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This month's issue features the link between human milk consumption and longer telomeres, a milk-like substance made by cockroaches, the slower digestion of dairy proteins, and the association of higher-fat yogurt with lower obesity.

Consuming Human Milk in Infancy Linked to Longer Telomeres

- **Telomeres—the protective ends of chromosomes—shorten in length as we age and have been used as predictors of lifespan generally, as well as the risk of developing some cancers and other health problems.**
- **A new study finds that consuming human milk early in life reduces the attrition rate of telomeres during the first few years of life.**
- **These results matters because it implies that breastfeeding has previously unappreciated benefits to cellular health.**
- **The study's authors suggest that human milk's apparent protection of telomere length results from its anti-inflammatory effects, whereas sugar-sweetened sodas may accelerate telomere attrition by promoting chronic inflammation.**

Telomeres can be thought of as tags on the ends of chromosomes that, in protecting those ends, are also guides to cellular aging and, consequently, to lifespan. Telomere length decreases as we age, dropping off most rapidly in the first four years of life. Now a team at the University of California, San Francisco reports that feeding an infant human milk appears to lower the rate of telomere shortening until at least the age of five.

The study, which is published in the current issue of the American Journal of Clinical Nutrition [1], did not specifically compare the effect of infant formula with exclusive breastfeeding. Instead, it set out to measure differences between a diet of human milk alone with mixed diets, and many mixed diets also included infant formula along with items such as fruit juice, flavored milks, and sodas.

The researchers found that any amount of human milk in the first four to six weeks of life was associated with having longer telomeres at preschool age. During those early weeks, an exclusive human milk diet was preferable. Among the young study participants, it appeared to increase telomere length at age four or five years by about 350 to 450 base pairs over a diet that included other foods or drinks.

At six months old—the age up to which the World Health Organization recommends exclusive breastfeeding—any level of human milk consumption (compared with no human milk consumption) was associated with longer telomeres at preschool age. The difference at this age was about 250 additional base pairs relative to the number of base pairs in children who consumed no human milk at six months.

Telomeres can be thought of as "tags" not merely because of their position marking the ends of chromosomes but also due to their structure. Their DNA part, contained within protective proteins, repeats the nucleotide sequence TTAGGG many times over.

Cells in a newborn's cord blood have the longest known human telomeres—averaging about 10 thousand base pairs [2]. But with every cell division, the process of copying DNA shortens telomeres because the enzyme that does the copying is unable to read the final part of the chromosome to which it is attached. A different DNA-making enzyme—called telomerase—steps in to replenish shrunken telomeres. But, over time, telomerase's replenishment is insufficient to make up for the shortening. Telomere length can, therefore, infer cellular age.

Telomeres can also be shortened by oxidative species found inside cells, the level of which is known to vary with lifestyle and environmental influences. For this reason, for example, adulthood obesity has been linked to accelerated telomere attrition—and a long-term reduction in so-called "bad" cholesterol resulting from gastric band surgery was recently shown to increase relative telomere length [3].

In the recent human milk study, the authors propose that consuming food and drink other than human milk (and water) in the first weeks of life triggers an inflammatory response in the immature infant gut, which in turn leads to oxidative damage to telomeres [1].

Both the repeating nucleotide sequence that occurs in telomeres and telomerase's molecular structure were discovered in the 1980s by Elizabeth Blackburn and her colleagues, who received the 2009 Nobel Prize in medicine or physiology for the work. Blackburn—a molecular biologist who is one of the authors of the new human milk study—has in recent years collaborated with medical researchers who are eager to understand telomeres' role in human health and longevity.

The latest research stands out because little is known about childhood influences on telomeres' attrition rate or how much such influences predispose attrition rates through adulthood.

One pair of studies that compared the telomere lengths of kids growing up in different neighborhoods in New Orleans found measurably shorter telomeres among children who were prenatally exposed to smoke (at home) with those who weren't [4]. They also compared the telomere lengths of children who grew up in "rough" neighborhoods (areas characterized by lots of noise, abandoned vehicles and so on) with those of children who grew up in "nice" areas [5]. But the children participating in these studies were all, in contrast to children in the new human milk study, past the period of most rapid lifetime telomere shortening.

The new study also highlights the effects of giving toddlers sugary drinks. The authors report a clear association between drinking lots of soda at three years of age and accelerated telomere attrition from four to five years of age that could not be explained by a possible role of soda in contributing to obesity. Why soda would have this effect on young children's telomeres is not clear, although it may have something to do with the prevalence of oxidative species in cells.

