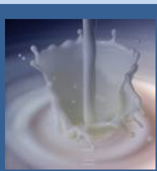
SPLASH! milk science update: July 2013 issue



SPLASH! milk science update

JUNE 2013 issue

This month's issue brings news of recently discovered similarities between human milk and cow's milk, a milk protein that battles cancer, the incredible diversity in lactation strategies, and the complicated transactions that occur with human milk sharing.

Enjoy!

Surprise: Cow's Milk Sugars Are Rather Like Human Ones!

- **The oligosaccharides found in human and cow's milk are much more similar than previously thought.**
- **The exact overlap of structures, by mass, is 40%. Specifically, that is the proportion of oligosaccharides found in human milk that are also present in cow's milk.**
- **Whey, the waste product from cheese making, could be a source of oligos for human health products.**

Pick up any textbook that runs through the sugars in milk, and you will read that human milk is unusual. It contains more oligosaccharides (medium-length sugars) than the milk of other mammals, and, in particular, most of its oligosaccharides have some subunits of fucose, a small sugar. Farmyard mammals, in contrast, do not make oligos out of fucose. At least, that was the conventional wisdom. But the distinction is now invalid.

Daniela Barile and her colleagues at the University of California, Davis, have diligently worked out the structures of all the oligosaccharides in cow's milk. They have found eight different fucosylated ones. And their library of structures will henceforth help researchers to rapidly identify rare oligos in all sorts of dairy products.

Moreover, their full list of cow's milk oligos has identified much greater 'overlap'—shared chemical structures—in the oligos of human and cow's milk than anyone thought likely. They report that about 40% of the human oligo structures, by mass, are present in both species' milk. This finding suggests commercial consequences: specifically, that cow's milk may be a useful source from which human-like oligos could be extracted in large quantities. The oligos could then be included in health-promoting products from infant formula to pills for immunocompromised cancer patients at risk of picking up germs in hospitals.

That cow's milk has many oligos in common with human milk is good news for making novel products based on it. However, the team's published research has so far only dealt with colostrum—the yellowy milk that appears in the first few days after birth. They have not yet analyzed mature cow's milk, which has a slightly different composition. Among other differences, mature milk has fewer oligos than colostrum.

The most obvious potential source of oligos for pills or formula is whey, the waste product of cheese making. Whey is produced in enormous quantities: for every kilo of cheese produced, ten kilos of whey are left over, and in some countries with lax environmental regulations, the whey is dumped in rivers. This damages river ecosystems because as the lactose in whey ferments, it uses up a considerable amount of oxygen, pulling the dissolved gas from the water and out of reach of aquatic organisms that depend on it for life. In the United States, cheese makers pay a lot of money to dispose of whey without damaging the environment.

At the moment, Barile is working on another paper about the structures of the oligos found in whey. If they are similar to human oligos—as those in colostrum are—the potential to use whey oligos in nutritional supplements is more promising. Barile's team has processed whey at all sorts of different temperatures and pressures in the hope of picking these data apart and making recommendations to industry about how to preserve the oligos. "With whey, you get different oligos depending on the process," says Barile. "A lot of cheese makers may be destroying their oligos and they don't know it."

"We have this nice possibility to solve an environmental problem by getting rid of a waste product of industry, at the same time as creating something useful," she adds.

An answer as to whether that really is possible should be available soon. For now, the composition of cow's colostrum certainly indicates that it will be.

