Clinical Benefits of Human Milk for Premature Infants

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The American Academy of Pediatrics recommends breastfeeding throughout the first year after birth for the full-term neonate and acknowledges the benefits of human milk in the management of premature infants (1). The beneficial effects generally relate to improvements in host defense, digestion and absorption of nutrients, neurodevelopment, gastrointestinal function, and psychological effects for the mother. The goal for nutritional support of the premature infant is to meet the intrauterine rates of growth (2). In doing so, several specialized needs of the premature infant must be considered, including metabolic and gastrointestinal immaturity, immunological compromise, and associated medical conditions that affect nutritional support. Human milk is capable of satisfying many of those needs for premature infants (3). However, careful attention to nutritional status is necessary. In this chapter I will focus on the benefits of human milk for the premature infant, comment on the need for nutrient fortification of human milk, and discuss the outcomes of feeding fortified human milk.

UNFORTIFIED HUMAN MILK

Clinical studies in nurseries throughout the world have suggested a decrease in infection in premature infants fed human milk compared with formula. Narayanan et al. (4) reported a lower incidence of a variety of infections in premature infants fed their mothers’ milk during the daytime (and formula at night) compared with similar infants fed formula exclusively. The lower rate of infection is reported irrespective of whether fresh or pasteurized human milk is fed (3). Early feeding of colostrum is also associated with a lower rate of infection compared with the early feeding of formula (3). Most recently, data from Mexico City suggest that premature infants have fewer episodes of necrotizing enterocolitis, diarrhea, and urinary tract infection, and needed less antibiotic treatment when fed their own mothers’ milk compared with similar infants fed term formula (5).

Necrotizing enterocolitis (NEC), a devastating acute intestinal inflammatory disease in premature infants, is less likely to occur in infants fed human milk. A very large, nonrandomized study of premature infants in hospital reported that the
incidence of NEC was significantly lower in infants fed human milk, either exclusively or partially, than in infants fed formula (6). That study reported clinical cases as well as confirmed cases, and in both circumstances the incidence of NEC was significantly higher in infants fed solely on formula. In another report, the disease appeared to be less severe and there was a lower incidence of intestinal perforation during the course of the disease in infants who had received human milk before diagnosis (7%) compared with those fed formula (39%) (7). These data suggest that the use of human milk may help prevent NEC in premature infants.

Specific factors such as secretory IgA (sIgA), lactoferrin, lysozyme, oligosaccharides, growth factors, and cellular components may affect the host defense of the premature infant. One of the major protective effects of human milk on the recipient infant operates through the entero-mammary immune system. It is reasonable to expect that exposure of the mother to the environment of the neonatal nursery through skin-to-skin contact with her premature infant may be advantageous to the infant. In this manner, mothers can be induced to make specific antibodies against the nosocomial pathogens in the nursery environment.

The reason for the protective role of human milk in NEC is unclear. One study associated a decreased incidence of NEC in premature infants with the feeding of a preparation of immunoglobulins A and G (IgA–IgG) derived from serum (8). The infants fed the IgA–IgG preparation had a significantly higher fecal excretion of IgA than controls, suggesting a local protective effect throughout the gastrointestinal tract. Our studies at the Children’s Nutrition Research Center in Houston also showed greater fecal excretion of IgA as well as greater excretion of lactoferrin in feces and both IgA and lactoferrin in urine of premature infants fed human milk compared with similar infants fed formula (9,10). In our studies, fecal excretion accounted for 9% of the IgA and 5% of the lactoferrin intake. Additional studies suggest that human milk–derived lactoferrin may be absorbed intact and excreted in the urine of premature infants (11). These results suggest that human milk may enhance the premature infant’s host defenses through local and systemic actions.

Diet also may affect fecal flora. Feeding of human milk to a compromised premature infant may result in a fecal flora that is less pathogenic than that of a bovine-derived formula. A less pathogenic flora would change the predominant nursery-acquired fecal pathogens to more beneficial, less pathogenic microorganisms.

