The Knowns and Unknowns of Human Milk Banking

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Abstract

The provision of donor human milk instead of formula is an important contribution to the nutrition and protection from infections for preterm infants. Systematic reviews suggest a lower risk of necrotizing enterocolitis with pasteurized donor human milk (PDHM) as opposed to artificial formula, although evidence supporting PDHM use from randomized control trials is limited. Human milk banks (HMBs) must have a risk management system to maintain a safe product especially as many operate in an unregulated environment. To ensure safety, the HMB in Australia has committed to meet the appropriate standards recommended in the Code of Good Manufacturing Practices (Blood and Tissues) and models risk management during processing on Codex HACCP (Hazard Analysis Critical Control Point) requirements. There is scope to continually reevaluate the screening of donors and quality standards recommended during HMB. This will be most effective if strong networks of HMBs are developed with regional reference laboratories to encourage compliance with safety guidelines. Further research and development is needed to refine technology for treating donor milk such as thermal ultrasound and ultraviolet light, aimed at the retention of full bioactivity. HMB networks will facilitate collection of evidence for refining HMB practice which should translate to improved outcomes for preterm and sick infants. Cost effectiveness is most likely when HMBs are associated with large neonatal intensive care units.

Introduction

Human milk (HM) performs the dual function in all mammals, providing protection and nutrition for the young. The primary advantage of mammals is their ability to reproduce and nourish their young in any environment that supports the adult. Evidence suggests that the nutritional components
evolved from the innate immune system [1]. The innate immune system is an evolutionarily non-antigen-specific, host defense system that provides immediate protection against invasive microorganisms. HM has many important immune properties, for example TLR (Toll-like receptor)-mediated innate immune responses are specifically and differentially modulated by HM [2]. TLRs are ancient innate immune receptors that are expressed by most human tissues, and are crucial for the recognition of pathogen-associated molecular patterns [3].

Provision of donor HM for preterm infants when mothers’ own milk (MOM) is not available is preferable to formula but pasteurization reduces the immune and nutritional benefits to variable degrees. The only human milk bank (HMB) in Australia was established in July 2006 with the opening of the Perron Rotary Express Milk (PREM) Bank at King Edward Memorial Hospital in Perth, Western Australia (WA). Previous efforts at HM banking ceased in the mid-1980s with the identification of transmission human immunodeficiency virus (HIV) via HM. After 4 years experience at the PREM Bank, we have had the opportunity to review our own data and re-assess what is known and remains unknown with regard to HM banking.

Somewhat to our surprise, we have quickly discovered that the community fully support HMBs. The PREM Bank was initially established with all equipment purchased from community donations. Media interest is limitless and almost exclusively positive. We have also found that mothers experiencing an oversupply actively seek us out and, as such, donations have always exceeded our processing capacity. We now also know that neonatal staff prefer to prescribe pasteurized donor HM (PDHM) rather than formula, as shown by steady increase in use since the milk bank opened in WA. The number of babies receiving donor milk has doubled over the past 3 years, but the duration of feeding and the average volume dispensed to each infant has remained reasonably constant. In 2009, the PREM Bank dispensed PDHM to 211 patients for an average of 15 days each. In 2009, 92 mothers donated 1,482 liters of milk. We now know that parents of preterm infants welcome PDHM when MOM supply is inadequate with only a few mothers in WA declining the options of donor milk instead of preterm formula (PTF).

We also know that our experience is not unique and that the World Health Organization and UNICEF have jointly supported the establishment of HMB as part of international efforts to promote and support breastfeeding: ‘Only under exceptional circumstances can a mother’s milk be considered unsuitable for her infant. For those few health situations where infants cannot, or should not, be breastfed, the choice of the best alternative – expressed breast milk from an infant’s own mother, breast milk from a healthy wet nurse or an HMB, or a breast milk substitute fed with a cup, which is a safer method than a feeding bottle and teat – depends on individual circumstances’ [4]. HMB is also referred to by the American Academy of Pediatrics [5] as a suitable alternative when an MOM is insufficient or unavailable. Despite the long history of
HM banking, evidence from randomized clinical trials (RCTs) is limited and includes trials in India by Narayanan et al. [6], in England by Lucas et al. [7], and in USA by Schanler et al. [8].