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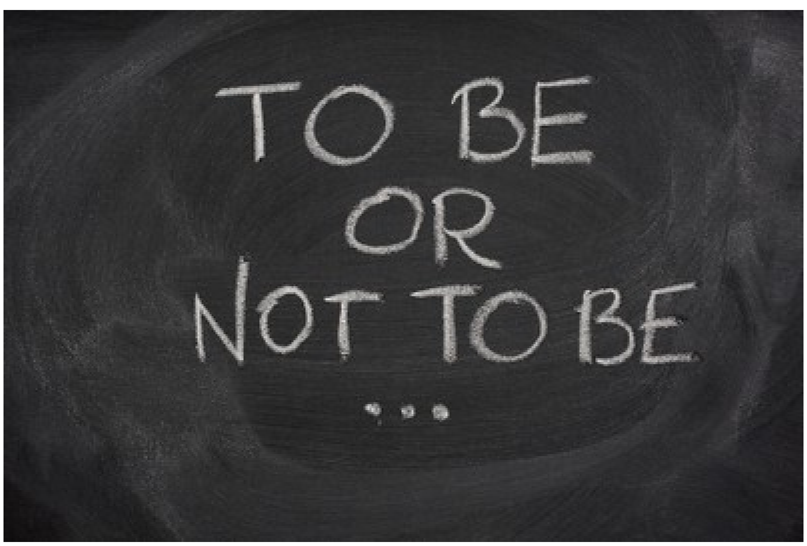
Milk Protein Kills Cancer Cells and Antibiotic-Resistant Bacteria

- **Human milk produces HAMLET, a protein-lipid complex formed in the infant's stomach from alpha-lactalbumin (protein) and oleic acid (lipid).**
- **HAMLET kills cancer cells by entering the cell's nucleus and fragmenting the cell's DNA.**
- **Using the same method of attack, HAMLET kills bacteria that cause respiratory infections in humans.**
- **When used in conjunction with antibiotics, HAMLET increases the sensitivity of bacteria to antibiotics, even antibiotic-resistant bacteria such as MRSA.**
- **The cow's milk counterpart, called BAMLET, also induces cellular damage to tumor cells.**



Wouldn't it be great if there were a nontoxic cancer treatment that effectively killed tumor cells without causing any harm to healthy cells in the patient's body? Or how about a chemical that could make antibiotics effective against bacterial strains that have become antibiotic resistant, such as pneumococci or MRSA (methicillin-resistant *Staphylococcus aureus*)? Solving just one of these tasks would be a medical miracle, and yet a team of American and Swedish researchers has shown that both are possible. Even more amazing is that the solution to these two seemingly disparate medical issues comes from the same molecule, a protein-lipid complex found in human breast milk called HAMLET (human alpha-lactalbumin made lethal to tumor cells). And unlike its Shakespearean namesake, the actions of milk-borne HAMLET are anything but tragic.

One part protein, one part fatty acid

Alpha-lactalbumin (LALBA) is the most abundant protein in human breast milk and is known primarily for its role in synthesis of the milk sugar lactose. In its "native" or folded state, this protein has no affect on tumor cells or bacteria. However, when LALBA unfolds and combines with oleic acid, an omega-9 fatty acid commonly found in human milk, it takes on a whole new set of skills.

In human infants, HAMLET is formed when the milk reaches the stomach; LALBA unfolds when it comes in contact with digestive acids and then combines with milk oleic acid. In the lab, researchers are able to create HAMLET by unfolding LALBA isolated from human milk with EDTA (ethylenediaminetetraacetic acid) and then adding oleic acid. Experiments with the “man-made” HAMLET have highlighted what this protein-lipid complex does for human infants as well as its numerous medical applications outside of the infant gut.

HAMLET takes on tumor cells

The tumor-fighting powers of HAMLET were discovered in 1995 by what the researchers called “serendipity” (Hakansson et al., 1995). They were investigating whether human milk proteins might block adhesion of bacteria to cancer cells and instead found that one of the milk proteins actually killed the cancer cells while leaving the normal cells unharmed.