Thus the relation between the feeding of human milk and the reduced incidence of infection or NEC reported in these descriptive studies indicates the particular suitability of human milk for premature infants.

However, the exclusive feeding of unfortified human milk in premature infants, generally infants with birthweights of less than 1,500 g, has been associated with poorer rates of growth and with nutritional deficits, during and beyond the period of hospital inpatient care (5,12–17). Because of the availability of commercial formulas designed to meet the nutritional needs of the premature infant, the use of unfortified human milk has declined. The recognition that growth and nutrient deficits can be improved with the use of nutrient supplements has led to a renewed enthusiasm for the use of human milk for premature infants (18–21).
Unfortified human milk may not supply sufficient quantities of nutrients for several reasons. The concentrations of several nutrients (e.g., protein and sodium) decline through lactation. The nutrient needs of the premature infant, however, do not decline until approximately 40 weeks of postmenstrual age. Therefore the decline in milk concentration results in an inadequate nutrient supply to the infant. The content of other nutrients (such as calcium and phosphorus) is too low to meet the considerable needs of the premature infant. Technical reasons associated with the collection, storage, and delivery of milk to the infant also result in a decreased quantity of available nutrients (e.g., fat, vitamin C, vitamin A, riboflavin). Lastly, the premature infant is usually tube-fed, making ad libitum feeding unlikely. Furthermore, fluid restriction is often imposed as part of the clinical management. Given the reasons cited, it should not be a surprise that inadequacies of calcium, phosphorus, protein, sodium, vitamins, and energy are observed in the premature infant fed unfortified human milk (5,12-17).

HUMAN MILK FORTIFICATION

Single and multinutrient supplementation of human milk has been associated with improvements in short-term growth and nutritional status. Mineral supplementation of unfortified human milk during the hospital stay increases bone mineralization during and beyond the neonatal period and prevents a decrease in linear growth (22–24). Supplementation with both calcium and phosphorus results in normalization of biochemical indices of mineral status—serum calcium, phosphorus, and alkaline phosphatase activity; urinary excretion of calcium and phosphorus (25,26). Sodium supplementation results in normalization of serum sodium (27). Supplementation with protein and energy is associated with improved rates of weight gain and improved indices of protein nutritional status—blood urea nitrogen, serum albumin, prealbumin (16,21).

Current practice suggests the use of multinutrient fortification of human milk. Nutritional outcomes of feeding fortified human milk in the United States indicate that premature infants receive less volume but greater intakes of protein and minerals, and experience greater gain in weight and increments in linear growth than infants fed unfortified human milk exclusively (19,28,29). Balance study data indicate that the use of fortified human milk results in net nutrient retention that approaches or is greater than the expected intrauterine rates of accretion. Fat absorption, however, has been lower than expected in some reports (26,30).

Lucas et al. (31) compared growth and nutritional status in premature infants who received fortified human milk versus partially supplemented (control) human milk. Premature infants fed human milk (birthweight < 1,850 g) were assigned to receive either a multinutrient fortifier (Enfamil Human Milk Fortifier, Mead Johnson Nutritional Group, Evansville, Indiana) or a control supplement (phosphorus 4.8 mmol/liter, sodium 0.3 mmol/liter, and multivitamins) mixed with their mothers’ milk. Many mothers were unable to sustain lactation for the duration of the study (average 40 days), so preterm formula comprised more than 50% of the milk consumed.
in both groups. Therefore the primary comparisons between groups may have been affected by the large quantity of formula given to the study infants. Nevertheless, there were no differences between fortified and control supplement human milk groups in growth outcome measures at 18 months of follow-up. Short-term differences were observed that were more apparent in an analysis of the data from infants who received more than 50% of their enteral feeding as human milk. The data suggested that the feeding of fortified human milk was associated with greater weight gain and a higher blood urea nitrogen (an index of normal protein nutritional status) than control supplemented human milk.

