REBUTTAL TO THE FDA ARTICLE
“Raw Milk Misconceptions and the Danger of Raw Milk Consumption”
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SUMMARY

The FDA recently published an article, “Raw Milk Misconceptions and the Danger of Raw Milk Consumption,” (posted at www.fda.gov/Food/FoodSafety/Product-SpecificInformation/MilkSafety/ConsumerInformationAboutMilkSafety/ucm247991.htm) in which it argued that most claims made in favor of raw milk are false, and that raw milk is unsafe to drink because it may contain pathogens and contribute to foodborne illness.[1] The FDA categorically rejects any claims that raw milk may reduce the risk of certain health problems even though its potential to do so is currently an area of active research. It claims that pasteurized milk is just as nutritious as raw milk, but ignores changes that occur to the biological activity of milk nutrients during pasteurization. Finally, it claims that raw milk is unsafe because it may contain pathogens even though pasteurized milk is by the same logic also unsafe because it also may contain pathogens.

Observational evidence suggests that raw milk may improve lactose tolerance, prevent the development of asthma and allergies, and may be more digestible than pasteurized milk for people who have difficulty digesting fat. Pasteurization decreases the content of iron, copper, manganese, and iodine in milk, and may diminish the bioavailability of calcium and phosphorus. It causes major losses of biological activity for vitamin C and folate, substantial losses for vitamin B_6, and may have similar effects for other vitamins. The available data for the prevalence of foodborne illnesses associated with specific foods are extremely poor in quality and rich in bias. Even taking these data at face value, however, raw milk may have the potential to protect millions of people from asthma and prevent hundreds of asthma-related deaths without causing major increases in the total burden of foodborne illness. These predictions need to be evaluated with high-quality, clinical research, which we will believe will proceed at a rapid pace only if the government abandons its antagonism to the producers and consumers of raw milk and instead encourages high quality scientific research and freedom of choice for consumers.

We evaluate each issue individually below. In general, we follow the sequence and format of the FDA document, occasionally modifying it to eliminate redundancy.

Does Raw Milk Improve Lactose Tolerance?

The FDA states categorically that “raw milk does not cure lactose intolerance,” but neither the references nor the commentary associated with this assertion are sufficient to support it. The commentary in this section states that raw milk contains lactose, that the lactase enzyme present in raw milk is produced by organisms that are not “probiotic,” and that the microbial profile of raw milk differs from that of yogurt, all of which are largely irrelevant to the question at hand. The lactase enzyme present in raw milk will digest lactose regardless of whether the FDA considers the bacteria that produce the enzyme to be “probiotic” and regardless of whether they are the same bacteria that are found in yogurt. This type of mechanistic speculation, however, misses the point. We cannot reject an argument about what happens when living human beings drink raw milk by discussing what is or is not in the milk.

In order to determine whether raw milk improves lactose tolerance, it is necessary to perform a randomized, controlled, clinical trial testing this hypothesis. Christopher Gardner and colleagues at the Stanford School of Medicine recently conducted such a trial,[2] but the results are awaiting publication and have not yet been publicly released. The web page for this study states that "many or most of [the claims of raw milk enthusiasts] are anecdotal and remain untested, including the claim that lactose intolerant adults can enjoy raw milk with minimal to no symptoms." In a survey of over 700 households in the Midwest participating in raw milk cowshare programs, we found that six percent of participating individuals had been diagnosed with lactose intolerance, and that over eighty percent of these individuals no longer suffer from symptoms after switching to raw milk.[3] This is an impressive piece of observational evidence that extends beyond isolated anecdotes and clearly justifies more extensive research, and we enthusiastically await the results of the Stanford trial.

The FDA states that people who are lactose intolerant lack the enzyme lactase, but this is an oversimplification. If we understand the complexity of lactose intolerance, we can more easily appreciate the many ways in which raw milk could play a role in reducing its symptoms. The discussion that follows is based on an extensive review published in 2005.[4]

Most of the world's population and about thirty percent of Americans have a condition called *hypolactasia*, the technical term for a decreased activity of the enzyme lactase. In rare cases, this results from a genetic defect that causes a complete loss of the enzyme, but in most cases it results from a gradual decrease in the activity of the enzyme after weaning. Most individuals with hypolactasia still have some lactase activity, ranging from five to ten percent of maximal levels in Chinese and Japanese adults to thirty to fifty percent in European adults. The loss of lactase activity is often heritable, but it can also be caused by a variety of intestinal disorders. The exact reason for the decline after weaning is unknown, but it could involve a decrease in the production of the appropriate message from the gene, a decrease in the production of the enzyme from the message, impaired processing of the enzyme once it has been produced, the presence of enzyme inhibitors in the intestine, and the loss of specific lactase-producing cells from the intestinal lining. These authors consider the loss of lactase-producing cells from the intestinal lining to be the most common reason for hypolactasia.

