This month’s issue features magnesium, the US military’s policy on breastfeeding, cow’s immune system, and camel’s milk.

**Magnesium in Milk: An Overlooked Mineral?**

- Magnesium plays a key role in many of the body’s functions, but the majority of Americans don’t consume enough of it in their diet.
- A new review indicates that magnesium plays a particularly crucial role in the activation of vitamin D, and magnesium supplementation may help avoid vitamin D deficiency.
- Another recent review suggests that milk may be an important dietary source of magnesium, and magnesium-fortified milk and dairy products could help overcome magnesium deficiency.

Magnesium is one of the most abundant minerals in the human body and plays a key role in many of the body’s physiological functions. Despite its availability in a wide variety of foods, magnesium is often reported as being consumed at inadequate levels [1].

A new review by H. Eustina Oh and Hilton C. Deeth suggests that “magnesium in milk and milk products is a major contributor of dietary magnesium and warrants more attention from researchers [2].” Magnesium in milk has so far been relatively overlooked by researchers compared to calcium, possibly because it is present in cows’ milk in about 10% of the concentration of calcium. Oh and Deeth suggest that “until recently it could be termed the forgotten mineral.” However, an ever-increasing number of studies have shown that magnesium is extremely important for the body’s functioning.

Magnesium is involved in protein and nucleic acid synthesis, bone growth, energy metabolism, regulation of blood pressure, and in the activation of hundreds of enzymes [3,4]. Dietary magnesium intake can help reduce the risk of type 2 diabetes, as well reduce the rate of heart attacks and strokes [5-7].

Consuming too little magnesium has been implicated in an array of health issues, including metabolic syndrome, skeletal muscle loss, kidney function decline, and depression [8-12]. Reduced intake of dietary magnesium is also associated with elevated blood pressure and higher stroke risk, whereas magnesium supplementation has been reported to lower blood pressure in adults [8,9].

Magnesium also interacts with many other minerals and nutrients. For instance, it influences extracellular calcium levels and the intracellular actions of calcium [13]. It also plays a crucial role in immunoregulation and bone mineralization by influencing the synthesis of the active vitamin D metabolites [14-17]. Magnesium’s interactions with vitamin D are a particularly important example of the crucial role this mineral plays in the body’s functioning. A recent review by Anne Marie Uwitonze and Mohammed S. Razzaque indicates that magnesium helps vitamin D activation and function. Vitamin D needs to be converted from its inactive form to an active form before exerting its biological functions, and this process is actively dependent on the bioavailability of magnesium [14,15]. The authors conclude that it is “essential to ensure that the recommended amount of magnesium is consumed to obtain the optimal benefits of vitamin D [18].”

Vitamin D and magnesium interact to maintain the physiologic functions of various organs, and abnormal levels of either nutrient can lead to serious organ dysfunctions [19-24]. Deficiency in either nutrient is associated with various disorders, including skeletal deformities, cardiovascular diseases, and metabolic syndrome [25-30].

The high prevalence of vitamin D deficiency is a major global health concern. High magnesium consumption reduces the risks of vitamin D deficiency in the general population [31]. “Vitamin D deficiency is presumed to be widespread, and consuming high doses of vitamin D supplement for a
prolonged period has undesirable side effects, so, the question is how can we reduce our dependency on vitamin D supplements and supplement-associated damaging effects,” says professor Mohammed Razzaque of the Lake Erie College of Osteopathic Medicine. “I believe that by taking the optimal amount of magnesium one can reduce the dependency on vitamin D supplements,” he says. “Without the optimal range of magnesium, endogenous vitamin D wouldn’t function to its full potential, and therefore, no amount of vitamin D supplement would reduce vitamin D deficiency-related complications,” says Razzaque.

Razzaque hopes for more studies of the interactions between vitamin D and magnesium in the future. “We need well-designed clinical studies to show that by consuming an adequate amount of magnesium one could reduce the morbidity and mortality related to vitamin D deficiency, perhaps without taking vitamin D supplements or taking a lower dose of vitamin D supplements,” he says.