The growth and nutritional status of premature infants fed fortified human milk versus preterm formula has been examined (29). The growth rates of infants (birth-weight \~1 kg, gestational age \~28 weeks) fed fortified human milk (Enfamil Human Milk Fortifier, Mead Johnson) were significantly lower (18 versus 22 g/kg\cdot d) than in infants fed preterm formula (Enfamil Premature Formula, Mead Johnson). Premature infants fed fortified human milk also had lesser increments in linear growth (0.8 versus 1.0 cm/week) and in average skinfold thickness (0.17 versus 0.25 mm/week) than infants fed preterm formula. To meet projected daily weight gains, the infants fed fortified human milk required milk intakes of more than 180 ml/kg\cdot d compared with infants fed preterm formula, who needed 150 to 160 ml/kg\cdot d to achieve those goals. The fluid intakes of infants fed fortified human milk were significantly greater than those usually recommended. Nutrient absorption and retention were measured by 72-hour balance studies at two time periods during the hospital stay, at 6 and 9 weeks of postnatal age. The fortified human milk provided nutrient intakes that approached or surpassed the estimates for intrauterine nutrient accretion (2,32). A correlation between calcium retention and bone mineral content of the radius was observed, suggesting that a greater quantity of minerals may affect bone mineralization. The data further suggested that the addition of magnesium, copper, and possibly zinc to human milk may not be necessary, as respective retentions were significantly above the intrauterine nutrient accretion rates.

The most marked difference between fortified human milk and preterm formula was in the absorption of fat. The infants fed fortified human milk had significantly lower rates of fat absorption than those fed preterm formula (62\% versus 91\% and 78\% versus 92\% at 6 and 9 weeks, respectively). The lower rates of fat, and therefore energy, absorption may have been the reason for the lower rates of growth in the infants fed fortified human milk (15,26,30).

It is unclear why fat absorption was so low. The addition of a large quantity of minerals to human milk may have created an unfavorable milieu for the human milk lipid system. The fat globule may have been disrupted by osmotic forces generated by the high mineral content of the fortifier. Such forces may affect the fat globule and liberate fatty acids. Moreover, free fatty acids may bind minerals. In the intestinal tract, soap formation caused by fatty acid binding to minerals may hinder fat absorption. Interactions between calcium and fatty acids have been reported during calcium supplementation of human milk for premature infants (33). Clinical data suggest that the large quantity of minerals in the fortifier affect fat absorption. Premature infants
TABLE 1. Comparison of selected fortifiers for human milk (prepared per 100 ml milk)

<table>
<thead>
<tr>
<th></th>
<th>PrHM*</th>
<th>EHMF†</th>
<th>SNC‡</th>
<th>Eoprotin§</th>
<th>SMAHMF‖</th>
<th>FM85#</th>
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<tr>
<td>Energy (kcal)</td>
<td>71</td>
<td>85</td>
<td>76</td>
<td>85</td>
<td>86</td>
<td>89</td>
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<tr>
<td>Fat (g)</td>
<td>3.6</td>
<td>3.6**</td>
<td>4.0</td>
<td>3.6**</td>
<td>3.6**</td>
<td>3.6</td>
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<tr>
<td>Carbohydrate (g)</td>
<td>7.0</td>
<td>9.7</td>
<td>7.8</td>
<td>9.8</td>
<td>9.4</td>
<td>10.6</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>1.8</td>
<td>2.5</td>
<td>2.0</td>
<td>2.6</td>
<td>2.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>22</td>
<td>112</td>
<td>97</td>
<td>72</td>
<td>112</td>
<td>73</td>
</tr>
<tr>
<td>Phosphorus (mg)</td>
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<td>59</td>
<td>50</td>
<td>48</td>
<td>59</td>
<td>48</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>2.5</td>
<td>3.5</td>
<td>6.3</td>
<td>5.3</td>
<td>4.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Sodium (mmol)</td>
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<td>1.0</td>
<td>1.1</td>
<td>1.9</td>
<td>1.1</td>
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<tr>
<td>Zinc (µg)</td>
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<td>1030</td>
<td>760</td>
<td>320**</td>
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<td>320**</td>
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<tr>
<td>Copper (µg)</td>
<td>60</td>
<td>122</td>
<td>130</td>
<td>60**</td>
<td>60**</td>
<td>60**</td>
</tr>
<tr>
<td>Vitamins††</td>
<td>Yes</td>
<td>††</td>
<td>††</td>
<td>††</td>
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<td>††</td>
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</tbody>
</table>