Researchers later identified that killer protein as HAMLET and found it could differentiate a normal from a malignant, or tumor, cell. Although it works its way inside the cytoplasm of all cells with which it comes into contact, only in tumor cells does it go beyond the cytoplasm and enter the nucleus (Gustafsson et al., 2005). Once in the nucleus, HAMLET interacts directly with the DNA as well as the proteins (called histones) that surround and package the DNA into chromosomes. The damage HAMLET causes to the cell’s DNA ultimately results in the cell’s death. More specifically, tumor cells exposed to HAMLET undergo programmed cell death, known as apoptosis. HAMLET breaks down the machinery needed for the cell to replicate, leaving the cell with no option but to commit cellular suicide (Gustafsson et al., 2005).

HAMLET has shown promise in treating multiple types of human cancers, including several in vivo experiments (reviewed in Gustafsson et al., 2005). For example, topical application of HAMLET reduced the size of human skin papillomas (pre-cancerous lesions caused by HPV) in 100% of the patients without causing any negative side effects. Additionally, HAMLET inhibited the development of human brain tumors (glioblastomas) grafted into rat brains. Postmortem analysis of the rats’ brain cells demonstrated telltale signs of apoptosis in tumor cells, including fragmented DNA, but no changes to the normal brain cells that surrounded the grafted tumor.

It seems strange that a molecule that targets cancerous cells would be found in human milk - how might it benefit human infants? Researchers speculate that HAMLET may be critical in helping infants regulate the growth and development of their gut mucosal tissue (Hakansson et al., 2011). With so much cellular proliferation (i.e., mitosis) going on during the first months of life, particularly in the maturing gut and its surrounding lymphatic tissue, there is the possibility for some cells to get carried away in the business of making copies. HAMLET would be able to effectively target these cells and eradicate them before they became malignant.

HAMLET causes cell death in bacteria

As if taking out potential cancerous cells isn’t enough, HAMLET also may help infants fight off infections. Hakansson et al. (2011) demonstrated that HAMLET has eyes for both malignant cells and specific bacteria that target the respiratory tract, including *Streptococcus pneumoniae* and *Haemophilus influenzae*. Interestingly, its method for eradication for both types of cells is the same – apoptosis - despite the fact that bacteria (as prokaryotes) lack the specific targets found in tumor cells (namely, a nucleus and DNA bound by histone proteins). Nevertheless, HAMLET goes after the bacterial DNA and causes it to fragment, leaving the bacterial cell with no choice but to shut down operations.

But wait, there’s more!

If the story ended here, HAMLET would certainly be regarded as one of the more amazing molecules found in human milk. But HAMLET is a bit of an overachiever and apparently is not content with simply causing cellular death in tumor cells and particular types of bacteria. Indeed, HAMLET appears to be able to do the impossible – it makes antibiotic-resistant bacteria susceptible to antibiotics.

Antibiotic use creates strong selective pressure for the evolution of resistant strains, and many bacteria have evolved resistance to multiple antibiotic classes, such as *S. aureus*, the bacteria that causes staph infection (the multiple drug-resistant strain is now known by its own acronym, MRSA). Simply creating new antibiotics only provides a short-term solution to this major public health issue. What is really needed is a way to make the current arsenal of antibiotics effective again. Enter HAMLET.

When HAMLET is used in conjunction with antibiotics, resistant strains of bacteria become sensitive to antibiotics (Marks et al., 2012, 2013). These results were not due to HAMLET applying its usual trick of inducing cellular death. Researchers purposely used very low concentrations of HAMLET (what they called “sublethal”) on bacterial colonies in the lab and still found a reduction in the size of the colonies. In conjunction with antibiotics, low levels of HAMLET appear to increase the binding and uptake of the antibiotics by the bacteria and also inhibit bacterial reproduction. Importantly, these results were found even in bacterial species that were previously resistant to HAMLET alone (e.g., MRSA). Indeed, Marks et al. (2013) noted that the one-two punch of HAMLET plus antibiotics was more effective in killing MRSA than *S. pneumoniae*, a bacteria that HAMLET can easily kill on its own.