What all this means for the importance of breastfeeding—and exclusive breastfeeding—on predicted human lifespan is hard to say. Although telomere attrition rates are linked to life expectancy, the details are messy. Telomeres are often different lengths on different chromosomes—and some research on cells known as fibroblasts suggests that it is not average telomere length—or even variance in their length—that triggers cellular aging processes, but instead, it is hitting a threshold of five telomeres below a threshold length that enables them to fully protect their respective chromosome ends [2]. All in all, though, the new study points to as-yet unappreciated mechanisms by which human milk likely contributes to cellular health.

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Cockroach Mothers Produce Nutrient-Dense Milk Crystals

- **The Pacific Beetle cockroach feeds its embryos a liquid that has been likened to milk because it fuels embryonic growth and development until birth.**
- **A new study reports that once ingested, the milk proteins are not immediately digested but form crystals that are highly nutritious and release nutrients over an extended period of time.**
- **Roach milk crystals exceed cow milk and many other mammalian milks in protein and caloric content.**
- **Inspired by roach milk, genetically engineered yeast may provide an alternative source of nutrition for humans of the future.**

A new study on cockroach milk [1] attracted a lot of attention from popular news outlets last month. And who can blame them? The idea of a milk-like substance coming from an insect is a pretty remarkable finding. But a cockroach making milk is, surprisingly, not news; scientists have known about cockroach milk for more than 40 years [2,3]. The recent study from Banerjee and colleagues generated so much "buzz" because they found that cockroach mothers, despite their diminutive size, produce a complete nutrient for their offspring that is higher in energy than milks from most mammals [1]. Using cutting edge X-ray diffraction techniques to take the closest look to date at the crystal structure of cockroach milk, the international team of researchers reported that cockroach embryos dine on a wide variety of amino acids, essential long-chain fatty acids, and carbohydrates. Cockroach milk, it seems, is more than just a drink; it is a highly nutritious meal. But if the thought of adding cockroach milk crystals to your smoothie is completely unappealing, don't fret. Thankfully, many of the features that make cockroach milk proteins so remarkable are also found in the milk of other mammals, including those sold in your grocery store dairy case.

One of these roaches is not like the others

Of the nearly 5,000 species of cockroach, only one is known to reproduce without laying eggs. The Pacific Beetle cockroach (*Diploptera punctata*) is viviparous, which means mothers provide nutrition directly to embryos as they grow and develop, and then give birth to live young [1,3]. In mammals, the placenta is responsible for nutrient transfer during gestation. In *D. punctata*, embryos are fed a liquid secreted from the wall of the brood sac, which is the insect equivalent of a uterus. Obviously, cockroaches lack mammary glands. But the liquid is nevertheless referred to as "milk" because of the role it plays in offspring growth and development.

Discovering an insect that produces milk is certainly a "Eureka!" moment, but scientists found something even more remarkable when they examined what happened after milk ingestion. Inside the embryo midgut, the milk proteins formed crystals, not unlike tiny nutritional diamonds. Cockroach milk, then, went from being a liquid when secreted, to a solid after consumption.

A crystalline structure offers two advantages. First, it allows for increased energy storage [1]. Folding clothes allows you to put more in your suitcase than if you simply threw them all in; in the same way, folding up the proteins and packing them into crystal structures allow for more nutrition to fit in the small roach stomach. The second advantage to forming crystals is the ability to hang on to that energy for a longer period of time [1,3]. Researchers observed that these crystals were not immediately digested but rather remained inside the cockroach gut. Like a nutritious cough drop slowly dissolving and continuously releasing flavor, roach milk crystals dissolve as the nutrients are needed by the embryo [1].

For an entomologist, understanding the nature of the milk crystals would help solve the mystery of how this roach species was able to evolve a completely unique form of reproduction. After all, viviparity would not be possible in *D. punctata* without the nutritional support usually provided by only the egg yolk [3]. But the composition and structure of the milk crystals is of interest outside the world of insects as well. Could the world's most nutritious food be hiding out in the stomachs of roach embryos?

Taking a closer look at cockroach milk proteins

Analyzing a liquid, like milk, is relatively straightforward. There are particular kits that can be used to determine what types of proteins are inside; certain fat-binding chemicals can be added to figure out how much fat and what types of fats are present; and it can be centrifuged to see what settles to the bottom. But crystal structure and formation are a bit trickier, especially if one is interested in examining a crystal inside a living organism (what scientists refer to as *in vivo*). Hence, the more than 40-year waiting period from milk crystal discovery to milk crystal structural analysis.