* PrHM = Preterm Human Milk (46).
† EHMF = Enfamil Human Milk Fortifier (Mead Johnson Nutritional, Evansville, IN); partial vitamin supplement.
‡ SNC = Similac Natural Care (Ross Labs, Columbus, OH): mixed 1:1 (vol:vol) with PrHM.
§ Eoprotin (Milupa, Friedrichsdorf, Germany).
# FM85 (Nestlé, Vevey, Switzerland).
** Indicates nutrient not contained in fortifier.
†† Complete multivitamins mixture: A, D, E, K, B-1, B-2, B-6, C, niacin, folate, B-12, pantothenate, biotin.

receiving a human milk fortifier (Eoprotin, Milupa, Friedrichsdorf, Germany) containing less minerals than the Enfamil Human Milk Fortifier have mean rates of fat absorption of 92% and rates of weight gain and linear growth greater than those reported for similar infants fed Enfamil Human Milk Fortifier (29,34). A comparison of the nutrient content of human milk fortifiers is given in Table 1. Although it is difficult to make comparisons between studies, the lower mineral content fortifier tends to favor better fat absorption and growth. Thus it appears that when fat absorption is improved, growth rates increase, and this may be achieved at lower milk intakes. The improvement of fat absorption would most probably favor even better mineral absorption.

Differences in rates of growth in premature infants receiving fortified human milk versus preterm formula have been reported, even for formulas containing lower quantities of protein and minerals than those available in the United States (35). However, in those studies bone mineralization did not differ significantly. Thus the slower rate of growth may not be a marker of poorer nutritional status. None of the studies suggested that the slower rate of growth of the fortified human milk–fed premature infant is detrimental. Indeed, it has been shown that these infants have a shorter period of hospital admission and less infection and necrotizing enterocolitis than infants fed preterm formula (35,36).

NONNUTRITIONAL OUTCOMES OF FEEDING FORTIFIED HUMAN MILK

Questions have been raised as to whether the addition of bovine-derived human milk fortifiers affects feeding tolerance in premature infants. Gastric residual volumes are
often used to assess feeding tolerance. The residual volume may be affected by gastric emptying. The data on gastric emptying, however, are controversial. Novel ultrasound techniques to assess gastric cross-sectional areas have yielded conflicting results (37,38). In contrast, Lucas et al. (31) clearly observed that the use of fortified human milk was not associated with feeding intolerance as manifest by abdominal distension, vomiting, changes in stool frequency, or volume of gastric aspirate when compared with control-supplemented human milk.

The feeding of unfortified human milk to preterm infants during their time in the hospital has been associated with greater intellectual performance scores at 7.5 to 8 years than in similar infants fed formula (39). The relation between diet and developmental outcome at 3 years of age also was reported for Australian premature infants who were born at less than 33 weeks of gestation (40). Human milk feeding had a beneficial effect on scores of intelligence and distractibility hyperactivity. Neurodevelopmental outcomes at 18 months, however, were not affected by human milk fortification in the study of Lucas et al. (31).

Visual function may be improved by feeding human milk to premature infants, possibly owing to the high concentration of very long-chain polyenoic fatty acids in the milk (41). Human milk also has significant antioxidant activity, including but not limited to such compounds as beta carotene, taurine, and vitamin E. Because of the antioxidant activity, the relation between diet and retinopathy of prematurity was examined (42). In this retrospective review of medical records, factors associated with the development of retinopathy of prematurity were studied and the diagnosis of retinopathy of prematurity was found to be significantly more common in formula-fed infants than in human milk–fed infants. The severity of retinopathy also was reported to be less in human milk–fed premature infants. Fewer infants fed human milk (exclusively or partially) progressed to advanced retinopathy, and none required cryotherapy or laser surgery (42). Most of the later studies were conducted in infants receiving fortified human milk. These results support the potential beneficial effects of human milk on neurodevelopmental function in the premature infant, whether receiving unfortified or fortified human milk.