Hypolactasia is an important part of lactose intolerance, but they are not the same thing. Lactose tolerance is determined not only by the ability to digest lactose, but also by the ability to efficiently absorb the glucose and galactose that result from this process and to prevent any of these sugars from being used by bacteria in the colon for the production of noxious gases, toxins, and other byproducts.

There are thus are a variety of mechanisms by which a dietary treatment such as raw milk could improve lactose tolerance besides providing preformed lactase enzyme within the milk itself. These include increasing production of the enzyme, increasing the activity of the enzyme once it has already been produced, increasing clearance of glucose and galactose from the intestine, or altering the gut flora toward a profile less likely to produce noxious substances either from lactose or from its metabolic byproducts. To give just one example of how raw milk might affect some of these parameters, it is an abundant source of undenatured lactoferrin, which stimulates the growth of lactase-producing cells, their expression of the lactase gene, and their lactase activity,[5] and inhibits the growth of pathogenic bacteria while encouraging the growth of probiotic bifidobacteria and lactobacilli.[6]

Discussing whether raw milk "cures" lactose tolerance is misleading because all individuals will have some limit to their tolerance of lactose. The question is whether raw milk improves this tolerance sufficiently in some people to allow them to consume the quantity of milk they desire without discomfort or undesirable health effects. The results of our survey suggest that raw milk's apparent ability to improve lactose tolerance is a major reason that people switch to it, and we look forward to the issue being further examined in clinical research.

Does Raw Milk Prevent or Treat Asthma?

As the FDA acknowledges, the PARSIFAL study found that children who drink "farm milk" are less likely to suffer from asthma and rhinoconunctivitis, a condition that causes a stuffed, runny, or itchy nose, post-nasal drip, and red, itchy eyes.[7] The FDA correctly notes that this study was not designed to distinguish between the effects of raw and boiled farm milk, and thus claims that the study has been "misused by raw milk advocates ever since it was published." The authors, however, considered the fact that much of the "farm milk" was raw and that the milk tended to be from grass-fed cows to provide the two most likely explanations for the reduced risk of asthma and rhinoconjunctivitis associated with drinking it.

The PARSIFAL study, moreover, is not the only relevant study to look at. The Study of Asthma and Allergy in Shropshire found a lower incidence of asthma among children who frequently drink raw milk, which reached borderline statistical significance ($P=0.06$),[8] meaning we can be 94 percent confident that the association was not a result of chance. The much larger and more extensive GABRIELA study found that asthma and allergies were inversely associated with raw farm milk but not boiled farm milk.[9] Thus, studies that have been designed to distinguish between raw and pasteurized or boiled milk have found a reduced risk of asthma associated specifically with raw milk.

The investigators of the GABRIELA study visited the farms and took milk samples. Compared to its boiled counterpart, raw farm milk was higher in total bacteria, lactoferrin, IgG antibodies, whey proteins, and TGF-□2, a compound that is known to suppress the inappropriate immune responses that underlie autoimmune and allergic conditions. Statistically, only the whey proteins were associated with a reduced risk of asthma.

The association between whey proteins and a reduced risk of asthma may relate to the ability of the undenatured whey proteins found in raw milk to increase our body's ability to make glutathione, which is the master antioxidant and detoxifier of the cell as well as a major regulator of protein function.[10] Glutathione is found in unusually high concentrations in the lungs, where it suppresses inflammation and acts as a natural bronchodilator, decreasing resistance in the airway and increasing air flow to the lungs, but glutathione status in the lungs of asthma patients is seriously impaired.[11] Undenatured whey proteins contain unique amino acid structures called glutamyl-cysteine from which our cells readily synthesize glutathione.[10] Studies wherein investigators have purchased milk from different sources have shown that high-temperature short-time (HTST) pasteurized milk contains thirty percent less total whey protein than raw milk,[12] and studies wherein investigators have applied different heat treatments to milk from the same source have shown that the remaining whey protein contains a lower proportion of the unique glutathione-boosting glutamyl-cysteine bonds, due to the selective destruction of beta-lactoglobulin and bovine serum albumin.[13, 14] Taken together, these studies suggest that pasteurization destroys about half of the glutathione-boosting potential initially present in raw milk.