Crystal structure is determined by analyzing the diffraction patterns created by X-rays. Like a crystal hanging in a window and diffracting sunlight across a room, X-rays penetrate crystal structures and their waves are diffracted into different directions based on the specific internal structure of that crystal. Researchers use these diffraction patterns to determine the structure and composition of a crystal.

Banerjee et al. [1] used cutting edge X-ray diffraction technology to take the highest resolution picture to date of the roach milk crystals. And what they discovered was a crystal structure like no other. The milk crystals were not composed of only proteins; the proteins were attached to carbohydrates (referred to as glycosylation) and fatty acids. And a closer inspection of the protein sequences demonstrated that they were extremely diverse in their amino acid composition. As such, these milk crystals are a complete food, providing all the essential macronutrients [1].

Milk vs. "milk"

Although the focus of the paper was to elucidate the specific properties of cockroach milk crystals, the authors could not resist seeing how cockroach milk stacked up against the real deal. One crystal was found to contain 3.7 x 10^{-5} joules (J), which is the equivalent of 8.8 kilocalories (kcal). Take 100 grams of roach milk crystals and compare it with 100 grams of milk from various mammals and what do you find? Roach milk crystals are more than three times higher in energy than the milks of many mammalian species, including cows, with the majority of that energy provided by protein [1].

Cockroach milk in the dairy aisle?

No need to panic dairy cows, you are not out of a job. Despite its complete protein package and high-energy content, cockroach milk is an unlikely substitute for cow's milk and its numerous associated dairy products. In addition to the logistical issues (just how many cockroaches would need to be "milked" to produce enough crystals for one human meal anyway?), there is a large cultural barrier. Cockroaches are seen in most Western cultures as a pest, not as food. Convincing people to consume the contents of their embryos' stomachs, no matter how nutritious, may prove impossible.

That does not mean they won't make their way into the human food supply. Dr. Ramaswamy, the corresponding author on the cockroach milk crystal study, discussed the possibility of genetically-engineering the crystals in a yeast substrate [4]. This represents a great example of translating science into public policy. The researchers have discovered a highly nutritious substance with potential to supplement or augment human diets. Using DNA sequences of the proteins present in the crystals, "synthetic roach milk" could be used to provide essential nutrients (particularly amino acids) to impoverished populations. All the nutrition, none of the roach.

But if you can't wait for a slow-digesting source of complete protein, take solace in the knowledge that one exists, and it is probably already in your refrigerator. It turns out that mammalian milk proteins employ many of the same tricks as the cockroach milk. The casein proteins in milk form protein bundles in the intestines that help slow their digestion and the subsequent release of their amino acids [5]. They may not shimmer like glitter, but they come in a much easier-to-swallow package.

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Dairy Protein Digestion: Life in the Slow Lane

- **Proteins take longer to digest in the stomach than do carbohydrates, and milk contains some of the slowest digesting proteins.**
- **Casein proteins are soluble in milk but form insoluble curds once they reach the stomach, making it hard for digestive enzymes to break them apart.**
- **Slower digestion also is associated with delayed release of the protein's amino acids into the bloodstream.**
- **Combined with the more quickly digested whey proteins, milk offers two sources of complete protein that help increase satiety and provide a consistent source of essential amino acids.**

Foods traveling from the mouth to the intestines are a bit like drivers off to work on a four-lane interstate. Some foods get in the fast lane and are quickly digested, whereas others stay in the slow lane, taking longer to reach their final destination. Why some foods are speed demons and others Sunday drivers depends on the particular properties of the nutrients in the foods. For example, proteins take longer to break down in the stomach than do carbohydrates, and milk contains some of the slowest digesting proteins of all. What makes milk proteins such slow pokes?

Milk's casein proteins actually go about making themselves more difficult to digest, forming small insoluble little balls, or curds, when they reach the stomach. Digestive enzymes have to work hard to break these curds apart, resulting in longer digestive times and slower release of the protein's nutrition. These properties of milk caseins may have evolved to benefit mammalian infants, but slowed digestion offers the benefit of increased satiety to milk drinkers of all ages. Eating foods, like milk, that take the slow lane may mean eating less food overall.

Protein digestion: one brick at a time

At the simplest level, proteins are strings of amino acids held together by peptide bonds. But the foods we eat contain proteins in their most complex form—those strings of amino acids are rolled into balls, which need to be unrolled and snipped apart in order for the intestines to absorb and then transfer the individual amino acids into the bloodstream.