A major concern with human milk fortification is that the added nutrients may affect the complex system of host defense. The relation between diet and the incidence of infection in premature infants has been examined. Human milk–fed infants had a 26% incidence of documented infection compared with 49% in formula-fed infants (43). The relation between necrotizing enterocolitis and human milk feeding has been discussed. Lucas et al. (31) determined that the use of fortified human milk was not associated with either confirmed infection or necrotizing enterocolitis. When the latter two events were combined, however, the group fed fortified human milk had more events than the control supplement group. Although it is difficult to conclude that the use of fortifiers is harmful, these data indicate the need for continued surveillance of these events (44).

In a review of prospectively collected data on morbidity and diet in premature infants in Houston, those infants fed exclusively on fortified human milk had a significantly lower incidence of necrotizing enterocolitis and sepsis, fewer positive blood cultures, and less antibiotic usage than infants fed preterm formula or a regimen of
alternate feedings of fortified human milk and preterm formula (36). Infants fed exclusively on fortified human milk had more episodes of skin-to-skin contact with their mothers and a shorter hospital stay. These data suggest that feeding premature infants with fortified human milk had a marked effect on the cost of medical care. The data further suggest that skin-to-skin contact may be the necessary link to promote an entero-mammary response in the premature infant. It may well become the practice to encourage mothers to have skin-to-skin contact to enhance their capacity to synthesize specific factors that counter the pathogens in the nursery environment.

The effects of nutrient fortification (Enfamil Human Milk Fortifier, Mead Johnson) on some of the general host defense properties of the milk have been evaluated. Fortification did not affect the concentration of IgA (45). Bacterial colony counts, however, increased over time of storage of fortified human milk (45). When fortified human milk was evaluated under simulated nursery conditions, bacterial colony counts were not significantly different after 20 hours of storage at refrigerator temperature but did increase from 20 to 24 hours when maintained at incubator temperature. The overall increase in bacterial colony counts by 24 hours, however, was small (approximately a 10-fold difference). These data did not suggest that changes are necessary in regard to the current practice of how fortifiers are used in the nursery, but they do suggest caution in handling human milk and the need to evaluate environmental effects as they arise.

CONCLUSION

Various methods have been reported and used clinically to augment the nutrient supply for the human milk fed premature infant. These methods include specialized multi-nutrient powdered mixtures ("fortifiers"), complete liquid formulas designed to be mixed with human milk, complete powdered formulas to be mixed with human milk, or alternate feeding of human milk and preterm formula. Although the optimum form of nutrition of premature infants is unknown, data are accumulating to suggest that human milk, fortified with additional nutrients, is appropriate for the tube-fed infant.

- The use of fortified human milk generally ensures adequate growth, nutrient retention, and biochemical indices of nutritional status in the premature infant when fed at approximately 180 ml/kg·d.
- Data are needed to determine the precise quantity of nutrients to be added as supplements. Nutrient interactions have not been explored in detail.
- Although large quantities of calcium appear to be needed, the exogenous calcium may affect fat absorption adversely.
- Although manipulation of milk may affect the intrinsic host defense properties of the milk, when compared with preterm formula, the feeding of fortified human milk may provide significant protection from infection and necrotizing enterocolitis.
- Lastly, the potential stimulation of an entero-mammary pathway through skin-to-skin contact may be a means of providing species specific antimicrobial protection for the premature infant. Several of these areas require further exploration.
Thus for premature infants, neonatal centers should encourage the feeding of fortified human milk, along with skin-to-skin contact, as a reasonable method of enhancing milk production while potentially facilitating the development of an entero-mammary response.