Although clinical research would be needed to show definitively that raw milk prevents or treats asthma, current evidence supports this hypothesis and lends credence to the personal experiences of the great many people who have found raw milk to be helpful in improving asthmatic symptoms either in themselves or in their children.

Does Raw Milk Prevent or Treat Allergies?

The FDA cites a double-blind, randomized, controlled clinical trial[15] in support of its claim that "raw milk and pasteurized milk do not differ" in their ability to provoke allergic symptoms and that "pasteurization does not change the allergenicity of milk proteins," but these conclusions conflict both with the data from this trial and with the conclusions of its investigators. The study included only five children, all of whom had an established milk allergy, and they were given each type of milk only once. With such a small number of participants and the lack of multiple challenges with each type of milk, the study clearly lacked the statistical power needed to detect statistically significant differences in the magnitude of allergic reactions. The authors nevertheless observed that when the children drank raw milk, their allergic reactions tended to occur with a later onset and for a shorter duration, and when they were given skin prick tests the raw milk resulted in less severe skin reactions. Although these differences were not statistically significant because of the limited power of the study, the authors appropriately concluded that "a tendency towards a lower threshold of reaction and larger skin reactions induced by the processed milk preparations might indicate an increased ability of pasteurized and homogenized/pasteurized milk to evoke allergy reactions in patients allergic to milk."

While this study clearly shows that it is possible for someone to have an allergic reaction to raw milk, it raises the possibility that there may be many people with a milder form of milk allergy that could tolerate raw but not pasteurized milk. It also supports the basic principle that pasteurization increases the allergenicity of milk and thus raises the question of whether people who drink raw milk from early childhood are less likely to develop an allergic reaction to milk in the first place.

Homogenization may be even more important in this respect. Indeed, the FDA cites a 2006 review in another section in support of its claim that homogenization has no impact on the nutritional quality of milk fat, but the review cited evidence that the homogenization of milk renders it capable of causing inflammatory reactions and anaphylactic shock in sensitized mice.[16] The authors suggested that this could be because the allergenic parts of milk proteins are usually tucked away inside large protein complexes in raw milk, but homogenization opens them up and causes them to stick to the milk fat. They were only able to find evidence that some ten percent of children with milk allergy could tolerate unhomogenized milk, but they suggested that "differences of primary immunization could be much more important in infants." To phrase their suggestion another way, most people with an established milk allergy cannot tolerate unhomogenized milk, but feeding unhomogenized milk to infants may be an effective way to prevent them from developing milk allergies to begin with.

When considering whether raw milk protects against allergies, however, we should take a much broader view and consider whether it protects against the development of allergies in general, not just allergies to milk. Several epidemiological studies suggest that this may indeed be the case:

- A study that surveyed just fewer than 1,000 children living in Crete found that among those without any exposure to farms, those who drank raw milk were about 70 percent less likely to test positive for allergies to cats, grass, mites, or olive blossoms using a skin prick test. This association was not found among rural children, probably because the incidence of allergies was already so low in these children to begin with.[17]
- A study of 320 adults living in Northern Germany found that among the two-thirds of the participants who did not visit farms in early life, those who had been drinking raw milk at the age of six years were 43 percent less likely to have IgE antibodies in their blood against pollen, animal dander, and mites. Among the third who did visit farms early in life, those who drank raw milk were 65 percent less likely to test positive for these allergies. The association only reached statistical significance in those who had visited farms, probably because the study was so small.[18]
- Among just under 300 children living in New Zealand, those who drank raw milk in the first two years of life were sixty percent less likely to develop allergic eczema and seventy percent less likely to develop allergic rhinitis, while there was no association between these symptoms and the consumption of pasteurized milk.[19]
- The Study of Asthma and Allergy in Shropshire found that among over 800 children, those who drank raw milk were seventy percent less likely to test positive for allergies to animal dander, grasses, or mites using a skin prick test. They also had on average sixty percent less total IgE in their blood, which is the type of antibody that contributes to allergic reactions Raw milk was the only food in the questionnaire that was associated with a reduced risk of allergies regardless of whether the children were exposed to a farming environment.[8]

These studies differ in how they defined the evidence for allergies and in their conclusions about whether the lower incidence of allergies among children drinking raw milk depends on the type of environment in which the children grew up. They nevertheless agree that this lower incidence exists. A recent review on the topic suggested that the rearrangement of protein complexes that occurs during homogenization, the altered fatty acid profile that occurs in milk from grain-fed cows, and the destruction of bacteria and whey proteins that occurs during pasteurization could all contribute to the destruction of the allergy-protective effects initially possessed by grass-fed raw milk.[20] Clinical research is necessary to confirm these protective effects and to elucidate the mechanisms behind them, but it is unsurprising to us that many parents do not wish to wait decades for this research to be published but wish rather to provide their growing children with the milk they believe is healthiest while their children's immune systems are still maturing.