Narayanan et al. [6] randomized preterm infants to raw or pasteurized HM ± formula and demonstrated pasteurization reduced the protective effects of HM (14.3 infection vs. 10.5%), but infants fed PDHM had lower infection rates than those fed formula (33.3%). Lucas et al. [7] randomized 502 infants weighting <1,850 g PDHM or PTF and demonstrated similar developmental scores (Bayleys) at 18 months which they interpreted as PDHM conferring advantage that was offset by the relatively deleterious effects of low nutrient content. The authors concluded that it is logical to combine the benefits of HM with that of extra nutrition provided in fortifiers. Schanler et al. [8] randomized infants 23–29 weeks’ gestation being fed MOM, to PDHM or PTF once tolerating >50 ml/kg per day if MOM supply was inadequate. Intention-to-treat analysis with 21% PDHM being switched to PTF for poor growth and infants still receiving 50% MOM, showed no benefit of PDHM in primary endpoint of late-onset sepsis and/or necrotizing enterocolitis (NEC). The study design and sample size have been criticized, and the authors agree further studies are required. Meta-analysis of randomized trials of PDHM vs. PTF found a lower risk of confirmed NEC with PDHM (as entire feed RR 0.25, 95% CI 0.06–0.98, as supplemental feed RR 0.3, 95%CI 0.11–0.87) [9].

It is unlikely that future evidence for HMB will come exclusively from RCTs of PDHM. Clinicians working in neonatal intensive care units (NICUs) with access to donor milk may have ethical difficulty randomizing high-risk patients to artificial formulae where the risks are known, and where their own clinical experience suggests fewer complications when donor milk is used. Because these PTF are constantly changing, it could always be argued that to ensure scientific rigor, RCTs would need to be repeated regularly to evaluate potential improvements. We suggest that it is time to accept the evidence of potential and reasonable clinical benefit of donor HM for preterm and ill hospitalized infants. The evidence to date carries enough weight to encourage the establishment HMBs where they are managed to an appropriate standard. We also propose that it is the responsibility of these donor HMBs and the NICUs to which they provide product, to engage in research to better assess potential benefits of donor HM and improve the products provided by HMBs.

What We Know about the Benefits of Pasteurized Donor Human Milk

For preterm infants [9, 10], PDHM reduces the incidence of NEC 4-fold and improves feed tolerance. This may be associated with reduced days of parenteral nutrition and earlier discharge from hospital. Pasteurization reduces the protective effects of HM, but feeding PDHM is associated with a
lower incidence of infections than feeding formula [6]. It is also known that preterm infants fed PDHM grow less well than those fed MOM [8, 10], but the significance of this is unclear. It is unknown whether the high IQ scores associated with feeding MOM to preterm infants [11, 12] relate equally to PDHM. For term infants, there is very limited evidence for benefit. HIV-negative infants, of HIV-positive mothers, fed PDHM had, in general, a larger thymus than infants of healthy mothers fed formula interpreted by the investigators as indicating a benefit due to immunomodulatory factors in breast milk [13]. PDHM has been used successfully to treat short gut syndrome [14]. There is no evidence to support the higher IQ with breastfeeding of term infants [15, 16] relate also to PDHM. There is no evidence that breastfeeding or feeding PDHM is useful in the prevention or treatment of CMP allergy [17, 18]. Breastfeeding is one of the few preventative measures for reducing childhood obesity rates [19], and this may be due to the lower protein content of HM [20]. There is little data on the body composition of infants fed PDHM, although there are theoretical reasons for a potential benefit of feeding PDHM instead of formula in reducing childhood obesity. It has been suggested that feeding PDHM improves quality of life for pediatric and adult patients with cancer [21], short gut syndrome, postsurgical feeding problems and numerous other conditions based largely on anecdotal evidence [22]. We conclude that there is some evidence of benefit for preterm infants (reduced NEC risk, decreased sepsis and neurodevelopment), and therefore these patients should remain the focus of donor HM banking. We are concerned that making donor milk available to outpatients or otherwise healthy term infants may result in donor milk becoming another alternative to mothers feeding their own infants. Conclusive RCT evidence in support of PDHM use in preterm infants seems unlikely, and focusing on collecting other physiological measures, for example ultrasound to assess gastric physiology, may be a better use of resources.