ACKNOWLEDGMENT

This review was supported by the National Institute of Child Health and Human Development, Grant No. RO-1-HD-28140, and the General Clinical Research Center, Baylor College of Medicine/Texas Children’s Hospital Clinical Research Center, Grant No. MO-1-RR-00188, National Institutes of Health. Partial funding also has been provided from the USDA/ARS under Cooperative Agreement No. 58-6250-1-003. This work is a publication of the USDA/ARS Children’s Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine and Texas Children’s Hospital, Houston, TX. The contents of this publication do not necessarily reflect the views or policies of the USDA, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. government.

REFERENCES


DISCUSSION

Dr. Putet: Can you comment on the difference in weight gain between the two groups. Do you think it is only a question of energy absorption?

Dr. Schanler: There were marked differences in fat and energy absorption in the two groups, and together with the differences in skinfold thickness this seems to be the reason why those babies were growing slower.

Dr. Rigo: When we analyzed our data comparing Enfamil human milk fortifier with preterm formula using metabolic balance techniques, we were surprised to find that the weight gain composition seemed somewhat different in preterm infants fed human milk fortifier than in those fed preterm formula. Although the protein deposition was similar, the water content of the tissue deposited seemed to be lower in the infants fed human milk fortifier. Do you have any idea why this should be? Is it to do with the sodium intake?

Dr. Schanler: In our study sodium intakes were roughly the same in the two groups.

Dr. Rigo: But the weight gain was significantly different not only because of differences in fat deposition. We think the lean mass deposition is also different, probably because of the different amount of tissue water.

Dr. Schanler: Nitrogen balance was slightly greater in the preterm infants fed fortified human milk. Probably there was more lean tissue deposition in that group.

Prof. Haschke: Necrotizing enterocolitis was only found in 1% of the infants fed the fortifier? This contradicts previous results where a substantially higher incidence was found. Could you comment on that?

Dr. Schanler: This could be a spurious result based on relatively small numbers. We are looking at this now prospectively. Also, you need to remember that distinct from other studies these infants were fed larger volumes of feed. Their diet was predominantly human milk. We only studied babies who were receiving more than 50 ml/kg·d of fortified human milk, babies who were receiving a mixture of fortified human milk and formula were not included. A problem with analyzing data from babies receiving fortified human milk is that it is hard to get pure groups of infants fed either fortified human milk or human milk exclusively. Babies usually receive formula and to some extent that complicates the observations.

Prof. Haschke: Fat absorption and retention and to some extent calcium and phosphorus retention were low. Do you think these were interrelated?

Dr. Schanler: I think they are related. Either the minerals are binding the fat or damaging the fat globule and binding the fatty acids in the milk, so making them unavailable to the infant, or this process is going on in the gut and the calcium is binding fat there. But it is probably the overall mineral content magnesium as well that affects fat absorption.

Dr. Faouri: Did you observe any differences between your two groups regarding bilirubin levels and the duration of jaundice?
Dr. Schanler: No, there was no difference in hyperbilirubinemia or the use of phototherapy.

Dr. Sedaghatian: How do you use your human milk? Do you store it, or do you give it fresh?

Dr. Schanler: We use mothers own milk. The milk is frozen after collection and then thawed and fortified before use for feeding. We don’t pasteurize it.

Prof. Lucas: We have been looking at our human milk data in relation to infection and found, surprisingly, that sepsis in premature babies was social class related. You might have expected that it would not be, as they are all looked after by the same nurses. But that of course creates potential confounding when you compare breastfed and formula-fed groups in a nonrandomized way, because of the greater positive health behavior of the social classes who breastfeed. Did you attempt to see whether your infection data were robust after adjusting for the early socioeconomic factors?

Dr. Schanler: No, we did not. But that’s an interesting point to study.

Prof. Cooke: Do you employ any form of bacteriological surveillance on human milk that you use to feed preterm babies, either if it is fresh or frozen or if it is processed in another way, and if so, what is that policy?