Cow's milk gets in on the act

If HAMLET has a flaw, it is that it comes from human milk and therefore is limited in large-scale clinical applications. However, LALBA also is found in cow's milk, and when it unfolds and combines with oleic acid, it forms a complex known as BAMLET (bovine alpha-lactalbumin made lethal to tumor cells). As its name suggests, BAMLET has been shown to kill several types of cancer cells in the lab and bladder cancer in rat models (Xiao et al., 2013). However, the way it leads to tumor cell death differs from HAMLET; BAMLET destroys the cell's lysosome (an organelle in the cytoplasm responsible for breaking down cellular waste) rather than the nucleus and thus does not directly interact with DNA or histone proteins (Rammer et al., 2010). Perhaps this difference in target is due to the fact that human LALBA and cow LALBA are not identical proteins (they share approximately 71% of their DNA (Xiao et al., 2013)). It is not yet known how this molecular difference affects BAMLET's ability to make resistant bacteria sensitive to antibiotics, but hopefully researchers will tackle that question soon.

This HAMLET has a happy ending

It seems remarkable that the combination of a protein and a fatty acid could produce a molecule that causes cellular death of tumor cells, without harming normal cells or causing side effects, kill specific types of bacteria that cause respiratory infections, but not harm good bacteria or normal cells, and make ineffective antibiotics once again effective in fighting bacterial infections. But perhaps most remarkably it has been hiding out all of this time in human milk, performing the important job of increasing infants' immune responses while keeping cellular growth in check.

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Xiao Z, Mak A, Koch K, Moore RB. (2013) A molecular complex of bovine milk protein and oleic acid selectively kills cancer cells in vitro and inhibits tumour growth in an orthotopic rat bladder tumour model. *BJU Int* **112**:E201-E210.

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Mining Animal Biodiversity to Improve Dairy Outcomes

- **Lactation emerged 200 million years ago, first in monotremes (egg-laying mammals) and then, 50 million years later, in marsupials.**
- **These species give birth to altricial young; postnatal development is regulated by progressively changing milk composition.**
- **More recently, the placental mammals (eutherians) have evolved with a longer pregnancy, mature young, and shorter lactation without significant changes in milk composition.**
- **The reproduction and lactation cycles of eutherians can vary considerably.**
- **This diversity of lactation strategies can be exploited to provide a better understanding of the regulation of milk production and composition.**

Dairy farmers everywhere would rejoice if scientists discovered a way to breed cows that continually produce milk. The answer to this biological riddle may lie in the study of other milk-producing animals.

Weird animals produce milk with various lactation strategies. Some produce all of their milk in just a couple days while others produce milk over five years. Some produce copious amounts of milk for a couple days and then not again for several weeks. By comparing the lactation strategies of different animals, researchers can identify exciting new methods of milk production.

The increasing availability of sequenced genomes and the opportunity to rapidly compare data between species provide new opportunities to better understand the bovine lactation cycle. Studying animals with lactation strategies different from cows or humans enables researchers to more easily identify mechanisms that regulate lactation and identify new milk bioactives that are not as readily apparent in cows and humans.

Egg-laying mammals also make milk

The monotremes (egg-laying mammals) split into mammalian phylogeny approximately 200 million years ago (Lefevre et al., 2010) and include the platypus (*Ornithorhynchus anatinus*) and echidna (*Tachyglossus* and *Zaglosus* genera), both of which are still found in Australia. The monotremes can be considered the first mammals and have a sophisticated lactation strategy. Both the platypus and echidna lay an egg that is incubated until hatching. After the egg hatches, the mother then initiates lactation to feed her very immature (embryo-like) young. Therefore, the milk must meet all of the requirements to provide nutrition and signalling factors for development of an immature young.

Birds produce "milk" too?

