Higher Milk Consumption Is Associated with Reduced Risk of Hip Fractures

- Previous studies of the association between milk intake and hip fractures have not shown a clear benefit for milk consumption.
- A recent longitudinal study of a large cohort of 123,906 U.S. adults followed over 32 years finds that milk intake and total dairy food consumption were both associated with a lower risk of hip fractures in older U.S. adults.
- The benefits of milk were not explained by its calcium, vitamin D, or protein content, and more studies are required to figure out what components of milk help lower fracture risk.

Bone density decreases with age, leading to an increased risk of hip fractures. Milk is considered helpful for maintaining bone health due to its high calcium, protein, and its fortification with vitamin D, and the 2015 Dietary Guidelines for Americans recommends that adults consume two to three cups of milk or equivalent dairy foods per day to protect aging bones [1].

However, the association between milk intake and hip fractures is far from clear-cut. No intervention studies have been conducted where one group of participants are given milk and then their risk of hip fractures is compared with that of a control group not given milk. The studies conducted so far have been prospective cohort studies, which followed individuals over time and collected information about their milk intake and whether they have suffered hip fractures to examine whether there were any associations between them. These cohort studies and meta-analyses of these studies have generally not supported an inverse relationship between milk intake and hip fractures [2-8].

“Previous studies of milk and hip fracture have not shown a clear benefit from milk, yet U.S. guidelines continue to recommend milk consumption for older adults,” says Professor Diane Feskanich of Brigham and Women’s Hospital and Harvard Medical School. “More recently, a study done in Sweden found an increased risk of hip fracture with higher milk intake in women but not in men, which I found surprising,” she says.

The Swedish study examined two large cohorts and found that women had a significant 9% greater risk of hip fracture for every glass of milk consumed per day, whereas no association was observed for men [5].

“This prompted us to do a similar analysis in our male and female cohorts,” says Feskanich. “There are differences in dairy consumption and hip fracture rates between Sweden and the U.S. and we did not want to assume that the Swedish findings would apply universally,” she says.

In a new longitudinal study, Feskanich and her colleagues found that among a large cohort of U.S. men aged 50 or older and women past menopause, higher milk and dairy intake were associated with a reduced risk of hip fracture [9].

“The Swedish study had gotten a lot of attention when it showed that hip fracture risk increased with higher milk intake in women,” says Feskanich. “So, our finding of a decreased risk with higher milk intake in both men and women shows that the book is not yet closed on this topic,” she says.

The new study examined the association between the long-term consumption of milk and other dairy foods and the risk of hip fracture in two large U.S. cohorts, the Nurses’ Health Study (NHS) of women and the Health Professionals Follow-up Study (HPFS) of men. In these two cohorts, 80,600 postmenopausal women and 43,306 men over 50 years of age were followed for up to 32 years.

Feskanich and her colleagues previously reported no significant associations between milk consumption and hip fractures in the NHS and HPFS cohorts [6-8]. However, their new study had increased statistical
power with additional years of follow-up and hip fracture cases compared with the previous studies, and also expanded the analysis to account for a variety of factors including sex, age, and other dietary intakes. In the new study, the researchers found that each serving of milk per day was associated with a significant 8% lower risk of hip fracture in men and women combined [9]. Higher total dairy food consumption, which consisted of milk, cheese, yogurt, cream, and ice cream, was associated with a significant 6% lower risk of hip fracture per daily serving of dairy foods in men and women. The data also suggested that higher cheese intake in women may contribute to a lower hip fracture risk, but the result was not statistically significant.

The study yielded some unexpected results. “Two things were surprising,” says Feskanich. “One was that the benefit of milk did not seem to be due to the calcium, vitamin D or protein content of the milk, i.e., when we added total calcium, vitamin D and protein intakes to our statistical models, we still found a lower risk of hip fracture with higher milk intake,” she says. “Future research would be useful which can examine what it is in milk that may lower fracture risk,” says Feskanich.