Despite the crucial physiological roles played by magnesium, more than half of the US population may be consuming inadequate amounts of this mineral [1]. Magnesium is widely present in both animal and plant foods, but the United States standard diet contains about half of the recommended daily allowance for magnesium [32,33].

Given magnesium’s various physiological functions, its interactions with other nutrients such as calcium and vitamin D, and its overall importance to human health, it is important to ensure that it is consumed in adequate amounts. The importance of magnesium in the diet and its inadequate consumption by a majority of the population have led to increased interest in finding dietary sources of magnesium and enriching such foods [34,35].

Milk and dairy products are already one of the main dietary sources of magnesium, particularly for children, contributing approximately 10–30% of the total magnesium intake [36]. Some studies have shown that the lactose in dairy products may help in the intestinal absorption of magnesium in human infants and in rats [37–39].

Milk can also be enriched with magnesium, and commercial magnesium-fortified ultra-high temperature (UHT) processing milk is already available [40]. A recent study discovered an added benefit of enriching milk with magnesium—it can help reduce bacterial contamination and spoilage, and increase the intestinal bioavailability of magnesium from milk [41].

Oh and Deeth suggest that milk and dairy products could be developed into a more efficient means to deliver increased levels of dietary magnesium. This may be in the form of magnesium-fortified milk and dairy products, and these could help overcome reported magnesium deficiencies and also help prevent vitamin D deficiency.

11. Welch AA, Kelaiditi E, Jennings A, Steves CJ, Spector TD, MacGregor A. Dietary magnesium is positively associated with skeletal muscle power and indices of muscle mass and may attenuate the association between circulating C-reactive protein and muscle mass in women. J Bone Miner Res. 2016 Feb;31(2):317-25.

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The Woman Helping Military Moms Breastfeed

- All branches of the US military now have a breastfeeding policy, intended to provide guidance and rules for mothers who wish to pump their milk.
- Although existing rules are a step forward, the onus is still on the mother to make pumping and storing possible, which remains challenging if she is in the field or deployed far from home.
- Other countries tend to not need pumping policies because their maternity leave periods are longer.

Back in the 1990s, when she had her first child, Robyn Roche-Paull was an aircraft mechanic in the United States Navy. She knew she wanted to breastfeed as long as possible, but her maternity leave was six weeks long, and then, in theory, she could be deployed to any part of the world. At that time, there was no military policy to facilitate pumping at her workplace, though she persevered. She would pump in the supply closet or the bathroom. “It was very, very difficult. The outlet I needed to plug my pump in was right by the bathroom door, and people would come in and out all the time—so the door was always opening to the hallway, with me standing right there,” she explains.

Despite daily struggles, Roche-Paull managed to breastfeed for a whole year while on active duty. The experience proved to be formative. Today, she works as a qualified lactation consultant and registered nurse with the US Army, and for eight years has been the executive director of “Breastfeeding in Combat Boots,” a nonprofit organization that seeks to support military mothers by providing advice, information, and inspiration for those who wish to breastfeed.

But the route to her current success has been bittersweet. When she and her husband decided to have more kids, there seemed little option but to leave her job. So, while her husband remained in the military,
One policy that would undoubtedly make a difference is longer maternity leave. After searching for years

Robyn Roche-Paull, Petty Officer 3rd Class - US Navy with her 8 week old son, 20 years ago. Courtesy of Robyn Roche-Paull.

The reason for the page’s popularity is not all positive—it also reflects unmet demand. Roche-Paull had struggled with a lack of military breastfeeding policy in the 1990s, and since then improvements have been slow to emerge. Only as of 2015 have all branches of the US military had rules and guidance for mothers who would like to breastfeed, and for their commanding officers. “Before it was sort of a free for all. If you had someone in charge who wasn’t supportive, then nothing happened—they didn’t do anything, they didn’t help you. The fact that we now have policies across all of the branches is huge,” says Roche-Paull.

