein in human milk that potently binds dendritic cell-specific ICAM3-grabbing nonintegrin (DC-SIGN) and blocks DC-SIGN mediated trans-infection of CD4+ lymphocytes with human immunodeficiency virus type 1, probably by offering multiple Le^x binding sites [36]. Other new bovine milk fractions of potential use in formulas are discussed by Lönnerdal in his chapter. In a more remote future, other bovine milk fractions may be enriched in bioactive substances such as enzymes, enzyme inhibitors, growth factors, cytokines, chemokines, binding proteins and immunoglobulins [37]. However, there will always be limitations to what can be achieved by modification of milks from other species. Some functions are species specific as are some compounds. As mentioned, the composition of the oligosaccharide fraction is very different in bovine milk compared to human milk, and some functional compounds and effects in human milk are absent from bovine milk.

With modern techniques in molecular biology, it is now possible to produce, also on a large scale, recombinant human milk proteins, which can be added to formulas with the potential to further reduce the gap in performance between breastfed and formula-fed infants. Examples of this are lactoferrin and lysozyme; in a recent study, a combination of both was found to shorten the duration of infectious diarrhea [38]. Another example is the fat-digesting enzyme BSSL. BSSL is secreted by the pancreas of all species studied and from the lactating mammary gland into the milk in some species, notably the human but not the bovine. BSSL is a key enzyme in neonatal fat digestion and thought to be the main reason for the more efficient use of fat from human milk than from infant formulas [39]. In a recent phase 2 placebo-controlled double-blind clinical trial in preterm infants, recombinant human BSSL was found to improve weight gain when added to an infant formula at a concentration typical for human milk. In another phase 2 study with similar design, the same principal effect was observed when recombinant BSSL was added to pasteurized human milk (Swedish Orphan Biovitrum, press release 2010-04-21, 2010-05-06). Since pasteurization inactivates BSSL, the addition restored the level of active BSSL in the milk. This illustrates its potential value for a further formula modification, particularly of formulas intended for very low birthweight infants.

New ingredients, some with potent biological activities and produced with new techniques are like to be expensive and they may also confer a safety risk. Moreover, a proven biological activity may not necessarily confer a health benefit on the recipient infants. Therefore it is – and will be even more in the future – extremely important to rigorously ascertain safety and efficacy before formulas with such ingredients are launched on the market, and the cost-benefit must be considered for formulas intended for infants at large, and particularly for formulas intended for infants in low-income countries.
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Discussion

Dr. Garg: Whenever we compare human milk with formula, we just supplement formula with one thing and see the effect on the outcome. Human milk has so many components that affect the same outcome, so maybe adding multiple components would give a beneficial effect that has not been shown with milk formula supplemented with a single factor.

Dr. Hernell: You are right. Human milk, as all milks, is very complex in its composition. We already know that there are differences in outcome between breastfed and formula-fed infants. To find out why that is so, we need to identify and characterize components in human milk that we think might have functional effects, and verify a potential effect if possible first in vitro and in animal models before we finally move on to randomized clinical trials. As I mentioned, many components have been added to infant formulas for a good purpose, and have also been proven to have an effect. However, for some of them the effect is not necessarily the same as a health benefit. To ascertain health benefits that make the addition of a new ingredient justified, we need to do proper clinical studies to prove the health benefit effect. The problem is that for that we need well-designed, sufficiently powered randomized studies, and these are very expensive. However, such studies are needed to prove efficacy as well as safety of new ingredients, even if they are present in human milk.
Dr. Gary: Regarding DHA in breast milk. To what extent is it beneficial to term infants?

Dr. Hernell: I think DHA is one of the components in human milk, and its concentration is reflected by the mother’s diet. I think most of us have been convinced that DHA in formulas like in human milk has a health benefit effect in terms of improved development of visual function and neurodevelopment, at least in preterm infants, and there are studies suggesting that exogenous DHA is also beneficial to term infants, even beyond infancy. Judged by recent meta-analyses and systematic reviews, the results are not as convincing as we used to think. Perhaps the effect is restricted to subgroups of infants that have not yet been clearly identified? It may also be that the effect is there for larger groups of infants but many studies have been underpowered, and there are so many other factors that interfere with neurodevelopment. Moreover, current methodology may not be sensitive enough to reveal small but significant effects.