“The other surprising thing we found was that the benefit from milk was mostly found in men and women with higher body mass index,” says Feskanich. “This was an ad-hoc analysis and needs to be examined and confirmed by others,” she says.

The study concludes that higher long-term milk consumption in older U.S. adults is associated with a lower risk of hip fracture, and this finding was not explained by the calcium, vitamin D, or protein content of milk. “I don’t think that a dietary recommendation can be made based solely on our research, but it does suggest that older adults may safely choose to include milk as part of their plan for bone health,” says Feskanich.

Further studies of milk consumption and hip fracture may also benefit from looking at a variety of populations. “Dietary recommendations may not be one-size-fits-all, and future research needs to target specific populations,” says Feskanich.

References:

Contributed by
Dr. Sandeep Ravindran
Freelance Science Writer
Sandeepr.com

Take It Easy: Neonatal Milk Hormones Influence Infant Social and Cognitive Behavior

- Research in rats and primates demonstrates that cortisol passed to infants from mother’s milk influences infant temperament.
- A new study on rhesus macaques demonstrates for the first time that the concentration of milk cortisol during the first weeks of life predicts cognitive performance in later infancy.
- Cortisol is a natural ingredient in milk whose concentration is unrelated to the mother’s stress level.

Email, texts, IM, Facebook, Instagram—in the age of social media, there is no shortage of ways to send a message from one person to another. But is mother’s milk the original social network? Many of milk’s
Ingredients are believed to act as signaling factors that convey a “message” from mother to infant. Over the last decade, researchers have worked on decoding these messages, with a particular focus on the hormone cortisol. Milk cortisol levels are associated with infant growth and infant temperament in rhesus macaques, and hypothesized to send the message to be more cautious and prioritize growth over behavioral activity [1-3]. A newly published study [4] expands on this hypothesis and tests whether milk cortisol levels during the first weeks of life predict behavior and cognitive performance months later. The results suggest that far from being an instant messenger, milk’s signal may have effects well after it is received.

You’ve Got Mail

Voles are small rodents similar in size and appearance to mice, and provide one of the most clear-cut examples of the maternal social network, better known as developmental programming [5]. Montane voles that live in the Western United States and Canada produce offspring mainly during the spring and summer months. Infants born in early spring grow rapidly and reach age at first reproduction quickly, whereas those born in late summer stop growing when reaching a particular body weight and delay reproduction until the following spring. These growth patterns are adaptive; offspring born in late summer are facing the approach of shorter, colder days when food sources will diminish and reproduction is unlikely to be successful. But without a calendar, how do the offspring know when they are born? In a series of elegant experiments, Horton [5] demonstrated that mothers were signaling photoperiod information, via the hormone melatonin, to their fetuses, which then directed postnatal growth and development. This groundbreaking research demonstrated that mothers can send messages to their offspring during gestation (“days will be getting shorter as you grow and develop”) and that fetal physiology is primed to receive these messages [5].

But the social networking need not stop after the offspring are born. The evolution of lactation among mammals, and particularly the extended period of lactation in primates, presents an additional opportunity for mothers to provide information to their offspring that may increase survival and reproductive success. Maternal physiological signaling in the postnatal period is referred to as lactational programming [1] (or as lactocrine programming [6] when discussing hormonal signals), and has been demonstrated in several mammal species. A specific signaling factor of interest is the stress hormone cortisol. Cortisol is present in milk, and infants have cortisol receptor genes in their intestinal tracts, setting up a perfect scenario for sending and receiving a signal. But what might mammal mothers communicate through milk cortisol levels?

