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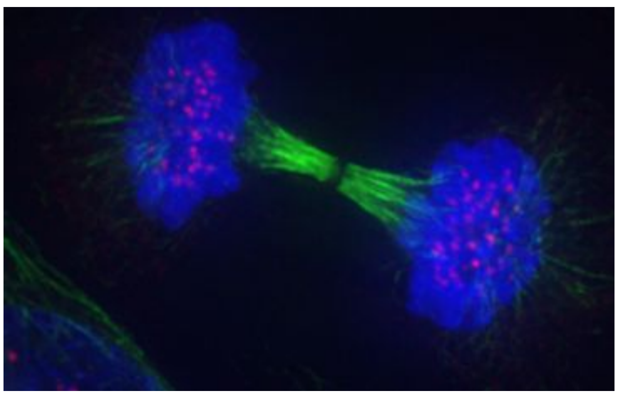
INTERNATIONAL MILK GENOMICS CONSORTIUM

This month's issue features double-powered milk-producing cells, a new way for milk to build bone, a one cow per poor family program, and when humans wean.

Milk-secreting Cells Have Two Nuclei

- **The luminal cells in the alveoli of breast tissue have been shown to contain two nuclei during the period that they secrete milk.**
- **An enzyme called Aurora kinase A, plus one of its substrates, appears to trigger the process of creating two-nuclei cells.**
- **The double-nuclei cells were found in five species of mammal, including dairy cows.**
- **The fact that these five species are distantly related implies that the evolution of double-nuclei luminal cells was crucial for the emergence of lactation.**

Occasionally in science a finding comes along that makes you wonder how no one figured it out before. That is the case with a discovery published in late April [1] by Australian researchers, who showed that milk-secreting cells in several distantly related—and presumably, therefore, in all—mammals, have two nuclei. The researchers demonstrated that these cells develop double nuclei because of a carefully regulated, incomplete cell-division process, involving unusually high levels of a particular enzyme. Quickly after lactation finishes, these cells commit suicide, allowing the breast to return to its pre-pregnancy state.



Cell with two nuclei

Lead investigators Anne Rios and Nai Yang Fu, both of the University of Melbourne and the nearby Walter and Eliza Hall Institute of Medical Research, in Victoria, Australia, were aware of a dissertation from the early 1980s claiming to have observed breast cells containing multiple nuclei [2]. The technology available back then left open the possibility that this observation was the outcome of how the tissues were prepared for microscopy. Rios, Yang, and their team brought a technology called three-dimensional confocal microscopy to the task, which allows researchers to measure the volume of different parts of cells.

Their investigation proceeded in a series of steps. First, working with different types of cells from the breast tissue of mice, the team demonstrated that only cells of one type—luminal cells—ever contain two nuclei, and that this feature appears in them on the same day that the cells start secreting milk. (Staining the cells revealed that these were the very same cells that produced lots of milk protein.)

Second, the researchers measured different features that made up the luminal cells' volume. This showed that the two nuclei in each of the cells were of the same size, and that the overall cell volume was much larger than that of single-nucleus luminal cells, presumably to accommodate the cellular machinery required to synthesize milk.

Turning to the question of how the cells got this way, there were two competing hypotheses: either two single-nuclei cells fused together, or one single-nuclei cell made a second copy of its nucleus as it embarked on the process of dividing—only for that process to remain incomplete. By triggering luminal cells to generate proteins that showed a different color in different cells, the researchers eliminated the fusion hypothesis (since no multi-colored cells appeared as the double-nuclei cells formed). Meanwhile, they separately showed that the double-nuclei cells live for an unusually long time given how metabolically active they are, adding support to the incomplete-division explanation.

The investigators then delved even deeper into the mechanistic details. The process of creating two nuclei had to be triggered by one of the hormones that signal the body to commence lactation, prolactin being the foremost candidate.