Does Raw Milk Contain Probiotic Bacteria?

The FDA document claims that raw milk cannot contain probiotic bacteria because milk contains bacteria from cows, while bacteria must originate from humans in order to be considered probiotic. This claim contradicts the definition of probiotic given by the World Health Organization (WHO), which states that "it is the specificity of the action, not the source of the microorganism that is important."[21] Researchers affiliated with the National Research Council of Italy recently isolated lactobacilli from raw milk that were capable of surviving conditions meant to mimic human digestion.[22] They referred to these bacteria as "potentially probiotic," and are currently investigating their functional properties in order to determine whether they could have positive effects on human health.

The FDA document further claims that bacteria are only present in raw milk to the extent it has been contaminated by manure, infected udders, milking equipment, or other environmental sources. This reflects the outdated belief that mammalian milk is naturally sterile. Human milk collected from healthy mothers using aseptic techniques contains probiotic bacteria, including lactobaciili and bifidobacteria,[23] and recent evidence suggests that the immune system purposefully transports these bacteria from the mother's intestine to colonize her mammary gland.[24] This transport also occurs in mice,[24] and probably occurs in cows as well. Cows and other mammals likely transport intestinal bacteria directly into milk to serve as probiotics for their young.

Is Raw Milk A Particularly Dangerous Source of *E. coli* O157:H7?

The FDA cites several outbreaks of *E. coli* O157:H7 traced to raw milk over the course of five years in which fewer than fifty people became ill, and concludes from this that "raw milk is not an immune system building food and is particularly unsafe for children." Since the data cited in this section have nothing to do with whether raw milk builds the immune system or whether children are more likely to develop food poisoning from drinking raw milk than adults are, we will instead address the question of whether raw milk is a particularly dangerous source of *E. coli* O157:H7.

Elsewhere, the FDA estimated that between 1996 and 2005, fresh produce was responsible for over 8,000 *E. coli* O157:H7 infections. Eggs were responsible for over 6,500; processed foods for over 3,000; and sprouts for over 1,500.[25] According to the FDA, then, these foods were altogether associated with about 1,700 cases of *E. coli* O157:H7 per year, whereas raw milk was associated with about ten. The CDC recently estimated that three percent of the population consumes raw milk.[26] Even if we take these associations at face value and assume that the proportion of the population drinking raw milk would grow to include everyone and that no advances would be made in preventing the contamination of milk, we could expect to trace about three hundred incidents of *E. coli* O157:H7 infection to raw milk per year. If the consumption of these other foods were to stay the same, they would still account for over five times as many illnesses as raw milk, and fresh produce alone would still account for three times as many illnesses as raw milk.

In a previous publication, we analyzed the literature associating raw milk with foodborne illness and concluded that this literature incorporates a systematic bias against raw milk.[27] These figures are thus likely to substantially overestimate the contribution raw milk would make to *E. coli* O157:H7 outbreaks. The poor quality of foodborne illness data is discussed in more detail below in the section entitled, "What Is the Potential Public Health Impact of Raw Milk?" Even taking these figures at face value, however, and assuming a worst-case scenario, raw milk cannot be construed as a "particularly dangerous" source of *E. coli* O157:H7, especially if we are to continue encouraging Americans to increase their consumption of fresh fruits and vegetables, from which they are – at least according to the FDA's data – more likely to contract this illness than from raw milk.

Does Pasteurization Damage the IgG Antibodies Present in Raw Milk?

The FDA cites a study showing that pasteurization causes IgG antibodies in milk to aggregate and bind to the receptors of human immune cells,[28] and claims that that the author of this study "hypothesized that the heat-aggregated immunoglobulins may actually have better immunological function."