Could monotremes be birds? This is a provocative question, and there is an interesting relationship between monotreme lactation and nutrient provision in some species of birds. Recent work has suggested that the sex chromosomes of platypus are more like that seen in birds than mammals. Interestingly, some birds, such as the pigeon, produce an essential nutrient substance in the crop sac (located next to the oesophagus) that is fed to their young and seems to be functionally similar to mammalian milk. The "lactation cycle" of the crop sac includes a growth phase during egg incubation, the onset of "milk" production at hatching, and sustained delivery of milk to the squab during the first five to 10 days. Prolactin, a hormone that is central to milk synthesis in mammals, also controls growth and function of the crop sac. Pigeon milk is similar to mammalian milk in that it contains protein, carbohydrate, lipids, vitamins, minerals, and growth factors. In addition, it includes antimicrobial proteins and other innate and adaptive immune factors that play a role in the development of their immune and digestive systems. When the squab is weaned, it begins to eat seeds, consumes crop milk less frequently, and the crop involutes and remodels in preparation for the next cycle. A recent study examined the transcriptome (all the genes expressed) of the pigeon crop (Gillespie et al., 2013) during the lactation cycle, and there was no evidence of expression of mammalian milk protein genes during lactation. However, the mechanism is an interesting example of evolutionary convergence to provide essential nutrients, protection from infection, and signalling for development of the young.

Marsupials produce different kinds of milk at the same time

The marsupial, which evolved about 150 million years ago, has a similar reproductive strategy to monotremes. They have a short gestation and give birth to an immature young, basically an exposed fetus. Lactation is very long relative to gestation and the mother progressively changes the composition of the milk nutrients and bioactives. This is necessary to signal the growth and development of the young. If a pouch young is transferred to a mother at a more advanced stage of lactation than its own mother, the suckled young grows faster and organ development can be accelerated.

Interestingly, the tammar can practise concurrent asynchronous lactation. The mother provides dilute milk for the neonate in the pouch and a more concentrated milk with a completely different composition from an adjacent mammary gland. This concentrated milk is produced for a larger young that has exited the pouch and is at heel. Both of the mammary glands are exposed to the same hormones and growth factors in the circulating blood suggesting milk composition and production can be controlled by a local mechanism in the mammary gland.

In contrast to the postnatal development of marsupial young, eutherians, such as the cow and human, have a long gestation and a relatively short period of lactation, and the composition of the milk does not change appreciably after secretion of the initial colostrum.

Fur seals can stop producing milk and start again, without another birth

Cape fur seal (Arctocephalus pusillus pusillus). Picture taken at Cape Cross, Namibia, Dec. 2003 (GFDL)

Usually when milking ceases or the young no longer suckles from the mother, the mammary gland stops producing milk and the structure of the mammary gland reverts to that seen before pregnancy. However, some species of fur seals give birth to their young on land, suckle the pup for a few days, and then the lactating mother forages for food in the ocean for up to four weeks. The pup remains on land and is fed for about three days when the mother returns from her foraging trip. In contrast to cows, the lactating seal can downregulate lactation while offshore and then resume milk synthesis and secretion after returning to shore to feed the young. Furthermore, each time the mother returns to feed the young, she increases milk production relative to her previous visit. Understanding how the seal regulates her mammary gland during this cycle may offer new promise for strategies to implement "once-a-day" milking of dairy cattle without loss of milk production.

Lessons for the dairy industry

Can we use the comparative genomics of these species to improve productivity in the dairy industry? Increasing milk protein production is an ongoing challenge for the dairy industry and small increments can significantly improve profitability.

Recent studies have shown the mammary gland of the fur seal is like a protein pump – it doesn't synthesize significant amounts of lipid and carbohydrate. Moreover, milk protein content of fur seals (10-20%) is more than double that of cow milk (3.0-4.5%). Therefore, this species may provide us with a clearer understanding of the genes regulating synthesis of milk proteins. A recent comparison of microarray analysis of mammary tissues (a snapshot of all the genes expressed in the mammary gland) from the offshore and onshore lactating Cape fur seal (*Artocephalus pusillus pusillus*) and the tammar wallaby and cow during early and late lactation (when we see increased milk protein production) identified the central role of folate in milk protein synthesis in mammary epithelial cells (Menzies et al., 2009). This analysis could now be enhanced with the considerably improved sequence data from new genomes appearing in publicly-available databases. This kind of approach will continue to provide opportunities to better understand the comparative genomics of the lactation cycle and to service the dairy industry.