To probe what was going on inside the cells, the researchers began by sequencing the RNA expressed in luminal cells in late pregnancy, and also during early lactation, to look for differences between the two cellular states. A key candidate emerged from this process: the cell cycle regulating enzyme, Aurora kinase A (AURKA), whose RNA code was found at much higher levels in the lactation-stage cells. Over-expression of AURKA had already been linked to the formation of double-nuclei cells, and to breast cancer (which is known to be generally very aggressive when it emerges during and just after pregnancy). In the Australian team's experiments, AURKA appeared only at the beginning of lactation—it was undetectable by the fourth day—implying that it acts as a switch, turning on milk production.

To underscore the role of AURKA, the team tried removing it by deleting its gene. As expected, this action completely eliminated double-nuclei cells from breast tissue and resulted in milk glands that made no milk. They also showed that AURKA's action depends on the presence of one its substrates, called PLK-1. Finally, the team demonstrated that AURKA's over-expression indeed results from the appearance of prolactin—more precisely, from the appearance of prolactin alongside epidermal growth factor, a protein that stimulates cell growth.

The molecular details of the mechanism mapped out, the researchers then wondered about the evolutionary importance of their findings. They identified two-nuclei luminal cells in the breast tissue of lactating creatures from opposite branches of the mammalian evolutionary tree. Lactating humans, seals, and wallabies have about 30% of their breast tissue composed of cells with double nuclei; in cows the proportion is 40%. This implies that the evolution of two-nuclei luminal cells was crucial to the evolution of the most mammalian of features—lactation—about 300 million years ago [1,3].

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Extracellular Vesicles in Milk Could Enhance Bone Formation

- **Milk is beneficial for bone health.**
- **Milk contains extracellular vesicles.**
- **The current study demonstrates that the extracellular vesicles stimulate bone formation.**
- **The vesicles may become a useful treatment for osteoporosis.**

Childhood mealtimes for many of us included a frosty glass of milk. Aside from being yummy, the wisdom of generations of mothers was to drink every last drop to build strong bones. Milk provides bone-building nutrients, but a new study suggests it does even more. The latest data just published in the *Journal of Nutritional Biochemistry* by a cadre of researchers under the direction of Fons AJ van de Loo, Radboud University Medical Center, the Netherlands [1], links the consumption of cow's milk containing tiny blobs of cellular material called bovine milk-derived extracellular vesicles (EVs) with the rapid growth of bone. If the findings hold up in human trials, it may herald a treatment for osteoporosis.

The problem

Bone is a living tissue. It is constantly being degraded by osteoclast cells and replaced by osteoblast and osteocyte cells. When we are young, these two processes run pretty much in tandem. But as we age, bone formation does not always keep pace. The result is osteoporosis—bone that becomes less dense and more prone to cracking and breaking. It is especially prevalent in women, with an estimated 30% of women being affected after menopause. Osteoporosis can also be accelerated in diseases including diabetes, lupus, and rheumatoid arthritis due to inflammation or prolonged anti-inflammatory glucocorticoid therapy. Osteoporosis is insidious, with no symptoms until the moment a fracture occurs. To explore possible treatment for osteoporosis, Dr. van de Loo and colleagues have for some time been investigating the possible involvement of EVs in cow's milk in improved bone formation [2,3].

A brief primer on extracellular vesicles

All cells release material from their surface. Typically, this involves "blebbing," where a portion of the cell membrane folds out and then pinches off. The result is a tiny, virus-sized sphere that contains material from the interior of the cell. Only a few decades ago, formation of EVs was viewed as random and of no importance. Instead, we now know that the release of these vesicles is an important way cells communicate with each other [4].

The communication has two general mechanisms. If the EVs have surface proteins that recognize proteins on the surface of the recipient cell, specific binding of the two proteins can occur. The binding sends a signal inside the recipient cell that can regulate cell metabolism or gene activity [4]. Alternatively, the lipid portion of EVs may meld together with lipid-rich regions of the recipient cell, with the vesicle's contents dumped into the recipient cell. This can also affect cell function. For example, small pieces of ribonucleic acid called microRNA can bind to the recipient's genetic material and block protein manufacture [4].