We agree that this study showed that heat treatment caused some ten to sixteen percent of the IgG to aggregate and that this allowed interactions with human immune receptors that would not occur with IgG from raw milk, but we find it puzzling that the FDA claims the author had hypothesized this to constitute "better immunological function" for two reasons. First, the author never used this phrase in the paper. In fact, he published a second paper with several colleagues showing that these heat-aggregated antibodies actually suppress the ability of human immune cells to manufacture their own antibodies.[29] This would seem to suggest poorer rather than better immunological function, but the authors simply concluded that "the physiologic significance of these findings is not yet known." The second reason we find the suggestion puzzling is because another author proposed in the *Lancet* that these heat-aggregated antibodies might contribute to the development of allergies.[30] The true effects of heat-aggregated antibodies are indeed unknown, but neither immunosuppression nor allergies constitute "better immunological function." Pasteurization clearly alters the immunological effects of raw milk in ways that are more likely to be harmful than beneficial.

Does Raw Milk Contain Enzymes That Facilitate Protein Digestion?

The FDA states that there are no protein-digesting enzymes (proteases) in cow milk that contribute to proper digestion of milk protein. We agree that cow milk does not appear at this time to contain factors that make important contributions to protein digestion, but some of the proteases that are destroyed by pasteurization may contribute to immune function.

The description of milk proteases that follows is derived from the 2003 textbook *Advanced Dairy Chemistry*.[31] The main protease in cow milk is plasmin. Plasmin originates in blood, which contains almost 700 times as much plasmin as milk. This suggests that the mammary gland does not actively and purposefully transport plasmin into milk. Plasmin activity in milk increases during infection of the udders, suggesting that the activity of this enzyme in milk is meant to be low. Plasmin can contribute to the digestion of milk protein, but pasteurization activates the enzyme from its precursor rather than destroying it. Ultra-high temperature (UHT) treatment, by contrast, inactivates much of the enzyme. A substantial portion of the protein-digesting activity of milk comes from other proteases produced both by the mammary gland and by white blood cells. Limited evidence suggests that at least one of these proteases, cathepsin D, may support the immune system of the newborn. Researchers who studied the effect of heat treatment on cathepsin D used a mathematical model to estimate that HTST pasteurization would destroy 92 percent of it.[32]

Williamson found that pasteurization or boiling of human milk did not have any effect on the absorption of nitrogen in preterm infants, suggesting that heat treatment does not affect the digestibility of milk protein.[33] It would be a mistake to conclude from this, however, that pasteurization does not destroy biologically important proteases since some of the proteases destroyed such as cathepsin D may play other important biological functions.

Does Raw Milk Contain Enzymes That Facilitate Fat Digestion?

High-quality studies have shown that pasteurization decreases fat absorption from human milk in preterm infants.[33, 34] This effect is most likely to be important in newborns, especially those born prematurely, and in children or adults who suffer from poor digestion of dietary fat. The FDA claims that this effect results entirely from the destruction of bile salt-stimulated lipase, a fat-digesting enzyme that is present in human milk but not in cow milk. These studies provided no evidence for this assertion, however, and it remains nothing more than an assumption.

Both human and cow milk contain another fat-digesting enzyme called lipoprotein lipase (LPL). The FDA cites a chapter from the 2003 textbook *Advanced Dairy Chemistry* for its claim that "there is no physiological role of LPL in milk lipid digestion or utilization," but this categorical rejection of any possible role for LPL in the digestion of milk fat directly contradicts the conclusions of the authors of that very chapter. Although they stated that LPL has "to date no *demonstrated* role for milk utilization by the offspring," (our italics), they nevertheless suggested numerous possible roles it might play, and concluded that it was extremely unlikely to not play any role at all.[35]

The milk-producing cells of the mammary glands manufacture LPL and secrete it into milk at the same rate they secrete other proteins into milk. The LPL within these cells is found primarily in the milk-secreting vesicles. The authors of the *Advanced Dairy Chemistry* chapter concluded that "it is hard to reconcile the data on synthesis and secretion of LPL with the view that its appearance in milk is a mistake, and that the enzyme has no useful purpose in milk." They went on to outline several possible functions of the enzyme:

- It may attach to the intestinal wall and help bind milk fat globules to the intestinal lining in order to facilitate their digestion.
- It may help transfer cholesterol and fat-soluble vitamins into the intestinal cells.
- It may help pre-digest milk fat globules to make them more accessible to the lipase enzymes produced by the pancreas.
- In human milk, LPL generates fatty acids that "have a powerful antiparasitic function," and LPL may play the same role in cow milk.