Dr. Schanler: We don’t have a strict policy. We culture milk in the first week it is brought into the nursery as an indicator of whether or not the mother is complying with the collection procedures. We almost never discard milk because of the results of a culture, but it has helped us re-emphasize to the mothers what technique should be applied.

Prof. Cooke: But if you don’t throw it away, then presumably you feed it, no matter what it has got in it. Our own work seems to suggest that from one collection to another on the same day, you can have positive and negative samples. So I wonder what you feel the value of occasion sampling is.

Dr. Schanler: We don’t have an answer to that question. What is your opinion about that? What should we do?

Prof. Cooke: Does anybody else in the room have a policy backed by any sort of science?

Dr. Schanler: The Human Milk Bank Association of North America has the same type of policy—that is, no routine surveillance, but do it to monitor collection technique.

Prof. Lucas: Neither the Human Milk Bank Association of North America nor the recent British directive recommends routine screening of mother’s own milk. The scientific rationale behind that is first that infection rates are, if anything, lower on unpasteurized human milk than on formula, and second that a Canadian study showed a very poor relation between the presence of organisms in the milk and infection in the baby. There really is no compelling data that human milk is a source of infection for premature babies.

Dr. Walker: Your collaborators in previous studies have defined a mechanism by which mothers produce antibodies in their milk against flora in their own environment, suggesting that there is a built-in protective process against infection. Have you looked at the milk sample to determine if there are antibodies directed against the organisms that colonize the infant?

Dr. Schanler: That is what we are doing right now.

Prof. Pohlandt: We heard from the audience and the panel that there is no scientific basis for bacteriological surveillance of human milk. But there have been sev-
eral papers on the vertical transmission of CMV. Do you think we can still use raw breast milk without checking the mother for CMV, taking into account the risk of vertical transmission to her baby? We have eight cases in our unit.

Dr. Schanler: We know that CMV is destroyed by freezing. I look for guidance in the audience. We are not really sure what is the best course of action.

Prof. Pohlandt: We have tested this in the lab. We found that a temperature of \(-20^\circ\text{C}\) does not destroy the infectious agent.

Dr. Schanler: Please report that. It is important.

Prof. Nowak: You said that you give your babies their mother’s own milk, which means that there may be a significant delay before they receive their first milk feed. Do you think this gap should be filled, perhaps with an IgA preparation? [1].

Dr. Schanler: In our nursery, the staff are reluctant to feed very early. By the time the babies start feeds, on day 4 or 5, there is breast milk available in the volumes that we are going to use. So, in our case, that is not a concern. The IgA study needs to be replicated; those data were almost too surprising to be believed. I know that an attempt was made to repeat it but it was stopped because of the hepatitis C scare.

Dr. Walker: There have been some follow-up studies in the United States [2], but they have not shown as good results as were originally reported in the *New England Journal of Medicine*.

Dr. Nowak: You have shown many benefits of human milk, particularly in relation to the occurrence of necrotizing enterocolitis. What kind of feed would you recommend when enteral feeding is reestablished after necrotizing enterocolitis? Human milk? Regular formula? Hydrolyzed formula?

Dr. Schanler: We routinely use human milk for all our babies post-NEC, moving to fortified human milk thereafter. I don’t know of any trials on this, but it’s an important area. Every textbook you read has one sentence on the nutritional support post-NEC, which is to use hydrolysate formula. There are few data to back that up. We routinely use human milk in those infants, and the only ones who don’t tolerate it are the ones who don’t tolerate any milk and need prolonged parenteral nutrition.

Dr. Rashwan: Is there any evidence of delayed gastric emptying when using fortifiers?

Dr. Schanler: We did not see any difference in indices of feeding tolerance between fortified human milk and formula. There is one report showing better gastric emptying with unfortified human milk than with formula [3]. There are a couple of very confusing reports looking at gastric emptying with ultrasound techniques: one showed no difference with fortified human milk and the other showed delayed emptying with fortified milk [4,5], but we did not see any difference.

REFERENCES