During lactation, cows gradually produce less milk and must become pregnant again to renew their milk supply. If it were possible to increase bovine milk production without a new pregnancy, like the fur seal does, the efficiency of milk production would be dramatically increased with a smaller environmental footprint. The greatest future innovations for the dairy industry may well result from the study of animals with unusual lactation strategies.

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Human Milk Sharing: Evolutionary Insights and Modern Risks

- **Allomaternal nursing is widespread across mammals and human cultures.**
- **The practice of wet-nursing was associated with infant mortality and economic exploitation.**
- **Natural selection may have favored allomaternal nursing.**
- **High demand for “grey” market milk is not without costs and concerns.**

Allomaternal nursing, the practice of infants suckling from a female not their mother, takes many forms. This behavior is not unique to humans and is widespread among mammalian species. Allomaternal nursing is thought to increase the fitness of females and infants, which would be favored by natural selection, but little research effort is directed to the topic. More recently, modern technologies of plastic containers, cold storage, and rapid shipping have created opportunities for milk sharing and milk selling widely among women. Some researchers and clinicians consider this unregulated trade of human milk a cause for concern--especially the risk of disease and toxin transmission to developing babies. Before that, though, let’s consider allomaternal nursing through historical, cultural, and evolutionary perspectives.

Historical perspectives

Wet-nursing was a prevalent practice before the advent of commercial formula. Throughout the Renaissance and into the early 20th century, poor women were hired to nurse the infants of wealthy women. Physiologically, the period of lactation, especially early and peak lactation, requires the mobilization of maternal body fat and skeletal minerals. When mothers are losing weight, ovarian function is suppressed and women do not experience a menstrual cycle (Valeggia & Ellison, 2009). Once mothers recover from this “depletion” of their bodily stores, they can conceive. In this way, interbirth intervals are often correlated with the duration of exclusive breastfeeding. By hiring wet nurses, wealthy women could shorten interbirth intervals and produce large families by forgoing the biological costs of lactation. The employment of wet nurses may have also been desirable because it allowed mothers to sleep through the night or/and attend long-lasting social functions in which infants were not welcome. In contrast, the poor women hired as wet nurses would often neglect their own infants and bias nursing behavior toward “paying customers.” The mortality rate for the biological infants of wet nurses was estimated to be quite high (Hrdy, 1992). Disentangling infant mortality due to wet-nursing from the immuno-socio-politico-economic context in which it occurred is tricky, especially when relying on historical records. Take home message: wet-nursing was contingent on wealth disparity and generally had the potential to have high costs for the wet nurses.

Cultural contexts

The practice of allomaternal nursing goes far beyond wet-nursing and is much more widespread among human populations than generally acknowledged. Within Islamic culture, there is the practice of “milk kinship.” This is a familial relationship, analogous in many ways to “godparents” among Catholics. In such instances, infants are nursed by a woman not their mother and consider her biological children “milk brothers” and “milk sisters.” In this way, lifelong social bonds are established and maintained throughout childhood, adolescence, and adulthood. And these relationships are in place in the event of the death of the biological parents (Parkes, 2005). Additionally, allomaternal lactation has been reported to be routine among many peoples including the Efe, Beng, and Aka in equatorial Africa, the Ongee of the Andaman Islands, and the Trobriand Islanders (Hrdy, 2009). Cross-nursing, when two women reciprocally nurse each other’s infants, is much less studied, but is known to occur among mothers in modern Western societies (Shaw, 2007).