Pasteurization destroys 97 percent of the LPL initially contained in raw milk.[36] The FDA claims that "it is desirable to completely inactivate LPL since any residual LPL activity can cause the development of rancid off-flavor, a serious quality defect in milk." Pasteurization certainly comes close to completely inactivating LPL, but it is not so obvious why we should sacrifice an enzyme that may play important roles in digestion and protect against parasites simply to avoid rancid off-flavor, when that off-flavor can be just as easily prevented by avoiding other aspects of modern processing. According to the aforementioned chapter of *Advanced Dairy Chemistry,*[35] this off-flavor develops when certain processing methods such as homogenization cause the enzyme to become activated within the milk, leading to lipolysis (breakdown of fat) before the milk is consumed:

> If the lipase were not destroyed by prior pasteurization, the conventional homogenization of the milk would result in rapid lipolysis and make the milk unusable. Induced lipolysis was not a serious problem when milk was collected by hand milking and transported to the dairy the same day. It has become more of a problem with the modern pipeline milking machines and holding of the milk for several days at the farms before transportation to a central dairy.

Pasteurization is thus required to make the milk safe for homogenization, but an enzyme that may promote proper digestion of the milk and protect against parasites is sacrificed in the process. Raw milk contains this enzyme in tact but because it is not homogenized or otherwise heavily processed, it also possesses a superior flavor.

Is Raw Milk Nutritionally Superior to Pasteurized Milk?

Pasteurization and homogenization compromise some aspects of milk nutrition but not others. We will therefore address each component of milk separately, following the format of the FDA document.

Milk Proteins

The FDA states that pasteurization does not compromise the nutritional quality of milk protein. As discussed in the section above, "Does Raw Milk Contain Enzymes That Facilitate Protein Digestion?" evidence from preterm infants suggests that we digest and absorb just as much protein from pasteurized or boiled milk as from raw milk. Pasteurization does destroy the biological activity of certain specific proteins, however, and these effects are discussed in the relevant sections below.

Milk Fat and the Effect of Homogenization

The FDA quotes a 2006 review as concluding that *"*regarding human nutrition, homogenized milk seems more digestible than untreated milk," but this quote never occurs in that review.[16] The authors noted that homogenized milk is more digestible than unhomogenized milk for subjects suffering from intestinal disease but that raw human milk is more digestible than homogenized formula for preterm infants. After reviewing more extensive and similarly conflicting data from animal models, the authors concluded that the "long-term effects" of the differences between the ways in which these animals digest milk fat globules from homogenized and unhomogenized milk "remain to be elucidated in humans." The evidence is thus insufficient to make any general statement about the effect of homogenization on milk fat digestibility, and it is disingenuous to suggest that the authors favored the belief that it increases digestibility when in fact they avoided making any clear conclusion at all.

We should note that the leading explanation for why homogenized milk would be more easily digested in the subjects with intestinal disease is that the fat-digesting enzyme produced by the stomach, gastric lipase, may be more able to digest the smaller milk fat globules. The normal role of this enzyme, however, is simply to initiate the breakdown of these globules so that the lipase produced by the pancreas can finish digesting them in the intestine. As discussed in the section above, "Does Raw Milk Contain Enzymes That Facilitate Fat Digestion?" the lipoprotein lipase (LPL) present in raw milk may fulfill the same pre-digestive role and may provide additional assistance to fat digestion within the intestine. Homogenization may thus make pasteurized milk more easily digestible for subjects with intestinal disease, but raw milk containing intact LPL may be the most digestible milk for most people overall.

Milk Minerals

The FDA claims that "there is no impact of pasteurization on milk mineral content," but the only study it cites in support of this claim that actually presents data for mineral content found that pasteurization led to a 15 percent loss of manganese, a 25 percent loss of copper, and a 35 percent loss of iron.[37] Additionally, although at least one study found that pasteurization had no effect on the iodine content of milk, at least three studies have shown that it incurs a twenty percent loss in this nutrient.[38]

The FDA claims that pasteurization has no effect on the utilization of minerals from milk, but the scientific literature is divided on this point. The most convincing evidence for the FDA's position is a study by Williamson and colleagues showing that neither classic pasteurization nor boiling affect calcium absorption from human milk in preterm infants,[33] and a study by Weeks and King showing that neither HTST pasteurization nor UHT treatment affect calcium absorption or bone mineralization in rats.[39] The findings of these studies conflict with the findings of Kramer and colleagues who showed in 1929 that classic pasteurization impaired the retention of calcium and phosphorus in adults and that drying milk impaired the retention of these minerals in both children and adults.[40] They did not test the effect of classic pasteurization in children.