The US Army was the last to put in place a policy. But, Roche-Paull acknowledges, it is the best because it embraces specifics. It states that moms who wish to pump should be provided with a locked room that has a table, a chair, and electrical outlet, and that the room cannot be a restroom. They should be given 15 to 30 minutes, every three to four hours.

In some ways, it is huge progress. Even as recently as 1972, women were discharged from the US Navy if they had a child. But all of the military policies—and each branch has different pumping regulations—still put the onus on the mother to make it work. “If you’re out in the field, or something like that, you’re gonna have to think outside the box,” explains Roche-Paull. “Where is there going to be a place to pump? Is it going to be in the tent? Is it going to be turned around behind a tree with your jacket pulled up around you?”

Storing milk is another issue. Often military moms can use a communal refrigerator, or keep their milk in insulated packs that come with most pumping kits. “I’ve worked [with] moms who were sent out for two or three weeks and they would take a big cooler with them. And they’d get ice from the cooks to keep the milk cold. If there’s a truck coming to deliver supplies and mom’s got a week’s worth of milk stored up, then she sends her cooler back with the truck—and dad picks it up at home base. And hopefully, she brought two coolers with her...” Roche-Paull relishes recounting these tales of resourcefulness and success—there’s the one about the officer who sent milk back from Afghanistan via DHL, and the pictures she was sent of a woman pumping at the firing range, her rifle rested up against the wall and guys shooting behind her. “But,” adds Roche-Paull with a pause, “it’s all on the individual.”

There’s very little data to characterize what this means for breastfeeding success in the military. One survey of the US Navy, published in 2009—after Navy breastfeeding policies were in place—found that almost two-thirds of enlisted women and half of female officers who started breastfeeding reported stopping because of a work-related issue [1]. Comparing the US Navy’s outcomes to the Department of Health and Human Services’ 2010 Healthy People objectives, the study concludes: “the reality of breastfeeding once the women return to duty shows an even larger difference from those goals; whereas the goal is 50% breastfeeding at 6 months; 30% plan to do so but only 13% actually do.”

Roche-Paull thinks that many of the remaining problems are cultural. “People often don’t understand why pumping needs to be done. There’s still a male-dominated culture—the sense that women don’t belong here, and now you are here, you want to do this totally feminine-women-thing. Why are we giving you breaks to go do this?” Sometimes senior women who do not have children, or who had infants when there were no breastfeeding policies in place, are among the least understanding, says Roche-Paull. “They kind of have this eat-your-young attitude. Well it didn’t work for me so I’m not going to let it work for you either.”

One policy that would undoubtedly make a difference is longer maternity leave. After searching for years
to find sister organizations to Breastfeeding in Combat Boots in other countries, Roche-Paull has realized that they probably don’t exist because militaries elsewhere tend to give new mothers much longer leaves before they are required to return to work. In Canada, for example, female military personnel get a year’s maternity leave. Roche-Paull has also been researching pumping and milk storage policies in other countries. “I’m having a hard time finding them. Again, because you all have great maternity leave policies, it’s a moot point.”


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A Cow’s Milk Reveals Her Health

- Milk contains natural defenses against microbes.
- The innate immune defense system in milk evolved to protect the mother and suckling offspring from infections.
- Molecular components of the innate immune system in milk are sensitive biomarkers of the health of the dairy cow.
- In the future, a milk sample may predict the cow’s health and allow more rapid management of disease.

Defense wins games. Ask any coach impatiently striding the sidelines. “The defensive line-up must be ever vigilant and able to rapidly neutralize the attacking incursion, which may come from any direction. You cannot wait for help from the cover defense! Any defensive lapse will be ruthlessly exploited by this opposition and all will be lost,” shouts the coach at spent and cowed players as the bell signals the end of their halftime break. Coaches could learn a lot more about defense from biology. An exemplar defensive strategy par excellence is used by mammals, especially dairy cows, where the defensive system is the animal’s immune system, the best in the league, and the opposition threat is microbial infection.