Allomaternal nursing among mammals

Allomaternal nursing is not just a cultural invention of humans but has been observed in many other mammals, over 70 species at last count. Roulin (2002) reviewed the prevalence of the behavior, although our knowledge could do with some updating from new research in the last decade. Identifying the benefits of allomaternal nursing is crucial because synthesizing milk is costly. Why would natural selection favor mothers who nourished young not their own?

Some species are characterized by cooperative breeding in which related or unrelated adults contribute to rearing infants of a dominant breeding pair. Contributions can include provisioning breeding females (and pups as they are weaned), babysitting, territorial defense, and in some species, females will nurse the dominant female's infants. Among meerkats, pups will suckle from allo-lactators who have lost their litter, have spontaneously started lactating, or are also attempting to rear their own litters (Scantlebury et al., 2002). The benefit to the pup is clear but for the allo-lactators is less so. The pups may be related to the allo-lactator and care toward them can evolve via kin selection. Similarly, living in a group has benefits--territorial defense from other groups and more eyes to spot predators--and allolactation may be a tactic for being allowed to stay in the group. Among some house mice, two females will share a nest and take turns between going on foraging expeditions and staying behind to protect and nurse all the pups at the nest. The females nurse their pups and the other pups equivalently. About half the time the two females are sisters, but these reciprocal arrangements are just as often between unrelated females. Moreover, the arrangement can be stable across multiple birthing seasons (Weidt et al., 2008). Allonursing has also been documented in capuchin and squirrel monkeys (Baldovino and Bitetti, 2007; Perry, 1996; Williams et al., 1994). These species are not officially considered cooperative breeders but habitually allow infants not their own to suckle. A single report from squirrel monkeys indicates that allo-lactators produce lower fat concentrations in milk than do biological mothers (Milligan et al., 2008). In that study, the allo-lactators' infants had died; it's unclear if low-quality milk may have contributed to infant mortality or if the reduction in milk demand changed milk synthesis.

Mother's milk is not only nutritive but is an integral component to defending the infant against pathogens and entraining the infant's developing immune system. Milk includes maternal antibodies, hormones, commensal bacteria, and special sugars for beneficial bacteria to consume. Infants who suckle from multiple females may be boosting their immune system from the diverse exposures they get from allomaternal milk. Cross-nursing among mothers allows for all infants to benefit without increasing the net costs of milk synthesis to the individual mothers.

Milk-sharing in WEIRD people: Dangers & demand

(Westernized, Educated, Industrialized, Rich, Democratic Nations (Henrich et al., 2010))

Many of the beneficial constituents in breast milk are not available in commercial formulas. As a result, there is increasing demand for donor milk in neonatal intensive care units and among mothers seeking alternatives to formula. A recent meta-analysis of randomized, controlled trials revealed that premature babies that consumed commercial formula were four times more likely to develop the dangerous infection necrotizing entercolitis than were premature infants that consumed donor milk (Ben et al., 2012). A number of nonprofit and commercial entities have developed milk banks that rely on donated milk from women screened for health and lifestyle. After donation, milk undergoes processing to make it safer (e.g., pasteurization). These processes, while important for protecting the recipient, can also neutralize some of the beneficial bioactive constituents in milk. Moreover, the overhead costs and clinical applications of these milk banks limit the general public's access to donated human breast milk.

Those in the general public clamoring for raw, unpasteurized human breast milk have turned to a vast online "grey" market for sharing and purchasing milk among strangers (Geraghty et al., 2011; Gribble, 2013). This generates a number of concerns for the health of the recipient and also the donor and the donor's infant. Milk can include viruses, pathogenic bacteria, drugs, and poisonous toxins. HIV, E. coli, and methamphetamine can also be present in expressed breast milk; although rare, the probability is above zero. And lots of potentially dangerous things in milk aren't quite so rare--such as BPA, cytomegalovirus, and over-the-counter drugs. Moreover, contamination can result from poor collection, storage, and transport methods. These concerns led the Food and Drug Administration to release a statement of the risks and state in 2010 that the "FDA recommends against feeding your baby breast milk acquired directly from individuals or through the Internet" (Use of Donor Human Milk, 2010). A recent survey of 41 recipients and 97 donors by Gribble (2013) revealed that although 85% of recipients of shared milk were aware that milk posed the risk of infectious disease, less than half of respondents were aware of drug or other kinds of contamination. In contrast, recipients named a number of their concerns with commercial infant formula that compelled their interest in purchasing human milk. Less than half of recipients had discussed milk-sharing with their health care provider. Although nearly all "donors" washed their milk pump before and after pumping, other tactics to prevent contamination were often overlooked, such as washing hands, nipples, freezing milk after expression, recording date of expressed milk on container, etc. (Gribble, 2013). Less than a third of milk donors had discussed milk donation with any clinician.