Dr. Sankaranarayanan: What would be the ideal omega-6 to omega-3 ratio in formula milk?

Dr. Hernell: I do not think we know the optimal ratio, if there is one. When the comments were written by ESPGHAN, the n-6:n-3 ratio was set to 5–15:1 because this range was considered representative of human milk. Perhaps the ratio does not need to be the same in formulas with and without added DHA.

Dr. Anderson: You talked about the modification of the infant formula again by adding many bioactives, and mentioned that there are great differences in protein composition and quantity in milk from different species. Formulas are different from human milk in not only protein quantity but also many aspects of composition. How important is the fact that infant formulas have a higher quantity of protein?

Dr. Hernell: The concern about the protein content in infant formulas has been that high protein content in early life may result in increased risk of obesity, and that’s a major reason why it is of interest to reduce the protein content in infant formulas to come as close as possible to the concentration in human milk. However, even if the concentration has been successively reduced, there is still a difference. The way to achieve a reduced protein concentration has been to improve the quality of the protein, allowing a reduction in the total concentration and still meet the needs of the infants. This method has been used by Nestlé and other formula manufacturers. They increased the proportion of α-lactalbumin, the major whey protein in human milk which has an excellent amino acid profile. Both quality and quantity are important. I have only touched on the potential biological effects of the various milk proteins besides being a source of amino acids. One can assume that these functional effects vary considerably with the quality of the proteins and also with peptides formed from some of them during their digestion.

Dr. Haschke: The lactalbumin-enriched formula was developed by Niels Räiha in 2000 [1]. Four clinical trials, which have recently been analyzed in a meta-analysis [2], indicate that growth of infants fed that formula was similar to that of breastfed infants and to the WHO growth standard for breastfed infants. Fortunately, the GINI study [3] now indicates that at 6 years of age, children who were fed a modern partially hydrolyzed formula (NAN-HA) during infancy, had weight, height, and BMI similar to exclusively breastfed infants. It seems that feeding with modern infant formulas with low protein concentration results in growth similar to that of the breastfed infant, which is important from the obesity perspective. Breastfeeding is now considered to protect from childhood obesity.

Dr. El Barbary: Is breast milk adequate for feeding preterm infants?

Dr. Hernell: That’s a very good question. The answer depends on how much preterm the baby is. If you have a very preterm infant, the mother’s milk will not meet
the needs of all nutrients of the infant, for instance of protein and calcium. Therefore, there is a need to fortify the milk or to use a formula intended for preterm infants. However, there are studies showing that with respect to long-term outcomes, preterm infants fed breast milk are doing better than those fed formula. How to optimize the nutrition of preterm infants is, in my opinion, an area where we need to learn much more. The more preterm the infant is, the more limited is our current knowledge. To meet the nutritional needs and provide the other benefits of breast milk will be the challenge.

Dr. Haralappa: To treat allergic diseases of infants, would you add hydrolyzed protein and probiotics to the formula?

Dr. Hernell: For the treatment of cow's milk protein allergy, I think most of us would recommend a formula based on extensively hydrolyzed protein. It has been more of a discussion what to recommend for prevention of allergy. Most scientific bodies, for instance ESPGHAN and AAP do not recommend any preventive strategy unless the infant is at high risk of developing allergy. For high-risk infants, breastfeeding is still the first recommendation. To recommend a formula is more difficult. It is debated how effective such prevention is and if formulas based on partially hydrolyzed protein have comparable effects to those of formulas based on extensively hydrolyzed protein, and if some formulas based on partial hydrolysates are more effective than others. I think we need more studies to give firm recommendations when it comes to prevention. With respect to probiotics, the data are still too inconclusive to give recommendations.