One compelling explanation that could reconcile the results of all three studies is that pasteurization impairs the bioavailability of vitamin D, which is needed for proper utilization of calcium and phosphorus. Kramer and colleagues showed that raw milk from cows raised inside barns produced results just as poor as those produced by dried milk. The cows were all eating identical diets regardless of whether they were raised indoors or outdoors, suggesting that vitamin D obtained from sunshine is what made the outdoor raw milk superior. Modern humans generally spend most of their time indoors, so the mothers who provided the human milk for the Williamson study probably produced milk that was just as deficient in vitamin D as the milk from the indoor cows used in the Kramer study. Weeks and King did not describe how the milk used in their study was produced, but since it was published in 1985 the cows were very likely to have been raised indoors. If in fact pasteurization impairs mineral utilization indirectly by impairing the utilization of vitamin D, then studies using milk that is already poor in this vitamin would clearly be expected to show that there is no effect of pasteurization. This finding would simply reflect the poor quality of the raw milk used and would in no way detract from the nutritional superiority of raw milk from cows raised on pasture.

Milk primarily contains vitamin D as the semi-activated form, called 25-hydoxyvitamin D or calcidiol, and to a lesser extent as the parent form, vitamin D, or as the fully activated form, called 1,25-dihydroxyvitamin D or calcitriol.[41] In fresh milk, these forms are all bound to vitamin D-binding protein or to the vitamin D receptor, which are present in the whey fraction of milk. It is only during subsequent storage that they gradually migrate into the cream.[41] Milk also contains a variety of other forms of vitamin D, including 24,25-dihydroxyvitamin D, 25,26-dihydroxyvitamin D, and vitamin D sulfate, but whether these forms have biological activity is controversial. Since the active forms of vitamin D are bound to specific proteins in the whey fraction, it is possible that these proteins contribute to the proper utilization of vitamin D and that they are damaged during the pasteurization process.

Vitamin D-binding protein is rich in the amino acid cysteine, and these cysteine residues contain sulfur atoms that can bind together to form disulfide bonds and thereby secure the three-dimensional shape of the protein. These bonds are usually vulnerable to heat and mechanical processing, so it is quite plausible that pasteurization could damage this protein, but to our knowledge no studies have specifically examined this question. Regardless of the exact explanation, however, the results of the Kramer study suggest that raising cows on open pasture improves the availability of calcium and phosphorus from the milk and that pasteurization destroys these benefits.

Milk Vitamins

The FDA states that pasteurization has little effect on the content of milk vitamins, except for vitamin C, which it dismisses as insignificant because of the low levels found in milk. The central flaw in this argument is that it focuses on the concentration of nutrients rather than their biological activity. Research that examines the biological activity of vitamins shows that raw milk does indeed make an important contribution to vitamin C status and that losses due to pasteurization are substantial not only for vitamin C but for other vitamins as well. We discuss these effects in more detail below.

Vitamin C

The FDA acknowledges that pasteurization destroys a substantial portion of the vitamin C in milk, but dismisses this as unimportant because “milk is an insignificant source for vitamin C.” One must wonder how it is, then, that raw milk prevents vitamin C deficiency in infants and young calves. A recent review in the journal *Pediatrics* remarked, “without doubt, the explosive increase of infantile scurvy during the latter part of 19th century coincided with the advent of usage of heated milks and proprietary foods.”[42] When the Hebrew Asylum in New York began using milk treated with classic pasteurization and eliminated orange juice from the diets of its infants, the infants began developing scurvy. Alfred Hess showed in the early twentieth century that raw milk, orange juice, and potatoes were each effective all on their own in preventing or treating scurvy, but pasteurized milk was not. These experiments clearly showed that raw milk is a valuable source of vitamin C.

Likewise, the textbook *Advanced Dairy Chemistry* notes that even though the vitamin C concentration is almost as low in human milk as it is in cow milk, "the plasma concentration of vitamin C in breast-fed infants [is] generally in the normal range, indicating that exclusively breast-fed infants are well protected against vitamin C deficiency."[43] The authors conclude from this that "breast-fed infants appear to be capable of maintaining a high plasma concentration of vitamin C independently of maternal and milk concentrations," but we suggest phrasing this in another way: the biological activity of vitamin C in raw milk is higher than a simple analysis of its vitamin C content would suggest.