Cow's milk contains a huge number of EVs. Pasteurization cuts down their numbers. Still, a glass of processed milk contains about 5 billion EVs that are derived from cells present in milk and from the mammary gland cells and the EVs remain bioactive. When that glass of milk is consumed, the EVs may travel through the stomach—they can survive that harsh environment—and reach the intestine where they are taken up. Or the journey may be short, with the vesicles taken up by mucosal tissue in the mouth. Which route is the primary route is still unresolved.

EVs and bone health

Bone remodeling has been studied in mice for a long time. Bone in mice is made of similar material and is organized similarly to human bone. As well, the regulation of bone formation and structure in mice and humans are similar [5,6]. One advantage of using mice as experimental animals is that they are a lot smaller than humans, so fewer EVs need to be supplied in the diet. Isolating EVs is a major task [1], so cutting down on the quantity required in feeding trials is definitely a good thing.

In the latest study to assess the possible effect of EVs on bone formation and structure, mice were used as the surrogates for milk drinking humans. Treated mice did not display any change in the tibia bone area, but there was an increase in the expression of sclerostin, a marker for the bone-producing osteocytes, which are formed from osteoblasts that become embedded in the bone network. At the same time, there was reduced expression of both type 1 collagen, an important constituent of bone, and osteonectin, which is associated with bone matrix formation. These reductions indicated that the bone that was forming was less dense that normal bone [7,8]. Indeed, microscopy examination of bone sections revealed an increased prevalence of a less organized type of bone matrix called woven bone, which is similar to the bone that is present in the developing human fetus [1].

With time, as occurs normally during fetal development, woven bone is replaced by stronger lamellar bone. Whether this occurred in the mice in the present study could not be determined because the study was not long enough, but other data that is not yet published by the researchers indicates that this likely does occur.

The current thinking is that the EVs in cow's milk stimulate the process of bone formation. While initially the bone that is produced is less dense, over time the hardier lamellar bone is established. If this does indeed occur—which further studies will focus on—EVs could someday be harnessed as a treatment for osteoporosis.

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Rwanda's One Cow per Poor Family Program Turns Ten Years Old

- **The Girinka program aims to reduce extreme poverty in rural areas of Rwanda by providing each poor family with a cow.**
- **The available evidence suggests that this program increased household income through the sale of milk and because fertilization of soils with manure has also raised crop yields.**
- **Girinka appears to have helped cut malnutrition rates as well, which were still 44% among Rwandan children in 2012.**

- **As in other African countries, mastitis rates are high among Rwandan cows, including those in the program. This is likely driven by a shortage of specialized personnel and training.**

A decade ago, the Rwandan government set up a program aimed at cutting poverty and improving health and nutrition in rural areas. The idea was simple: given a cow, a poor family suddenly has milk to drink and manure with which to fertilize crops. Today more than 130,000 cows have been distributed through the program [1], which goes by the name "Girinka." While Girinka has its shortcomings—including high rates of mastitis—its overall impact has been remarkably positive.

Crossbreeds of African cows with higher-producing breeds, such as Jersey, have been used in the Girinka program.

Rwanda is a small country in East Africa where the economy is largely based on semi-substance agriculture, irrigated by rainfall. Rwanda is also landlocked, which makes importing and exporting costly goods—and, like its East African neighbors, educational achievement is quite low. For these reasons, diversifying the economy presents challenges, and development through agriculture is the obvious path forward. At the same time, however, the United Nations Food and Agriculture Organization reports that 40% of the country's soils are highly susceptible to erosion—so simply working the soil harder wouldn't be effective [2]. Despite the obstacles, in the last few years, the Rwandan government has been working through a very ambitious plan to become a "middle-income" country by 2020.