Infection is the ultimate challenge to an animal’s survival. Typically, there are no armistices in these battles, just total victory, or total defeat for the individual animal. Over many past generations, the outcomes of these battles drove an evolutionary arms race between the immune system of an animal species and infectious microbes. Occasional changes (DNA mutations) in the latter that increased microbial infectivity were eventually countered by advances (DNA mutations) in the immune system of the animal, but all this takes a great deal of time. The arms race continues unabated. Luckily, the mammalian immune system of today, through the process of evolution and natural selection, is exquisitely adapted to defense against microbial challenges. Mammals have multiple defensive components in their immune system that work together like a well-drilled team to robustly protect an animal from the ever-present threat of microbial infection.

The Three Armies of the Mammalian Immune System

There are three major components of the mammalian immune system that defend the body from microbial incursion. The first component is the secretion of protective antibodies from immune cells that are sensitized to specific microbial invaders (humoral immunity). The second component enlists immune system cells that are trained to seek out and destroy specific microbial invaders (cell-mediated immunity). Both of these components are primed for defense by the memory of past battles with specific microbes i.e., the immune components must first be trained to recognize specific microbes before they can destroy them. These two components are exquisitely efficient at killing or neutralizing specific invading microbes that they recognize from past incursions, and hence they are called the adaptive immune system. However, the Achilles’ heel of this defensive strategy is its impotency when confronted by new microbial invaders that have never before been in contact with the animal’s immune system. It takes time for these two immune components to learn to mount a good defensive response, time that can be exploited by the microbial invasion. The third immune system component, innate immunity, plugs this defensive gap as it
rapidly responds to new microbial threats. The innate immune defense component does not require memory of past microbial invasions, it is ever ready for defense, and importantly, the activity of the innate immune component is largely indiscriminate in its targeting of microbes; it annihilates anything that is broadly recognized as foreign within an animal. Innate immune defense is brief, brutal and unsophisticated, often causing some collateral cell damage while saving the day. This is an evolutionarily ancient and formidable front line of defense against microbial invasion in all animals.

**Milk Defense**

In dairy cows and other mammals, there is extension of all three immune system defense components into milk, but in particular the innate immune component [1-5]. The innate immune component in milk guards against opportunistic infections caused by microbes such as bacteria, fungi, and viruses lurking in the local environment of a cow. The mantra of The Game of Thrones television series that “winter is coming” (the external threat is real and certain), is never truer. These microbes can be restrained by good dairy industry hygiene practices, but they are an ever-present potential health threat to cows. The innate immune component in cow’s milk protects the mother from mammary tissue infections (mastitis) and it may also protect the suckling calf while its adaptive immune system is developed and trained [6]. Protection of lactating cows from infections improves the efficiency of milk production and it is important from an animal ethics perspective.

A major challenge to the dairy industry is the maintenance of the health of cows during the periparturient period (around birth), a time when the physiological foundation for optimal lactation is established [7]. During this period the cow is vulnerable to infections such as mastitis and uterine diseases [4]. Scientists suggest that this increased susceptibility to infections is caused by profound physiological, metabolic and hormonal changes in the cow accompanying birth that together cause periparturient immunosuppression within the cow [7]. Pre-emptive good hygiene management of cows at this time is a mainstay of the dairy industry. However, there is also need for preclinical identification and early treatment of infections during this at-risk periparturient period. A team of investigators recently suggested the need for a simple test using milk that reports the broad-spectrum health of the cow, and enables early treatment of any infection before it becomes established and causes clinical symptoms, especially the loss of milk production [4]. These investigators and others suggest that a molecular test based on innate immune system proteins in milk may provide the answer [3,4].

**Milk Reveals Cow Health**

Recently, German investigators identified a large number of innate immune biomarkers (proteins) in milk that can be used to monitor the general health of dairy cows [4]. The study was published in *Advances in Dairy Research* and highlights research from sixteen investigators, led by Joerg Lehmann, from several research institutions primarily based in Leipzig, particularly the Fraunhofer Institute for Cell Therapy and Immunology. The aim of the study was to identify and validate potential bovine biomarker candidates detectable in milk for the evaluation of the general health status of dairy cows.