In rats, rhesus macaques, and humans, milk cortisol is associated with infant temperament, but the message sent by mothers differs among species [1-3]. In rats, higher cortisol intake via milk was associated with more exploratory behavior and less anxiety during adulthood, whereas among rhesus macaques and humans, higher milk cortisol was associated with a more fearful or less confident temperament during infancy [1-3]. Differences between the meaning of the message sent to rats and that sent to primates may relate to differences in life history. Compared to rats, primate infants have a protracted period of growth (even when scaled for body size); they rely on milk for energy (both for growth and for behavior) for a much longer period of time than do rats. Information about how much energy may be available for the entirety of the lactation period would allow primate infants to calibrate their growth rates to maternal reserves [1], just as developing voles calibrate their growth using maternal signals on birth season [5].

Not so Instant Messenger

In rhesus macaques, Hinde and colleagues [1] propose that milk cortisol levels send a message from mothers to infants about how to allocate energy received in milk. Specifically, they argue that rhesus macaque mothers that may be limited in their resources (e.g., first time mothers that are still growing) would improve the chances of their offspring surviving to reproductive age by sending the message to “take it easy”—be cautious when it comes to behavior and put any available energy from milk into growth
Hinde et al.’s hypothesis for energetically conservative infants is based on milk collection at 1 month and 3.5 months of age and infant behavioral assessments at 3.5 months of age. But if the message that mothers are sending is meant to convey an adaptive strategy throughout the lactation period, this message is predicted to be persistent. To this end, a new study by Dettmer et al. [4] investigated whether cortisol levels in rhesus macaque milk during the first weeks of lactation were predictive of behavior and cognitive performance between 4 and 8 months of age. At this phase of development, rhesus macaque infants are increasing their independence from their mothers while also developing neurological changes associated with complex social behavior [4].

Contradictory to Hinde et al.’s [1] findings, Dettmer et al. [4] found the higher milk cortisol levels were not associated with overall social behavior patterns. Indeed, one of the only associations noted for a particular behavior was more play and engagement in social behaviors, between 4 and 8 months of age, in daughters (but not sons) that received higher levels of milk cortisol.

Conflicting findings between these two studies [1, 2] on the association between milk cortisol and social behavior in infant rhesus macaques need not mean a return to the hypothesis starting board. Each study used a different method for assessing behavioral traits such as cautious, nervous, and confident. Hinde et al. [1] used a bio-behavioral assessment that required separating infants from their mothers and social groups, whereas Dettmer et al. [4] observed the infants interacting within their social groups. Might a more stressful environment bring out more observable behavioral differences between those infants receiving high and low levels of milk cortisol? The studies also differed in the timing of milk collection, with Hinde et al. [1] considering the effects of milk both during early (1 month) lactation and peak lactation (3.5 months). It is possible that some behavioral traits may be more responsive to messages sent later in lactation or, as Hinde et al. found with sons, to changes in the message, such as an increase in milk cortisol over time [1]. Clearly, it is a complex system.

Case in point: the cognitive tests did support previous research on milk cortisol in rhesus macaques [1]. The test used by Dettmer et al. [4] was ideal for their hypothesis, as it looked at how quickly a monkey was able to learn a task, and also measured impulse control. A box with only one opening sat at the bottom of a plexiglass board and the monkeys were trained on over 100 trials to reach straight ahead and grab a food reward out of the box (with the box opening facing the monkey). Then, the experimenter moved the box so the opening was on the left or the right—to reach the reward, monkeys had to reach around the board rather than straight ahead. Researchers measured whether the monkeys reached impulsively straight ahead or to the correct side, as well as how long it took them to solve the task. Both higher milk yield (i.e., how much milk the mothers produced) and higher milk cortisol levels predicted a less impulsive test performance [4].

These results from Dettmer et al. [4] add to the growing body of literature that suggests a relationship between milk cortisol levels and infant phenotype. Moreover, this is the first study to demonstrate downstream cognitive effects due to natural variation in milk composition [4]. As predicted, the message sent by milk cortisol was persistent and not only relevant at the time it was sent. The small sample size in this study (34 infants, only 12 of which were cognitively assessed) limits the ability to speak about sex differences in response to milk cortisol, as observed by Hinde et al. [1], or to identify windows of sensitivity for milk signals. However, the results provide an excellent point of departure for designing future studies intent on capturing these complex relationships between milk signals and infant responses.