Imagine that a protein is a skyscraper awaiting demolition. Although a wrecking ball and some explosives might be the quickest way to knock it down, doing so will damage the individual bricks used to construct the building. For proteins, the bricks are the amino acids the body needs to manufacture other proteins (e.g. muscle fibers, antibodies, hormones). Proteins, thus, must be broken down, brick by brick. (This can explain why proteins appear to have a more satiating effect than carbohydrates—they spend more time in the stomach than do carbohydrates, which require little processing by the stomach [1].)

Stomach acids help to unfold all the twists and turns of the amino acid chains, allowing digestive enzymes produced by the stomach's wall to get to work breaking the peptide bonds apart. The easier it is to get to the individual amino acids, the quicker the protein can be processed. As such, proteins with less structural complexity have quicker digestive rates.

Taking it slow: milk casein proteins

As proteins go, individual casein proteins from milk are fairly simple in their structure, lacking the high degree of coils, turns, and folds found in many other proteins [1,2]. In theory, they should quickly move through the stomach and transfer their amino acids to the bloodstream soon after ingestion. In practice, however, researchers have found the exact opposite.

Casein proteins in milk form small spheres, called micelles, with the hydrophilic (water-loving) portions of the protein on the outside of the sphere and the hydrophobic (water-fearing) portions on the inside. With hydrophilic structures on the outside, the micelles are soluble in water (or milk, which is mostly water) [1,2]. But when the micelles reach the stomach, "one of the most ingenious events in nature takes place" [2]. The digestive enzyme chymosin snips one of the bonds on the exterior protein (known as the kappa subunit), leaving only the hydrophobic subunits inside [1]. Without their protective layer, the now insoluble proteins form a curd. (If the term curd sounds a lot like curds and whey, there is a reason. In the process of making cheese, chymosin is also responsible for producing casein curds). Thus, by effectively turning a liquid into a solid, the enzyme makes casein proteins more difficult to digest.

Why would proteins that evolved to help nourish mammalian infants want to take *longer* to move through the gut and release their nutrients? There are obvious benefits to rapid digestion; nutrients and energy become available quickly after consumption, fueling immediate needs. Indeed, whey protein in milk is regarded as a "fast" protein [3] because its amino acids appear in the bloodstream relatively quickly after digestion (one of many reasons milk's whey proteins are promoted as recovery foods after exercise). One of the disadvantages to fast delivery, however, is the need to replace those nutrients more frequently. Evolution solved this problem by equipping milk with complementary "slow" casein proteins. In addition to keeping the infant feeling satiated, slower digestion also means a slower release and subsequent absorption of casein's amino acids. By having complete proteins that take both the slow and fast lane, milk provides mammalian infants with a nearly consistent supply of amino acids needed for their growth and development.

Filling up on cow's milk

When a human adult drinks a glass of cow's milk, chymosin acts the same way it does in an infant. Curds are produced, and these take longer to break down into individual amino acids. So, does this mean that casein proteins keep adults feeling full for a longer period of time than other proteins, such as whey? Surprisingly, there is not a consensus on the satiating effects of casein from the nutritional research [1].

A 2013 review of clinical trials on the effects of casein, whey, and other dietary proteins on appetite found that, although several studies supported the hypothesis that casein would be more satiating than whey, many actually found the opposite [1]. One reason for these confounding findings was the time period used to assess satiety. If satiety was measured within 1–2 hours after ingestion, whey seemed to be more effective, but if was measured 3+ hours after, casein kept the participants feeling more full [1]. With longer-term supplementation (days compared with hours), casein supplementation influenced overall food consumption. Participants supplemented with casein proteins consumed less total food at the end of the 7-day study period compared with those on a whey supplement [1].

Taken together, the studies reviewed by Benndtsen et al. [1] suggest positive effects of both whey and casein on appetite regulation. For those looking to reduce total food intake, the results of the longer-term studies are most encouraging. After all, weight loss or maintenance is not about how much food is consumed over the span of hours, but over weeks, months, and years. Milk is the only food to deliver both proteins simultaneously. If milk proteins can help reduce snacking in the short term and total food consumption in the long term, it could be an ideal food choice for those looking to reduce their total energy intake without compromising nutrition.