What Do We Know about Human Milk Fortifiers Produced from Human Milk

Sullivan et al. [23] randomized 207 infants with birthweight <1,250 g in the USA to three groups. Two groups received only HM (MOM ± PDHM + HM-based fortifier starting at 40 or 100 ml/kg per day milk feeds), and one group received HM + bovine products (MOM ± PTF + bovine milk-based fortifier). Infants fed HM + bovine products had a higher incidence of NEC than those fed exclusively HM products. There were no differences in feed tolerance or growth between the groups. The rate of NEC in the HM + bovine products was relatively high compared to contemporary outcomes. The bovine products included formula and fortifier. The HM-based fortifier is commercially available from a private company in the US.
The Safety of Human Milk Banks – Management and Regulation

HMBs should be managed and regulated in such a way as to ensure that appropriate measures are undertaken to allow response to unforeseen risks. In the mid-1980s when HIV was identified in HM, most HMBs closed. In Australia, HMB management at that time did not allow a rapid response to this unforeseen risk. The informality of the screening process and the lack of complete record keeping, donation traceability and document and process control were insufficient to respond to this new threat. Since the emergence of these new diseases, similar industries have developed management strategies to allow public confidence in the safety of these valuable services. Blood/tissue banking and the food industry have risk management tools (e.g. Australian Code of Good Manufacturing Practices – Blood and Tissues and Codex HACCP, Hazard Analysis Critical Control Points, requirements) that can be adapted for use during HMB management.

Many countries continue to struggle to maintain the credibility and confidence of clinicians in milk banking safety and efficacy due to the lack of a regulatory body governing the operation of HMBs [24]. In countries such as Brazil, where governments have specific legislation regulating milk banking, these difficulties appear to be significantly reduced [25]. During the establishment of the first HMB in Australia, we encountered barriers as existing legislation did not recognize HM as a Therapeutic Good or Food [26]. Thus, the two bodies regulating the production of these products, the TGA (Therapeutic Goods Administration) and FSANZ (Food Standards Australia New Zealand) did not have a legal framework to regulate HMB. Each State has control over food manufacturing. In WA, the PREM HMB was established with a rigorous quality and safety system based on HACCP. Governments in the eastern states of Australia have not yet endorsed HMB. As part of the current Australian government’s response to the ‘Best Start Report’ [27], the Australian National Breastfeeding Strategy (2010) was developed which recommends national regulations for HMBs be developed based on the WA guidelines. These new national regulations will also be consistent with the Biological Tissue Framework [28]. It is highly unlikely that it will be an option in Australia to feed raw donated milk. Regulation will mandate that the milk be treated to manage the risk of viral transmission and to reduce bacterial contamination.

The Safety of Human Milk Banks – Processing of Donors and Donations

In general, HMB in most countries commit to screening milk donors for the same blood-borne viruses as required by blood banks. Rationalization in some centers has led to dropping of screening for HTLV and restriction
of hepatitis B screening to surface antigen. HTLV is destroyed by pasteurization and freezing, and false positives are associated with influenza vaccination. In Australia, women who have lived for 6 months or more in the UK between 1980 and 1996 are excluded as breast milk or blood donors because of the risk of transmission of variant Creutzfeld-Jakob disease, while countries immediately affected by the bovine spongiform encephalopathy epidemic continue to operate HMBs without evidence of harm. Other reasons for exclusion of donors include an assessment of any medications or pharmacologically active herbal products a donor mother may be taking that may be transferred to breast milk. Much is known about the transfer of common medications into breast milk, and exclusion of donors based on maternal drugs is rarely necessary but proceeds on a case by case basis [29–31].