Don’t Stress Out

One of the most interesting findings of these research studies on milk cortisol composition and infant development has nothing to do with infants at all but rather their mothers. Cortisol is probably best known as the stress hormone. Human mothers may be concerned how their own response to stressors (from being a new mother, to living in a violent environment) may end up having a negative effect on their developing fetus or breastfeeding infant. But Dettmer et al. [4] found no relationship between milk cortisol and cortisol from maternal hair samples (which is associated with maternal cortisol levels). Indeed, Hinde et al. [1] found that maternal rank (a proxy for stress) was also not predictive of milk cortisol. Mothers are not passing their stress on to their offspring; higher milk cortisol is not necessarily associated with chronically stressed mothers. Rather, the association of both maternal experience (e.g., first-time mothers) and maternal body mass with milk cortisol supports the argument that cortisol signals for conserving energy and not necessarily for the development of anxiety. This should reduce the stress for breastfeeding mothers (or those who intend to do so in the future). Cortisol is supposed to be in milk.
Health scientists have shown that bone density of humans peaks about age 30 and then slowly declines with age, eventually leading to increased risk of osteoporosis, characterized by reduced bone density, which in turn causes greater risk of fractures late in life [9]. This is a major health issue affecting many elderly people as fractures are often an invitation to opportunistic infections causing more serious life-threatening challenges. The scientists unequivocally demonstrated that an adequate and well-balanced...
diet helps to slow this inevitable onslaught on the elderly [9]. However, Cooper and colleagues comment that the most effective delaying tactic may be the attainment of a higher bone density much earlier in adult life and even during childhood and fetal development [1-3]. They suggest that with a higher bone density starting point, the unrelenting age-related decline in bone density after 30 years of age will not reach the critical threshold for increased risk of bone fractures until a later age in the elderly. Increased bone density of children and young adults is therefore the key to good bone health much later in life.

**Vitamin K<sub>2</sub> Contributes to Bone Health**

There is considerable evidence that vitamin K<sub>2</sub> contributes to bone health in adults [10, 11], although Vermeer and colleagues noted that there were few investigations in children [12]. For example, O’Connor and colleagues demonstrated that vitamin K<sub>2</sub> status in a small population of healthy Danish girls aged 11-12 years was associated with increased bone mineral content [13, 14], while the Vermeer group concluded that improved vitamin K<sub>2</sub> status in healthy children over a two-year period was associated with a marked increase in bone mineral density [14].

Scientists involved in several investigations demonstrated that vitamin K<sub>2</sub>, and to a lesser extent vitamin K<sub>1</sub>, are essential for making a specific type of molecular modification on a protein named osteocalcin, which is secreted from bone-forming cells or osteoblasts [15, 16]. The molecular modification allows this protein to bind calcium in bone and thereby become an integral component of bone. Other scientists noted that in the example of postmenopausal women, there was an association between unmodified osteocalcin in blood and increased risk of bone fracture [17]. Doctors now routinely use the concentration of unmodified osteocalcin in blood as a marker for bone loss or resorption occurring in various adult diseases such as osteoporosis.

**Confounding Health Recommendations**

Vermeer and colleagues highlighted three confounding health authority issues relating to the recommended Adequate Intake of vitamin K. This research group is based in The Netherlands at Maastricht University and has published extensively, including scientific papers in the *British Journal of Nutrition*, the *European Journal of Nutrition*, and the journal of *Food and Function* [12, 15, 18]. First, health authorities recommend an Adequate Intake of vitamin K based on the level required for optimal blood coagulation. However, Vermeer and colleagues concluded that this level is insufficient for optimal vitamin K-dependent modification of osteocalcin and therefore, the recommendation potentially compromises optimal bone health. Secondly, they noted that the recommended Adequate Intake often applies to the total vitamin K level and may not reflect the functional and bioavailability (stability and ease of absorption into the body) differences between vitamin K<sub>1</sub> and vitamin K<sub>2</sub> [18]. Thirdly, the group highlighted paucity of information on the vitamin K status of children, who experience rapid bone growth, unlike adults, and may therefore have different requirements.