Dr. Sankaranarayanan: I agree with you that breast milk is one of the best prebiotics. But the amount of oligosaccharides in breast milk, is it optimal? Are there any studies? And what would be the ideal amount of oligosaccharides in infant formula?

Dr. Hernell: In human milk, the oligosaccharides are the third largest fraction, so they constitute a large fraction. They are also very complex in structure, and the composition varies between mothers, depending on, for instance, what blood group antigens they are expressing. The optimal concentration as well as composition is unknown, and it also depends on what effect you are looking for. I gave the example with calicivirus and the milk lipase BSSL; some mothers confer a protective effect via their milk and others do not depending on the glycosylation pattern. So far, it has not been possible to copy the oligosaccharides in milk, and to do this would be very expensive, I guess. What formula manufacturers do instead is to try to find other sources of oligosaccharides which are much less complex and much less diverse. How much to add to a formula is also a matter of how much are you allowed to add because that is specified in the infant formula directive, at least in Europe.

Dr. Klassen: A comment to the question related to partial hydrolysates. I wanted to bring to your attention that very recently two meta-analyses have been published on the preventive effect of hydrolysates. I want to underline the point Dr. Hernell made that the effect has to be demonstrated in clinical trials for each single hydrolysate. Some hydrolysates were shown to actually reduce the risk of development of atopic dermatitis to the level of breastfed children, so I think this is a somewhat important effect.

Dr. Mouane: I have a question about protein hydrolysates. You told us the degree of prevention depends on the hydrolysates, so what is the right one? Could you be more precise?

Dr. Hernell: I think the best answer you can get right now is conveyed in Dr. Klassen's statement.

Dr. Klassen: It's basically looking at the scientific evidence, as Dr. Hernell said in his talk. We should consider evidence from randomized placebo-controlled clinical trials. To my knowledge, clinical trials are selected for meta-analyses according to
quality criteria. Thus, it is only the clinical data that really count, in my view. It is not sufficient to have just animal data. This might be a good indicator, but can be limiting in establishing the evidence.

Dr. Haschke: The meta-analysis you are asking for comes out in the May 2010 edition of *Journal of Pediatric GI and Nutrition*, so you can make up your mind based on this.

Dr. Jongpiputvanich: I have read in the literature that breast milk also contains probiotics. Would you like to comment on that? And what is the mechanism behind breast milk probiotics?

Dr. Hernell: Before I started, I deleted one slide. That was actually a slide showing the front page of a paper in *BMJ* that we wrote in 1980; it was called ‘Human milk banking. To heat or not to heat.’ It says in the abstract that our study shows that human milk contains pathogens, but they seem to make no harm. From there, we have in 30 years switched from thinking that they do not cause harm to that they may even be beneficial and are meant to be there. But how they get there, I think is still an open question. If you read the paper, we found that breast milk samples at that time could contain $10^5$ CFU/ml bacteria, but such milk didn’t cause any harm to the baby. When we instructed mothers to carefully clean the nipple and the areola before sampling, the bacterial counts were significantly reduced but not to zero. How for instance bifidobacteria present in human milk get into the milk, I think is still an open question. My guess would be from the outside.

Dr. Gibson: You gave an excellent summary table of the various effects of various additives that are being put into infant formulas. Testing the efficacy of some of these things has proven very difficult, particularly in the case of term infants where they have blood reserves on the one hand and on the other hand they have endogenous capacity, and I am thinking particularly of say DHA, the omega-3 fats and nucleotides. What are your thoughts about the efficacy of some of these things? Are they cosmetic or do they play a real role?

Dr. Hernell: I think if you look at nucleotides and read the literature, it’s very difficult to say yes they are beneficial, they do have a health consequence. On the other hand, if you look at subpopulations of infants, it may be that they do benefit from exogenous nucleotides, but I don’t think it is something that you need to add to an infant formula intended for healthy term infants, that’s how I read the literature. Concerning DHA, you know that better than I do, I think it’s pretty much the same; it’s very difficult to prove that you really have a health consequence in healthy term infants, which does not necessarily exclude such an effect.

References