Back in 2006, when Girinka began, Rwanda was recovering from widespread droughts the year before that significantly dented harvests and led to food insecurity in some districts. Among the districts that received a large share of the cows was Bugesera, which struggled more than most during the drought, since it had faced a famine known locally as "Kinga umwuzukuru araje" at the turn of the century. In his thesis, Vincent Kayigema, of the University of KwaZulu-Natal in South Africa, evaluated Girinka's impact in Bugesera [3]. Kayigema found that the program has "notably improved its beneficiaries' livelihoods," and that manure as a source of fertilizer is clearly having a benefit. That, in turn, he argues, is aiding Rwanda's climate resilience because it makes the soil structure better able to hold together during extremes of sun, wind, and rain. (Another study by Sung Kyu Kim et al focusing on Ngoma district reports that over 90% of beneficiaries are using manure as fertilizer [2].)

A number of other researchers have studied Girinka's impact, each focusing on poor residents in a different district of Rwanda. Kenyetta University student Mutarutwa Nkusi Christian [4] estimates that Girinka has improved average annual household incomes by roughly 115,325 Rwandan francs (or about $175) in Gatsibo district—another part of the country that has received a lot of cows from Girinka. That amount matters in a country where average household income is about $400.

But wealth can be thought about in a more holistic way than raw income, and when evaluators apply this kind of logic to Girinka, it is cast in an even more favorable light: "Ownership of cattle, especially in the Rwandan context, contributes to the enhancement of social status. The provision of cattle to poor households elevates the poor not only financially but personally and socially as well," writes Michelle Rugema of the University of Cape Town in her study of Kayonza district [5]. In other words, Girinka, when understood as a contributor to feeling rich, improves beneficiaries' lives a great deal.

Among those who stand to benefit most from the program are members of female-headed households. Rwanda has a relatively large number of such households as a direct result of the 1994 genocide, writes Emmanuel Hakizimana [6]. Not only did the genocide create many widows—and its aftermath saw many families in which one parent is in jail or exile—but between 250,000 and 500,000 women were raped and deliberately infected with HIV, and of those, many ended up with kids and no partner.

While Girinka seems to have had a positive impact on income—and is generally reported to have been fairly administered—it is still criticized. One complaint is that the cows the families receive often have or have developed mastitis (infection of the udders)—although the exact proportion is unclear. (The Rwandan Ministry of Agriculture did not respond to an email requesting this proportion.) Mastitis leads to high levels of white blood cells in the cows' milk. Not only is the condition unpleasant for cows, it causes their milk to be of lower volume and lower quality. People who drink milk from a cow with mastitis are more likely to suffer stomach upsets than otherwise, unless the milk is first boiled. Moreover, the milk probably contains fewer minerals like potassium and calcium, as well as bioactive components like lactoferrin—all important for healthy nutrition.

Girinka's mastitis issue should be put into context, though. In 2007, Jan van der Lee compared mastitis rates across East African countries—therefore his work was published at a time when Girinka could not have had much impact on Rwanda's overall mastitis prevalence. Van der Lee writes that as much as 60% of cows at that time suffered from the problem. His publication also shows that Rwanda is hardly an outlier: Kenya has a 40% mastitis prevalence, and Ethiopia, 80%. Mastitis is particularly common near to Ethiopia's capital, Addis Ababa, where rates were as high as 84% to 94% when van der Lee wrote his report [7].

Although Girinka cannot be blamed for creating the problem in Rwanda, that is not to say that the policy has paid sufficient attention to mastitis. Most scholars who have investigated the program levy the criticism that there are not enough veterinarians to take care of the cows, to help the cows to be as productive as they can be for their impoverished owners, or even to administer Girinka. For example, Rugema [5] notes that, "In Mukarange sector, there is only one veterinary officer who is responsible for visiting and following up beneficiaries, providing veterinary services and support, collecting and tracking new applications, running the day to day administration on the ground as well as reporting back to district offices."