Bacterial cultures of milk are not consistently performed in all HMBs, and the bacterial count limits for rejecting milk vary between HMBs and from that recommended [32]. In Australia, and most countries, neonatal units do not routinely culture or pasteurize MOM. The risks of feeding heavily contaminated MOM to very preterm infants are unknown. Law et al. [33] cultured 10,128 samples of MOM from 96 mothers fed to infants with birthweights <2 kg in the first 2 weeks of life. They detected no growth in 19% of samples, only Gram-positive bacteria in 74%, only Gram-negative bacteria in 1% and mixed Gram-positive and -negative bacteria in 6% of samples. Gram-negative bacteria were present in at least one sample of milk from 51 of 96 mothers’ milk (53%). There were few adverse events that could be related to ingestion of bacteria in raw milk, but colonization of the gastrointestinal tract by Gram-negative species may have occurred after ingestion of the same species in 48% of 62 babies exposed [33]. Botsford et al. [34] reported 36% HM (MOM and donor) grew Gram-negative bacteria after continuous tube feeding to preterm infants, and found that this was associated with feed intolerance and suspected sepsis.

In Australia, all donor milk is screened before and after pasteurization, and all donor milk is pasteurized. From the past 4 years of operating the PREM Bank, we do know that rigorous bacterial screening of donor milk will result in approximately 26% pasteurized milk being discarded (fig. 1).

This rigorous bacterial screening regime has shown that bacterial content of donated milk varies greatly between donors and even between individual donations by the same donor. Most of the donor milk cultured and pasteurized, and on occasion discarded as ‘unsafe’ by the PREM Bank, has been donated by other mothers of preterm infants in our unit and, as such, has been fed raw to their own infant apparently without incident.

The issue of culturing milk after pasteurization is most controversial. The PREM Bank has processed 1,919 batches of donor milk since establishment in 2006. Every batch has been cultured before and after pasteurization and, of these, 43 showed bacterial growth after pasteurization. Twenty-six of these
43 passed the prepasteurization bacterial screen. *Bacillus* species grew in 32 of 43 postpasteurization cultures, including *Bacillus cereus*, a known food-borne pathogen. Postpasteurization obviously precludes use, and these batches are discarded. The germination of the vegetative spores of *B. cereus* is a well-documented consequence of heat treatment during food production [35, 36]. Only 7 of the 32 samples that grew *Bacillus* after pasteurization grew *Bacillus* before pasteurization. Without routine postpasteurization culture, one batch showing growth of a known food-borne pathogen would be released every 66 batches. At the PREM Bank, this would occur once every 5 weeks of processing. A similar issue with *Bacillus* culture after pasteurization of HM has recently been reported from the Austin HMB in Texas, USA [37]. We recommend post-pasteurization cultures for all donor milk dispensed to neonates.

Due to the risk of bacteria contamination and associated heat-stable toxins, all HMBs should consider implementing strict screening standards. In the case of the PREM Bank, the decision was driven by the risk assessment required during HACCP development. Although current evidence would suggest a low likelihood of bacteria that had been present in donor milk prior to pasteurization causing a clinical issue for a recipient of donor milk, the extreme vulnerability of our recipients currently dictates this cautious approach to bacterial screening. To ensure the viability of HM banking and its ability to operate in the most efficient manner possible, revision of bacterial screening of milk remains an issue requiring further research. The PREM Bank is currently developing real-time polymerase chain reaction method for the specific and rapid detection and quantification of bacteria and pathogens to allow milk

*Fig. 1.* Volume of PDHM rejected (black) due to bacterial quality in the PREM Bank.
which is heavily contaminated or contains pathogens to be identified and discarded prior to pasteurization.

Alternative approaches are used internationally to increase efficiency and reduce cost while maintaining acceptable safety. In some countries, milk is streamed to be fed raw or pasteurized to very preterm and term infants based on level of contamination and risk to patient. For example, in Germany, donor milk with $<10^3$ CFU/ml is used for feeding infants $<1,500$ g either raw or pasteurized, whereas milk containing $10^4$–$10^5$ CFU/ml is analyzed for pathogens and pasteurized for feeding older babies if pathogens $<10^4$ CFU/ml [38]. This appears to be a pragmatic approach to minimize the waste of donations, but in the context of evidence-based practice, may be difficult to implement in some countries.

Most HMBs pasteurize donor milk at 62.5°C for 30 min to eliminate bacteria and viruses. However, raw milk is used for preterm infants in some countries: raw donor milk has been used for feeding preterm infants for many years in Norway where donors are screened for HIV, hepatitis B and C, HTLV 1 and 2, and CMV, and the milk screened to ensure that it is free of pathogens and has low bacterial counts [39]; in Sweden, raw donor milk is used in 5 of the 27 HMBs for preterm infants [32].