The investigators used an interesting approach to the discovery of these biomarkers [4]. First, they identified large groups of healthy and diseased cows in early lactation from normally high-performing commercial populations of dairy cows. The diseases they identified were varied in terms of disease agents, affected tissues, and severity. Lehmann and colleagues identified about forty different diseases, some were systemic affecting nonmammary and sometimes multiple tissues, and others were due to intramammary mastitis. The investigators argued that using this population of cows, any disease biomarkers discovered in milk would identify a broad spectrum of common cow health issues and may be able to discern intramammary from systemic infections. The latter possibility was not a primary aim of the study. Second, they identified gene activities (the abundance of each messenger RNA (mRNA), the intermediary between a gene and its corresponding protein) in milk cells from cows with systemic extramammary disease or intramammary disease that were different in the milk cells obtained from the healthy cow group. The investigators reported that the process generated a long list of 1,891 genes with mRNA levels in milk cells that were affected by disease. Many of these genes coded for innate immune proteins. Third, the investigators substantially narrowed down the list to a smaller group of high priority genes by selection for only those genes ultimately generating proteins that are secreted out of cells and into milk, and which are known to be involved in inflammatory responses. The gene prioritization process worked well as the investigators reconfirmed single gene results from some previous studies [3]. Fourth, the investigators then measured the quantities of a number of specific proteins present in milk derived...
from these high priority genes to confirm their association with disease. In all, the investigators discovered a substantial number of candidate protein biomarkers in milk that report cow health. Some but not all of these proteins are involved in innate immunity. This is a valuable list that may have many future applications. Finally, the investigators demonstrated that a combination of the quantities of a few of these protein markers in milk was better able to detect the early signs of disease than the quantity of any individual protein—it’s about the team, not the individual player.

**Implications**

Joerg Lehmann and colleagues concluded that a combination of biomarker proteins in milk could be used as a broad-spectrum measure of cow health [4]. This test using milk could provide an early indication of preclinical infections in cows and allow earlier treatment to minimize adverse production impacts from common diseases. The investigators also stated that an automated, cost-effective and high-throughput method for accurate biomarker quantification still needs development. The coach may now have a decisive early warning system to head off attacking disease incursions.


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**Camel’s Milk Offers Hope Against Diabetes**

- Camel’s milk has been consumed for millennia by populations in the Middle East and India.
- There are studies claiming that camel’s milk offers protection against a long list of medical ailments.
- The evidence that camel’s milk reduces the symptoms of diabetes is reasonably persuasive, although more studies are needed to identify how the underlying biological mechanisms might work. A little over a decade ago, an article appeared in a journal devoted to diabetes research claiming that the disease did not exist among the camel-milking drinking Raica community, a group living in the desert of northwest India, in the state of Rajasthan. The study had surveyed more than 2,000 people. The defining factor in the Raica community’s healthy blood glucose levels appeared to be their camel milk consumption, not genetics, nor a holistically healthy lifestyle [1]. Since that article was published, its authors have buttressed their initial conclusions. Raica community members who do not drink camel’s milk can indeed develop diabetes. The same researchers tracked down a small number of them via a Rajasthani hospital outpatients department. Just as was the case for non-Raica individuals with type II diabetes in their follow-up study, three-months of drinking half a liter of camel’s milk a day reduced the severity of diabetic Raica community members’ disease. The change was evident in various measures, such as post-meal glucose levels and levels of hemoglobin A1c (which is a marker for glycemic control) [2]. Diabetes is one example of a long list of ailments against which camel’s milk has been reported to be medicinal. Other studies suggest that it can fight infections, from diarrhea-causing germs in children [3] to intestinal worms that commonly afflict sheep and goats in North Africa [4]. Some find that it can even
help to alleviate symptoms of autism [5] and reduce the risk of various cancers [6, 7, 8]. The quality of these studies varies. Nonetheless, the demand for camel’s milk outside the regions where it is traditionally consumed is rising. Camels are now the fifth most important dairy animals in the world according to the United National Food and Agriculture Organization [7].