A shortage of specialist personnel creates other problems, such as a lack of training Girinka's beneficiaries in animal husbandry and in how to best make use of the products that a cow can provide. "Our experience in the field is the average dairy cow or dairy goat owner has almost zero training in mastitis diagnosis, prevention, control or therapeutics. So, even if the Girinka program cow is mastitis free, she will not stay that way during or after her first lactation," said Jim Cullor, a professor of dairy food safety at the University of California, Davis, in an email. That is a shame because Jonathan Argent and colleagues [1] have measured the additional benefit to receiving training (as opposed to only receiving a cow). Six years into the program, they find an enduring impact on levels of milk production, milk yields per animal, and also on household income. Asset accumulation—the production of calves—was also greater where Girinka beneficiaries had been trained. (But, unfortunately, Argent and his coauthors didn't measure the impact of training on the prevalence of mastitis.)

In general, Girinka offers a valuable learning experience for poverty-reduction programs in other countries that have bad soils and people living on very low incomes. The evidence is imperfect since there are few—if any—proper baseline studies against which the present day situation can be compared. But as part of a collection of development programs intended to reduce extreme poverty, Girinka appears to have raised the self-esteem of many of its adult beneficiaries, provided them an opportunity to start building assets, and improved the health of their children.

Girinka aside, there is still plenty to be done to improve the lives of rural and impoverished people in Rwanda; in 2012, the level of chronic malnutrition among the country's children was 44% [8]. But extreme poverty was reduced from 45% to 24% in the decade between 2000 and 2010. That's a hugely important change—and it was, in part, due to Girinka [9].

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Cultural Motherhood: When to Wean Part II

- **Across 100+ human cultures, breastfeeding typically ends between two and four years of age.**
- **Breastfeeding practices reflect a mix of cultural traditions and modernization.**
- **Milk composition during multi-year lactation is mostly unknown.**
- **The impact of breastfeeding initiation and duration varies across environments and disease ecologies.**
- **Human lactation is highly flexible; there is no "one size fits all."**

The "evolved" age of weaning is a topic of debate not only among the general public but clinicians and scholars as well. Weaning, however, is not an event—it is a process. When that process begins and how long mothers and infants negotiate milk transfer varies across mother-infant dyads [1,2]. While insights can be gained from consideration of our primate relatives (see Part I), comparisons across populations, and across mothers within a population, provide important insights into the human condition and the complexities of infant weaning.

Weaning in a biocultural context

The World Health Organization recommends infants breastfeed for up to two years of age or longer. Indeed, evaluations of dozens of cultures reveal that breastfeeding cessation occurs typically between two and four years of infant age [3-5]. These findings are largely consistent across hunter-gatherers, horticulturalists, agriculturalists, and pastoralists [6]. Pastoralists who heard dairy animals are particularly noteworthy. The genetic underpinnings of the lactase enzyme that allows mammalian infants to digest the lactose of mother's milk has been shaped by cultural practice among humans. Individuals who produced lactase post-weaning and lived in populations with cows, goats, camels, mares, and/or sheep were able to digest animal milks, thus gaining protein and fat in their diet [7]. This complex interplay between the human genome and cultural practices is known as gene-culture coevolution. Interestingly, the use of domesticated animals across cultures is associated with a later age of introducing solids but does not accelerate or delay weaning [6]. Instead, breast milk is complemented by dairy milk for young infants. Among the Datoga of Tanzania, dairy, such as fresh and soured goat or cow's milk is introduced around three and a half months of infant age and breastfeeding ended in their second year of life for a majority of infants [8].