### Nutritional Adequacy and Variability of Pasteurized Donor Human Milk

In 1980, Björkstén et al. [40] demonstrated that pasteurization reduced the bioactivity of breast milk. In our HMB, the retention of IgA, lactoferrin and lysozyme after classical pasteurization at 62.5°C was 72.3 ± 3.6, 21.8 ± 3.3 and 39.4 ± 11.5% (n = 22) [41]. It is possible to optimize the pasteurization temperature and improve pasteurization design to improve the quality of PDHM; for example, pasteurization at 57°C for 30 min retains 90% bioactivity and removes 99.9% of bacteria [41]. Bile salt-stimulated lipase is also inactivated by classical pasteurization, which will also remove the filaments from the HM fat globule [42]. These factors contribute to reduced fat absorption from PDHM vs. raw milk [43, 44].

The composition of donor milk is highly variable with mean (coefficient of variation) values for fat, protein and lactose being 4.16 (21%) g/100 ml, 1.35 (24%) g/100 ml and 6.71 (9%) g/100 ml, respectively (n = 50, PREM Bank). Most very preterm infants being fed HM are supplemented with HM fortifiers containing protein, calories and minerals. PREM Bank measures the nutritional composition of donor milk, and the data are used for nutritional audits and occasionally for individualized fortification. Standardization of nutritional product from HMB is possible but rarely practiced [45]. Infrared spectroscopy is a useful analytical method for determining the macronutrient content of HM, and recently the mid-infrared HM analyzer (Miris AB, Uppsala, Sweden).
requiring 2- to 3-ml milk samples has been validated for human fresh and frozen milk and for pasteurized HM [46].

The Influence of Establishing a Human Milk Bank on Breastfeeding Rates in the NICU

It is important to confirm that PDHM is replacing formula not MOM in the NICU. We performed an audit of breastfeeding rates at discharge home in infants born <30 weeks gestation and surviving >3 weeks. In the 6 months before we established our HMB, 45/74 (61%) of very preterm infants were breastfed on discharge vs. 60/80 (75%) in the 6-month period one year after the establishment of our HMB. 15% of very preterm infants received formula as their first feed before the HMB opened vs. none after. Of infants who receive some PDHM, 60% go home breastfeeding. In our NICU, consent for feeding PDHM is obtained by the lactation consultants who also support the mother to express her own milk. Increased awareness of the benefits of HM may be a contributing factor to the increased breastfeeding rates of mothers of preterm infants discharged from the NICU after establishment of an HMB [47].

Cost Evaluation

There have been previous attempts to compare the cost of operating an HMB with the potential cost savings derived from the reduction in incidence of NEC in NICU [48, 49]. In countries where the background rates of NEC are low and hospital costs differ, it may be difficult to transpose these cost/benefit models. However, simple comparisons can be made. In the US, private non-profit milk banks charge USD 3.00 per 30 ml of PDHM; this charge covers the cost of donor screening, milk processing and transport. This equates to approximately AUD 120 per liter of donor milk. Following our NICU standard feeding regime for a hypothetical 24-week CGA infant fed exclusively donor milk, we would expect to require 10 l of donor milk until discharge. Thus we could attribute a cost of AUD 1,200 to provide donor milk for this hypothetical infant. This cost equates to less than a single day’s care in our NICU. Given that many of the complications attributed to artificial formula use may increase the complexity of care and length of stay, providing PDHM needs only to prevent a few of these complications to recoup the investment many times over.