**“Healthy” Children May Be Deficient in Vitamin K<sub>2</sub>**

In their initial investigation, Vermeer and colleagues examined the effect of a modest vitamin K<sub>2</sub> dietary supplementation for a period of eight weeks on 28 healthy children aged six to ten years and compared them with a similarly sized un-supplemented control group [18]. The investigators measured the vitamin K-dependent modification of osteocalcin in the children’s blood. They reported that during the testing period, the blood from the vitamin K<sub>2</sub>-supplemented group of children had increased vitamin K<sub>2</sub>, decreased unmodified osteocalcin and increased modified osteocalcin levels compared with the control group. The investigators implied that vitamin K<sub>2</sub> caused greater incorporation of modified osteocalcin into bone. There were no changes in other bone health markers or blood coagulation activity in the vitamin K<sub>2</sub>-supplemented children.

In a second and larger investigation, the Vermeer group measured the vitamin K status in the blood of
896 healthy children and adults by measuring unmodified levels of osteocalcin [12]. Surprisingly, the children had a six-fold higher level of unmodified osteocalcin in their blood compared with adults and the adult level was largely unaffected by age.

Implications

The Vermeer group demonstrated that “healthy” children are likely to be markedly deficient in vitamin K [12, 18]. The investigators speculated that the lack of optimization of bone growth of children caused by this deficiency may, in later life, increase the risks of osteoporosis (low bone density) and associated bone fractures. They commented that high bone growth rates of children compared with the process of general maintenance of bone mass in adults may be responsible for the striking differences in their unmodified osteocalcin levels. The good news provided by the Vermeer group was that moderate dietary vitamin K supplementation of children and adults decreased the level of unmodified osteocalcin in their blood, implying that there was greater incorporation of modified osteocalcin into bone [18]. Thus, vitamin K supplementation may improve bone health in the young, an outcome that could pay handsome rewards much later in life. The latter expectation has not been formally proven, therefore, Vermeer and colleagues suggested the need for a large population study to establish whether low dietary vitamin K status in children was directly associated with bone density and fracture rates of the elderly [12, 18]. This type of investigation could take some time.

Perhaps past generations had it right. Their children regularly drank full cream milk rich in vitamin K, and calcium, and they exercised in vitamin D enriching sunshine much more than many of today’s often sedentary children. These solid foundations for bone formation may need to be rebuilt in the current generation. Recently, investigators also demonstrated that vitamin K is important for cardiovascular health and metabolism [5, 12, 15, 16], indicating that this vitamin may have complex and central roles in healthy aging. Time for a glass of milk.

All these vitamins aren’t to keep death at bay, they’re to keep deterioration at bay—Jeanne Moreau.


Contributed by
Dr. Ross Tellam (AM)
Research Scientist
Brisbane, Australia
Could Cheese Be the Answer to the French Paradox?

- The “French Paradox” describes the French diet, marked by significant quantities of saturated fats from cheese and alcohol from wine, which does not seem to have resulted in a higher mortality rate due to coronary heart disease or cardiovascular disease in the French population.
- Previous studies often focused on the antioxidant properties of components in red wine as a solution to the French Paradox.
- More recent studies find that milk components in cheese stimulate the production of an intestinal enzyme called alkaline phosphatase, which reduces gut and systemic inflammation and may improve cardiovascular health.