Problematically, the value of human breast milk when sold online is contingent on volume, not composition. This leads to a number of concerns. Additional income may induce women to upregulate milk synthesis through pumping, potentially compromising their own health and the composition of milk available for their own baby, as happened historically with wet nurses. The composition--or quality--of the milk can't be evaluated by the recipient. The complex biochemistry involved in measuring the concentration of constituents--including contaminants--is restricted to a handful of highly specialized laboratories. I expect that most people are providing healthy, safe milk via the internet. But when profit is involved, some people may exploit the system. Just as the unscrupulous drug dealer cuts cocaine with talcum powder, internet milk may be padded with cow's milk or tap water. Although we know that in general milk contains hundreds, maybe thousands, of bioactive molecules, a systematic description of everything in human milk does not exist (Neville et al., 2012). Studies have shown that concentrations of constituents in milk vary across lactation within mother or among mothers at any given time, but we don't entirely know how much or why (Hinde & Milligan, 2011). Some constituents may vary in relation to the woman's physical and psychological health, the sex of her infant, and other things we still don't know. Although there may be benefits to allomother's milk from an evolutionary perspective as discussed above, when observed in other mammals, allomother's milk usually supplements mother's milk; it is not usually a replacement.

Moving forward

Online milk selling exists at the intersection of socio-political context, economic factors, feminist perspectives, and medical consequences (both beneficial and detrimental for developing infants). These are complex issues and require substantial consideration and discussion. Just as in every domain of milk research, answers and solutions are never simple or easily determined.

So what are some possible solutions? Expand the current national network of milk banks, donor programs, and private industry that mirrors the management of our national blood supply. (American Red Cross, I am looking in your direction.) Just as many hands make light work, many mammaries produce substantial volumes of life-saving donor milk at low cost per lactating woman. This would generate a larger supply of donor milk. Such a plan would have to guard against potential problems of the commercialization of human fluids (very tricky). This solution also requires the improvement of processing techniques so as to retain the bioactivity of milk constituents. We also need to responsibly increase awareness of the risks involved with online milk sharing both for donors and recipients. A key element of this is not just educating parents but also health care providers to be able to effectively, and with nuance, discuss milk sharing with their patients. Parents who want to feed their baby breast milk are buying internet milk because they don't want to use formula. If a formula more representative of human milk were available (cost effectively), perhaps fewer parents would take the risk of internet breast milk. Commercial infant formulas need to better reflect the complex biofluid that is human milk. Advantageously, many companies are interested in doing just that.

And we need to do more for families who steadfastly demand breast milk for their babies. We need to establish, with the reality of online exchanges in mind, best practices for milk handling from collection to storage to shipping to preparing for feeding. Some websites that host milk-sharing profiles include "tips," but these fall far short of best practices. The reality is that milk sharing is part of our evolutionary and cultural heritage because, as with all aspects of child-rearing, infant feeding takes a village--the lactation biologists unlocking nature's milk recipes, the food scientists formulating alternatives, clinicians caring for vulnerable patients, employers providing maternity leave and pumping stations, and healthy women donating their over-supply; all of these people contribute to optimizing infant health. This is our modern village, and we can do more to support all of our neighbors.

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