The Way Forward

Standard pasteurization at 62.5°C reduces bioactivity of immune factors in HM by about 50%. At least 57°C is required to destroy bacterial cell wall,
and temperatures above this damage proteins. BSSL is destroyed at 45–55°C. Alternative technologies for treating HM need to be developed to better retain bioactivity. We are assessing new methods developed by the food and dairy industry. Interestingly, these technologies are used to improve taste and smell of dairy products, not bioactivity. Ultrasonic pasteurization (22–100 kHz) induces inertial cavitation and results in the formation of microscopic bubbles which rapidly collapse producing shock waves and localized heating. These mechanical forces disrupt cellular membranes leading to cell lysis. We have shown that combining ultrasound with low heat (45°C) will result in a significant increase in bacterial inactivation, especially of *Staphylococcus epidermidis* which has some resistance to cavitation. Thermo-ultrasonic pasteurization reduces bacterial contamination while retaining secretory IgA, lactoferrin, lysozyme and BSSL at 90, 78, 80 and 45%, respectively. In addition, this technology homogenizes HM, which will prevent fat separation and loss of energy during tube feeding [50]. Further improvements are required to better retain bioactivity especially of BSSL. We are currently developing methods based on ultraviolet light. The preliminary findings are encouraging and may result in a safe high-quality product to be trialed as a priority in the care of preterm infants.

HMBs are most successful when developed as part of a package to promote breastfeeding, and this is likely to provide the way forward for the further development and regulation of HMB in Australia. The establishment of the PREM Bank was only possible because of generous financial contributions from the community and, unsolicited donations of breast milk. The ongoing costs are incorporated into the budgets of the NICU and pathology department of our hospital, the only tertiary perinatal centre in WA. The government has commended the contribution of PREM Bank to the health of the community by presenting prestigious State and Health Department awards in our first few years of operation. Networks of HMB have been established in countries such as Brazil and Sweden with some coordination of activities. In our region of the world, PREM Bank is supporting the development of milk banks in Melbourne, Sydney, Brisbane, New Zealand and the Philippines (with UNICEF). Networks facilitate quality control and training, encourage collaboration and contribute to maintaining standards and reducing costs. A reference laboratory within each region or country could monitor compliance with safety guidelines, liaise with Government and coordinate educational activities. We have become the reference laboratory for our region, and the lessons that we have learnt and the protocols that we have developed are readily transmissible to other units.

Collaboration between HMBs and between networks will lead to data collections and clinical studies which will provide evidence for refining and improving the process of HM banking and ultimately clinical outcomes related to feeding preterm and sick infants.
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References

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Discussion

Dr. Mohanty: What would be the cost of decontaminating 1 liter of bank milk?
Dr. Simmer: In American figures it is USD 120, but we can't actually cost it in Australia because it's just incorporated in our unit, and the nurses and the doctors and the equipment are all part of it. But the actual pasteurizer, there are cheaper versions being developed. We visited with the WHO the milk banks in the Philippines, and they just make a very simple water bath, so the standards and the risk-benefit ratio are different in different parts of the world.

Dr. Mohanty: Have you ever detected HIV virus in the milk?
Dr. Simmer: We have never found an HIV-positive mother on screening donors. But we wouldn't take the milk from an HIV-positive mother. CMV is very common in Australia, but that is destroyed by pasteurization.

Dr. Gottrand: Another use of human milk from a milk bank is for an infant with the short bowel syndrome, but the data supporting that this milk helps intestinal adaptation are insufficient. Could you comment on this use, and do you have any experience?

Dr. Simmer: At our Children's Hospital NICU, where babies with short gut syndrome go, we do use human milk. There was at first a little bit of resistance, clinicians wanting to use the elemental formula, but human milk, particularly when you are fed small quantities, is better.

Dr. Lack: You have shown some quite convincing data about protection of breast milk in the very sick newborn, but the question remains, these protective effects are they due to protective beneficial effects of the breast milk or is it cow's milk protein, for example, that may lead to a cellular form of allergy or reaction in NEC? In some of these other conditions, you always have to question is it the beneficial effects of the milk that are protecting you or is it something negative in cow's milk, it's constituents or protein? If it's the latter, then trying to recreate the best form of human breast milk might not be the best approach, and I wondered are there any trials for example trying to prevent NEC with extensively hydrolyzed milk formula or elemental amino acid-based formulas?

Dr. Simmer: Most of the babies do get a bovine protein fortifier anyway, so I think the human milk is protective. There are a lot of good things in human milk. A long time ago, elemental formula was associated with NEC compared with normal formula because it has a high osmolality, and also the elemental formulas are made for GIT pediatric patients and often have long-chain fats, elemental formulas are not really made for preterm infants. The preterm formulas are pretty good, but not as good as human milk. Why would you use another formula as the preterm formula is made perfectly for a preterm infant?