There may be nothing more iconically French than the image of a luscious cheese board and bottle of aged red wine. But for those of us living in a hyper-health-conscious culture, constantly bombarded with diet and nutrition trends and fads, it would be difficult to see a wedge of Camembert and glass of Pinot Noir as anything other than an indulgence. And certainly not as a “healthy” choice. Yet decades of research show that a French diet, including a high intake of saturated fat from cheese and alcohol from wine, may lower incidence of mortality from coronary heart disease (CHD). Though researchers have long looked to the beneficial properties of antioxidants in red wine to explain this French Paradox, the benefits may actually lie with components in cheese. In particular, a recent study found that a potent intestinal enzyme, alkaline phosphatase (IAP), may be stimulated by dairy products to fight cardiovascular disease (CVD) [1].

The French Paradox was first formally identified in 1992 when cardiologists Serge Renaud and Michel De Lorgeril [2] posited that the high intake of saturated fat common in the French diet was mitigated by the average level of alcohol consumption (20–30 per day). They noted that alcohol inhibited platelet aggregation, which in turn reduced the risk of CHD. Subsequent studies supported this “red wine hypothesis” and looked further into the polyphenols, especially resveratrol, that may protect cardiovascular function and health [3-5]. Benefits of moderate consumption of red wine have been correlated to reduced CVD, type 2 diabetes, and possibly neurodegenerative diseases [4]. So by the end of the twentieth century, it seemed that the answer to the French Paradox could be found in the biochemicals of wine, and specifically in the properties of those biochemicals as they could minimize or even block the potentially negative effects of high consumption of cheese.

Yet Ivan M. Petyaev and Yuriy K. Bashmakov, both medical doctors, offered a more comprehensive solution to the French Paradox in 2012, when they noted that “multiple other factors seem to be implemented in the French paradox” [6]. “These include smaller portion size, lower number of eating occasions, regular gardening and exercise and higher intake of fruit and vegetables rich in flavonoids, phytosterols and dietary fiber.” But also, and perhaps more significantly, they argue that the French consumption of cheese, “especially of molded varieties,” may be the key to the so-called paradox. The ripening process of Roquefort, Camembert, Gorgonzola, and other varieties of molded cheeses is characterized by a more intense proteolysis than that of non-molded cheeses such as Gouda and Cheddar [6]. Ripened molded cheese contains andrastins A-D, which inhibit the cholesterol biosynthesizing enzyme farnesyltransferase; andrastin A may also have anti-cancer potential as an antitumoral compound [7]. Petyaev and Bashmakov note that it is through the extended ripening period of molded cheeses that the most advantageous properties appear, including the anti-inflammatory and probiotic benefits to humans [6].

Most recently Jean-Paul Lallès, biochemist and Director of Research at the French National Institute for Agricultural Research in Rennes, France, further supported the “dairy products” hypothesis by suggesting that milk components, including casein, calcium, and lactose, stimulate production of the IAP [1]. IAP impacts processes in the intestine as well as beyond it and is notable for its anti-inflammatory action. As inflammation in the body is reduced, metabolism and cardiovascular health may improve. Studies involving exogenous administration of IAP show that it is effective in treating inflammation of the bowel, as well as acute or chronic kidney disease in humans and animal models [1]. Lalles notes that “both experimental and clinical observations support the notion that IAP is a key anti-inflammatory enzyme able to control both gut and systemic inflammation.”
Alkaline phosphatase is also present in non-human milk, but it is inactivated during pasteurization. “Milk-AP has long been the ‘gold standard’ marker for pasteurization,” notes Lalles, “due to its heat-sensitivity greater than that of most such pathogens” [1]. Finally, and perhaps not insignificantly, low concentrations of alcohol stimulate IAP, which may further support the role of alkaline phosphatase in the French Paradox.

When it comes to lifestyle choices and nutrition, we have often looked for particular diets and profiles that offer the best outcomes for longevity and health. The seemingly indulgent diet of wine and cheese produced a kind of nutritional mystery long dubbed the French Paradox. But as recent research continues to show, the role of dairy in cardiovascular health is significant, and for the French, the answer may lie within the cheese.


Contributed by
Dr. Katie Rodger
Managing Editor

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