Caseins and cockroach crystals

There is another "milk" that could provide a satiating protein for humans, but it might not be as appetizing as are dairy milk, cheese, and yogurt. In an elegant example of evolutionary convergence, mammalian infants are not the only animal offspring that utilize a slow-digesting protein. Pacific Beetle cockroach embryos are fed a milk-like substance from their mothers, and researchers recently reported that the proteins from this liquid transform into high-energy crystal structures in the embryo's gut [4]. Although casein curds and roach milk crystals are not structurally similar, both effectively slow the release of the nutrients in the digestive tract of the offspring. Making milk a meal, rather than just a drink, appears to be an important evolutionary innovation for organisms as different as roaches, humans, and cows.

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Eating Whole-fat Yogurt Is Associated with Lower Obesity in an Elderly Population

- **Researchers have previously studied the association between yogurt consumption and obesity, but so far the results have been inconclusive, and few studies have compared the effects of low-fat and whole-fat yogurt.**
- **A new study finds that consumption of whole-fat yogurt but not low-fat yogurt is significantly associated with a decreased waist circumference and a higher probability of reducing abdominal obesity in an elderly population.**
- **The researchers suggest that the results may be due to some inherent benefit of the fat in whole fat yogurt, or because low-fat yogurt often contains more sugar.**
- **The researchers conclude that whole-fat yogurt may offer some benefits for managing obesity in an elderly population but point out that consuming any type of yogurt is expected to have positive effects on health.**

For those on a diet, it might be natural to reach for low-fat rather than whole-fat yogurt. But the results of a new study might make that decision a little more complicated, at least in some populations. In the study, Carmen Sayón-Orea and her colleagues at the University of Navarra found that eating whole-fat yogurt was associated with a decrease in waist circumference and a greater probability of reducing abdominal obesity in an elderly population at high cardiovascular risk [1]. The researchers didn't find a similar association with low-fat or total yogurt consumption.

Researchers have previously studied the associations between yogurt consumption and obesity, but the results have been inconclusive [2–5]. In addition, few studies have looked at the effect of low-fat versus whole-fat yogurt. "We wanted to clarify the role of these kind of yogurts," writes Sayón-Orea in an email.

Sayón-Orea and her colleagues previously found that for young, healthy individuals consuming a lot of whole-fat yogurt was associated with a lower risk of becoming overweight or obese [6]. "We decided to replicate our research in an elderly population," she writes.

In the new study, the researchers used questionnaires to assess the consumption of total, whole-fat, and low-fat yogurt in 4,545 elderly individuals at high cardiovascular risk. They found that higher consumption of whole-fat yogurt but not low-fat yogurt was associated with a decrease in waist circumference and a higher probability of reducing abdominal obesity. The results are consistent with those of previous studies showing the benefits of whole-fat yogurt consumption [6–8].

"The different association regarding whole-fat and low-fat yogurt consumption might be explained by some benefit inherent to the fat contained in whole-fat dairy products, or because of a higher sugar content of low-fat yogurts," writes Sayón-Orea. In Spain, where the study was conducted, low-fat yogurts contain added sugars, she adds. "If people decide to consume low-fat yogurt, it's very important to check if it's high-sugar or low-sugar, and always prefer low-sugar yogurts," writes Sayón-Orea.

Another possible explanation for the study's results that the researchers couldn't rule out is that participants who consume low-fat yogurts have special lifestyle characteristics. "For example, people who perceive that they are gaining weight might change their consumption to low-fat products," writes Sayón-Orea.

The researchers conclude that whole-fat yogurt may offer some benefits for managing obesity, particularly in an elderly population. But according to Sayón-Orea, consuming any kind of yogurt is likely to have health benefits. "I do believe that any kind of yogurt is healthy because the mechanism by which yogurt is beneficial to health is the content of calcium, the lactic acid and the probiotics," she writes.

Yogurt tends to be rich in calcium and also contains lactic acid that can promote calcium absorption. There's some evidence that the high calcium and protein in yogurt can influence appetite, and that calcium may also reduce fat production and absorption, and increase fat excretion and oxidation [9–12]. These mechanisms could explain some of yogurt's beneficial effects against obesity and metabolic disorders.

"Another possible mechanism that could be implicated in these beneficial effects might be the role that microbiota may play in the development of obesity and cardiometabolic diseases," writes Sayón-Orea [13,14]. "Some bacteria that are used as probiotics in yogurt, such as *Lactobacillus acidophilus* and *Bifidobacterium bifidus*, may help to prevent or treat some diseases, including obesity," she writes.

The researchers plan to expand on their current work by exploring the effects of yogurt consumption and different types of yogurt on other disorders. "The next outcomes that we might explore could be hypertension and cardiovascular disease," writes Sayón-Orea.

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