Dr. Lack: So, an elemental formula could be presumably adapted to make it more suitable if it was something about milk protein.

Dr. Simmer: Yes it could be, and you can even buy preterm formulas with hydrolyzed protein if that's what you want. Most of us are a bit nervous about it because there have been trials reporting poor growth of preterm infants fed hydrolyzed formula.
**Dr. Saavedra:** I have a comment relative to elemental or amino acid-based formulas for premature infants. We have been dealing with short bowel patients, and we started using amino acid formulas to see if we could get them off parenteral nutrition faster than with either hydrolyzed or intact protein formulas. There are no good control studies in children with post-NEC short bowel syndrome, but even though it appears we could get them off parenteral nutrition faster, these kids who are now 10–12 years old, they can’t get even close to any whole protein because they are extremely allergic as opposed to children who we had on hydrolysates who are tolerating protein much better. We were actually tolerizing these babies by using hydrolyzed or intact proteins, which we could not do if we just used amino acid for a long period of time.

**Dr. Jones:** I was intrigued by your comment that there was bacterial contamination in normal breast milk in mothers and that you should pasteurize it. That goes to the whole hygiene hypothesis argument that doesn’t seem to do healthy children any harm. My question is, is pasteurized and homogenized bank milk better than untouched bank milk?

**Dr. Simmer:** One of my colleagues has moved to head a unit where they pasteurize the milk of CMV-positive mums (mums’ own milk). I think that this protocol could well cause more harm that good. However, our milk rooms in our NICUs have been run like a kitchen and not to the standard of a human milk bank. I think we could improve our food handling standards in the hospital milk room.

**Dr. Stettler:** A few years ago, there was a paper from Germany that showed that children who had been fed bank breast milk from diabetic mothers were more likely to become overweight or obese than those who had been fed breast milk from non-diabetic mothers [1]. I would like to know if you are familiar with that study, if you followed that literature and whether that has an implication on your practice.

**Dr. Simmer:** I am not familiar with the paper, and it’s not a question that we asked donors. Women with diabetes do have more trouble establishing lactation, than non-diabetic women, so they would be infrequent donors.

**Dr. Harding:** You are using banked milk and adding a bovine fortifier, but there are clearly possibilities for human milk fortifier. Where do you see that going?

**Dr. Simmer:** Dr. Van Goudoever will talk about this too, but we have used the ultrafiltration method and you need a lot of human milk. You also have to pasteurize it and protein quality may be reduced. I really think we have to improve pasteurization technology before we move onto further processing human milk. Dr. Van Goudoever?

**Dr. van Goudoever:** It’s the same answer; we are on the edge of basically of producing our own human milk-based fortifier. Active freeze drying is the process we are doing, and we do it on pasteurized milk. But it’s complicated. Like Dr. Simmer says, you have to add all kinds of vitamins, minerals, so as a neonatologist you are trying to mimic Nestlé so to say, and that’s hard.

**Dr. Simmer:** And we don’t have any evidence to support freeze-drying milk. The actual bovine fortifiers are pretty good, and we’d need to do the trials human versus bovine. The bovine fortifier is going to be a lot cheaper than the human milk one.

**Dr. van Goudoever:** So, we agree on having more studies.

**Dr. Simmer:** On human milk fortifier, yes. I’d find it hard to randomize a thousand babies to formula if you had human milk there, but it’s not impossible.

**Dr. Harding:** It will also be interesting to debate what the outcome measure should be for such trial.

**Dr. Were:** In areas where we do not have pasteurizers and we also do not have fortifiers freely available because of cost, how long would you be able to store mothers’ own milk so that we can give the milk she lactated in the first 3 weeks to the baby for the subsequent 2 weeks? Do you have any information about that?

**Dr. Simmer:** In the freezer, 3 months.
Dr. Nagesh: We have a problem regarding the cost of running a human milk banking facility. A lot of units in India use single donor unpasteurized breast milk for a single baby after taking informed consent. What are your thoughts on this?

Dr. Simmer: I am not opposed to that. I think as a director of a unit I wouldn’t encourage it, and I don’t think our government would be particularly happy. But on a one-on-one basis, if both parties are happy with it, I would be comfortable. Certainly in our aboriginal community that happens quite a lot. So, officially we wouldn’t condone it, but on an individual basis I would be comfortable with it.