Among indigenous communities modernizing from traditional lifestyles, approaches to breastfeeding have been affected. Mayan women, in the Puuc region of the Yucatan Peninsula of Mexico were traditionally subsistence maize agriculturalists, but more recent adoption of mechanized farming, access to labor market economy, establishment of a village clinic, and greater population density has changed their diet, economy, and health [9]. Whereas once these women almost exclusively delivered babies in their home, more mothers are giving birth in clinics and experiencing Cesarean deliveries. With these health changes, formula feeding is increasing and mothers are delaying breastfeeding, even if just by a few hours after birth. Moreover, younger mothers introduced complementary foods earlier and stopped breastfeeding earlier despite advice from health care providers [9]. Complementary foods typically included boiled carrots, potatoes, squash, and chicken, as well as tortillas, pureed beans, and crackers. Interestingly, colostrum was viewed differently depending on access to clinical staff. Among younger mothers whose adulthood was marked by the introduction of a local clinic, colostrum was viewed as beneficial similar to a vaccine, but older women who had become mothers before clinical care was locally available, viewed feeding colostrum as good because it helped to bring about the transitional milk [9].

For Tsimane forager-horticulturalists in riverine forests of Bolivia, modernization is associated with more intensive breastfeeding, as mothers living in remote villages in the forest and along the river introduce weaning foods at earlier infant ages than do women living in more modernized conditions closer to developed areas [9]. These introductory weaning foods are typically watery stews of plantain or rice and meat or fish. A majority of Tsimane mothers stop breastfeeding between 12 and 26 months of infant age, with a mean of ~19 months [9]. Whether mothers lived remotely, however, was not associated with the cessation of breastfeeding.

Taken together, these studies reveal that modernization does not have a consistent effect on breastfeeding practices, but they highlight how public health programs can be most effective at assessment and implementation when they consider traditional practices and beliefs within the context of cultural transitions.

Known knowns and known unknowns of extended lactation

Most research effort into the effects of breastfeeding has been directed to understanding the effects of exclusive breastfeeding the first 4–6 months (current WHO and CDC recommendations are for exclusive breastfeeding for the first 6 months)… but in terms of the latter parts of multi-year lactation, we know relatively little. We don't even systematically know what the milk composition is in mothers who sustain lactation for multiple years.

Mandel and colleagues recruited women who continued to breastfeed after the first year [10]. They sampled milk from 34 mothers who varied in how long they were lactating (between 12 and 39 months of infant age) and found that the percentage of milk fat was higher the longer lactation had been sustained [10]. They stated that the "The long-term effects of such high fat intake have not been studied." Kay Dewey's 1984 [11] study on breast milk composition from 12 to 20 months was able to look at many more aspects of milk, including many minerals. In general, the milk composition was similar in the second year of lactation to that in the first year, when mothers were producing more than 500 ml of milk a day. However, very few of these mothers were producing that much during the second year of lactation, most had significantly decreased their milk production.

Importantly, the two studies described above were conducted in “WEIRD” populations: Westernized, educated, industrialized, rich, and democratic, but most people aren’t WEIRD [12]. In 1978, Jeliffe and Jeliffe reviewed milk production across multiple populations, including poorly nourished communities in the Global South. Milk volume is seemingly much lower as lactation progresses. This is to be expected, as young consume solid foods and suckle less often, milk flow through in the mammary gland decreases, causing a down-regulation of lactose synthesis [13]. The lactose is responsible for pulling water into the mammary gland (yay osmotic pressure!), so as lactose synthesis decreases, milk volume decreases. Recently, Quinn et al. showed that among Filipino women breastfeeding up to 18 months of infant age that milk produced for older infants was higher in fat content and lower in lactose than during early lactation, consistent with expectations of the weaning process [14].

These studies primarily studied milk up to two years of infant age, rarely three to four years of age. And they investigated macro-constituents in milk; percentage fat, percentage protein. What about the fatty acid profile? Amino acids? And what about hormones? Cells? Immunofactors? Microbes? Oligosaccharides? There are hundreds, if not thousands, of constituents in milk that we are still describing during the period of exclusive breastfeeding [15-17] much less constituents in milk during complementary feeding. We are still unlocking what these constituents do when ingested by the newborn, much less toddlers and children. The information on breastfeeding for five or more years comes from rare self-selected cases, an extreme tail end of a continuous distribution of weaning ages.