Other than the particular case of the Raica community, is there strong evidence that camel’s milk can help to treat diabetes? The simple answer is that there are various encouraging experiments and trials, most of which report a protective effect, but they generally involve a small number of participants. When it comes to type I diabetes, for example, Parvin Mirmiran and her colleagues at universities in Tehran, Iran, conclude in their review of the field that most studies have reported a reduction in average insulin dose in response to drinking camel’s milk [9]. For type II diabetes they find that the evidence is slightly less clear than for type I diabetes, though it is still positive on balance.

One of the most recent and optimistic trials of camel milk in people with type II diabetes involved randomly selected patients who were being treated at a hospital to the west of Tripoli, in Libya [10]. Forty-two men aged between 40 and 65 were included in this study, all of whom received the hospital’s usual outpatient treatment of dietary changes, exercise and regular injections of insulin. Twenty-one of the men were asked to drink half a liter of fresh camel’s milk each day, on top of following the usual treatment.

The results were impressive. For three months the fasting glucose levels and insulin doses of all of the men were monitored. By the end of the period, those who consumed camel’s milk had 13% lower blood sugar than those who hadn’t—and the researchers previously checked that the two groups had basically the same average blood sugar levels at the start of the study. Unsurprisingly, therefore, the camel milk-drinking men didn’t need to inject as much insulin: they saw a steady decline in the amounts that they needed over time—and after three months, it was 25% lower than at the outset. Moreover, a battery of blood tests comparing the two groups at the end of the three months demonstrated highly significant improvements in the camel milk group relative to the control group, for every measure tested except for cholesterol levels—that is, the researchers observed improvements in levels of hemoglobin A1c, bilirubin, urea, creatinine, triglycerides, and many more indicators of metabolic health.

What is it about camel’s milk that might account for its apparent benefits for diabetics? This is where existing research is even less conclusive. One contributor might be zinc. Camel’s milk contains a lot of it relative to cow’s milk, and zinc is known to enhance insulin’s interaction with its receptor [6]. Another is likely to be an insulin-like molecule in camel’s milk that is understood to be protected from human stomach acid. This is because it is encapsulated by lipids [11]. Moreover, this molecule is probably easily absorbed into the bloodstream after it has run the gauntlet of the stomach because camel’s milk does not coagulate—become lumpy—in an acidic environment (unlike cow’s milk) [11].

At least two studies have recently homed in on new details. A research group based in Saudi Arabia, at King Abdel-Aziz University, in Jeddah, conducted an experiment on laboratory rats, inducing diabetes in some of them [12]. They sourced camel’s milk from a farm in Mecca principedom and fed it to the rats. The scientists then followed shifts in the gene expression patterns of these animals. In addition to the improvements in blood glucose and other benefits that researchers elsewhere have documented in human studies, this group was able to observe changes in the expression of various genes—notably genes called CPT-I, FASN, PK, and IRS-2—as well as stimulation of insulin production and secretion from the rats’ pancreases. A joint research project between Saudi researchers and others at the University of California, Irvine, meanwhile, has found that camel’s milk has an especially high level of freely available gamma-aminobutyric acid (GABA) [13]. GABA has separately been shown to prevent and reverse diabetes in animal models, probably because it helps to lower autoimmune inflammation and restore pancreatic beta cells.

These high levels of free GABA content might also offer a mechanism by which camel’s milk could provide some protection against cancer. As the authors of the Saudi-US paper point out, GABA has been shown to inhibit the migration of cancerous cells in the colon. As with the gathering evidence around camel’s milk as a defense against diabetes, that is an exciting avenue for research. If camel’s milk is as medically useful as this early work proposes, it offers hope to much of the world’s population that cannot afford the bulk of modern medicine’s solutions.


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