Dr. Nagesh: But is pasteurization not required then?

Dr. Simmer: No, you have got one donor to one baby, you don’t have to pasteurize that milk as long as the recipient mum is aware of the risk, even though it’s low.

Dr. Haschke: One comment on the cost structure of donor’s milk. You were saying that in your unit is grossly subsidized and you cannot really estimate how much it costs, considering the whole logistic procedure. You mentioned the figure of USD 120 per liter in the US. We visited the milk bank of the University of Iowa and tried a cost analysis, where we assumed that the university wouldn’t subsidize everything (e.g. students collect the milk, the University provides the car, housing, etc.). Our estimates were in the range of USD 300–500 per liter. This implies that the donating mothers are not getting any money. I find it somehow unethical to sell human milk protein and not give the mothers anything who donate the milk. What is your position on commercial human milk protein?

Dr. Simmer: I am uncomfortable with mums donating milk and a company making money out of it. It’s not the way most milk banks work around the world, so I wouldn’t be that happy with it. The cost of handling donor milk is just absorbed into the running costs. We are never going to get pasteurized donor milk as cheap as formula. We do not plan to sell it to term babies. When you compare the costs with how extremely expensive intensive care is for those little preemies who are getting NEC, then I think the cost of HMB becomes acceptable.

Dr. Haschke: I agree with you. One thing which should be done is a health economic analysis based on a real simulation of conditions which apply. Even if the cost per liter of milk comes out higher, there could be a benefit for the population.

Dr. Simmer: I have been looking for PhD students to do just that. It would be good information to have.

Dr. Lack: You mentioned about restricting this to the very sick, but given that a lot of the benefits of breastfeeding have been demonstrated in the well baby and if you believe the data on prevention of atopy or IQ data, and we don’t know how much breast milk is necessary to produce these benefits, would there be an argument made to extend this sort of banking delivery, and would there be the capacity to deliver it?

Dr. Simmer: We have to practice evidence-based medicine. Personally I am not that convinced about the atopy side of things and breast milk. I think there are many advantages of breast milk, I am not sure about reducing asthma. If we stay evidence based, it’s the preemies who benefit, and they are in-patients. The whole thing of becoming a commercial company and selling milk is just not where most milk banks want to go. We started feeding pasteurized donor milk to patients less than 32 week gestations when we didn’t have enough mothers’ own milk. There were more patients than milk. Those at the highest NEC risk were prioritized. But now that we have got a bigger pasteurizer, we are liberalizing use to 33–34 weekers because they are still preemies and they are still in our hospital. So, we are using it more but only for in-patients, including the short gut type babies, who might be 3 or 4 months postterm but they are still in hospital.

Dr. van Goudoever: How are parents responding when you say you are 26 weeks of gestational age and then you go up to 32 weeks and then stop?
Dr. Simmer: We tell them at the beginning, that we have only got so much and at 34 weeks it will be stopped; If the clinician thinks that baby is particularly small and had a lot of problems, you are allowed to have donor milk for longer.

Dr. Goqwana: Are we right and are we not creating some problems when we say it’s a milk bank? And a second question: If women are on medication for whatever reason, and that medication is secreted into the breast milk, do you accept the milk?

Dr. Simmer: I know, usually when we talk about banks, we think money, but there are also blood banks, and human tissue banks. There are screening questionnaires for the medications that the mums are on, and we use Tom Hale’s book. There are very few medications really that you have to refuse the milk, but we look at how much is secreted in the milk and the category of drug. We check all that.

Dr. Stathatos: Are there any collection standards to decrease the possibility of contamination with bacteria?

Dr. Simmer: There is Medela produces a microwavable bag for collecting milk. We have done a study but I haven’t got the data with me. On preliminary look, I don’t think it made much difference. It would be a good area to study. It’s not just skin contamination, there is also subclinical mastitis in mums who are expressing. Bacterial contamination varies from week to week, so you can’t just test the mum’s milk at 10 days and say, ‘that’s clear, we won’t test it anymore’; you have to keep testing it.

Reference