Irwin Bernstein said it best, “The plural of anecdote is not data” [18].

The impact of breastfeeding: context, context, context

Most of what we know about the effects of breast milk comes from studies comparing formula and breast milk feeding or comparisons of the duration of exclusive breastfeeding. The amount of the differences between formula and breast milk groups depends on context. For the very low-birth weight, premature infant in the neonatal intensive care unit at high risk of necrotizing enterocolitis, breast milk can potentially mean the difference between life and death, and can influence the length of hospital stay, and the hospital costs [19,20]. For kids in communities with high prevalence of infectious diseases, limited access to clean drinking water, nutrient scarcity, breast milk constituents can reduce the risk of lethal diarrheal disease [21] or malnutrition [22].

Moreover, since many studies collect data at a single point in time, rather than longitudinally, we can’t always identify at which age each individual infant reaches a threshold weaning state. Much like primatologists predict weaning occurs when birth weight is tripled or quadrupled, other milestones or thresholds may influence weaning. We recently observed no differences in health and growth parameters among Tanzanian children weaned before or after two years of age [23]. What we can’t know, was whether or not the condition of those individuals who weaned later would have faltered if they had been weaned earlier. Full-term, typically-developing, healthy babies of experienced mothers growing up suburban “WEIRD” populations have the luxury of milk mattering less than for the millions of babies whose early life experiences present more obstacles and challenges.

Similarly, since nutritional and environmental impacts have the strongest impacts earlier in development, as kids age, the effect of breast milk on cognition, health, behavior, and growth is expected to decrease. This is the crux of developmental programming. The age at which the benefits of each extra day of breastfeeding during complementary feeding converge to “no added value” for immune function, nutrition, metabolism, and psychological well being… we don’t have data to know. And whether or not continued breastfeeding should cross zero to detrimental consequences, I am not aware of any research that supports those claims either. Indeed, in a ground-breaking study that interviewed toddlers and children who were still breastfeeding, the older children reported that breastfeeding was a source of psychological comfort and was “better than chocolate” or “ice cream” to them [24].

Constraints, obstacles, and options

Within our WEIRD American culture, we need to stop pretending that all mothers have all options. Aside from some medical conditions that hinder breastfeeding, many mothers cannot meet their breastfeeding goals because of economic realities, lack of social support, cultural barriers, and limitations in the medical training of their clinicians. Fewer than 350 hospitals in the US are designated “baby friendly” by offering “an optimal level of care for infant feeding and mother/baby bonding.” Some states don’t have ANY baby-friendly hospitals. Furthermore, the recommendations for exclusive breastfeeding for 6 months is challenging when one lives in a country without paid maternity leave. The Affordable Care Act mandates insurance coverage for high quality pumps, break time and break space for pumping, and storage space for collected breast milk… but employers are differentially compliant with these protections. In short, mothers may have economical, medical, cultural, and social constraints that impact the length of their lactation period.

So where does this leave us?

In 2005, Dror Mandel and colleagues [10] began their paper with the following sentence: “The optimal duration of breastfeeding is unknown." Given the wide range of variation and continued limitations in the state of our knowledge, the idea that there is a specific adaptive age for weaning is not supported. There is no one way; there is no one size fits all.

So many people approach breastfeeding topics as black and white. But behavioral biology is entirely shades of gray—and way more than 50. Biological systems are exquisitely complex. Humans as biocultural organisms are confronted by the realities of the cultural and individual contexts in which we produce and rear our young.

Grappling with that complexity, as lactation biologists, neonatologists, and food scientists can tell you, precludes excessive claims relying on logical fallacies, intuitions, or non-existent data. Such claims are predicated on "all else being equal." But all else is never equal, and how any given mother weighs each of her considerations will ALWAYS be specific to her individual situation. There is no one way; there is no "one size fits all."

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