The belief that the value of a particular nutrient from a given food can be determined simply by determining its concentration is a fallacy because it ignores not only the rate of the nutrient's absorption and utilization but also its interactions with the other nutrients within the food. For an illustrative example, vitamin E supplementation increases plasma and tissue levels of vitamin C,[44, 45] possibly by sparing it from oxidation, or by suppressing oxidative stress in the mitochondria, the part of the cell that contributes to the recycling of vitamin C.[46] When oxidants derived from poor metabolism or inflammation reach the blood, vitamin C is the first thing to start disappearing.[47] Iron, copper, and manganese are cofactors for enzymes that neutralize reactive oxygen species that would otherwise oxidize vitamin C, and glutathione helps recycle vitamin C once has been oxidized.[48] We reviewed the loss of these minerals that occurs during pasteurization above in this section under the subheading "Milk Minerals," and we reviewed the glutathione-boosting power of raw milk above in the section, "Does Raw Milk Prevent or Treat Asthma?" Anything within raw milk that protects against oxidative stress, infection, and inflammation or improves metabolism is likely to boost vitamin C status, which clearly emphasizes the need to assess its nutrient value by feeding it to live humans or animals and not simply by assessing the concentration of individual nutrients within it.

Folate

Although the concentration of folate in milk is relatively low, just as with vitamin C it is sufficient to prevent folate deficiency in human infants and other mammalian young. In the 1980s, researchers noticed that folate deficiency was extremely rare in breast-fed infants but was common in infants fed homemade cow milk formula, even though the loss of folate during the production of the formula was too small to account for this difference. Other researchers subsequently showed that milk contains a folate-binding protein that increases the uptake of folate by some fifty percent in upper intestinal cells, more than triples the uptake of folate by lower intestinal cells, and has twice as large an effect in the presence of calcium and chloride, which are present in milk. Pasteurization of goat milk destroyed these effects. Similarly, the investigators did not test folate-binding protein from raw cow milk, but when they isolated the protein from pasteurized cow milk it was inactive.[49] These experiments were performed in intestinal cells taken from rats. At about the same time, other researchers showed that goat milk colostrum nearly completely inhibited the uptake of folate by isolated bacteria typical of the intestine, and suggested that the function of folate-binding protein was to prevent the overgrowth of certain intestinal bacteria.[50] These results taken together would suggest that in a live animal or human being, folate-binding protein from raw milk would ensure that the vitamin is absorbed rather than left in the intestine to feed bacteria.

Subsequent research into the effect of heat treatment on the concentration of folate-binding protein in milk has produced conflicting results. Wigertz and colleagues showed that UHT treatment destroys 98 percent of the folate-binding protein while HTST pasteurization destroys only twenty percent of it.[51] They similarly found that UHT treatment destroys twenty to forty percent of the folate while HTST pasteurization destroys ten to twenty percent of it.[51] Others studies, however, have shown that classic and HTST pasteurization destroy ninety percent of the folate-binding protein.[52] Ngyren-Babol and colleagues recently attempted to reconcile these findings by showing that the free protein denatures at less than 50°C, which is easily reached by all pasteurization temperatures, whereas the folate-bound form of the protein denatures at higher temperatures ranging from 72 to 84°C, depending on the form of folate to which it is bound.[52] HTST pasteurization just barely reaches these temperatures, while UHT treatment greatly exceeds them. Since milk contains half of its folate-binding protein in the free form and half bound to folate, and since it contains a variety of different forms of folate, the effect of pasteurization may be rather unpredictable and depend on the specific composition of the milk.

Ngyren-Babol and colleagues also suggested that the heat-treated protein could retain its ability to bind folate but nevertheless form aggregates. We could therefore speculate that heat treatment might alter the biological activity of the protein without destroying it entirely and even without destroying its ability to bind folate. This could explain the early results showing that folate-binding protein isolated from raw milk but not from pasteurized milk enhanced the absorption of folate in intestinal cells taken from rats.[49] Indeed, a recent clinical trial found that the availability of folate from pasteurized milk was lower than that of any other food tested, including fortified bread, supplements, lemon mousse sprinkled with yeast flakes, and milk that had undergone fermentation, which degrades the folate-binding protein.[53] Supplementing the fermented milk with folate-binding protein derived from a commercially processed whey protein concentrate decreased the availability of folate almost to the low level of folate from pasteurized milk. These results suggest that pasteurization converts folate-binding protein from a beneficial booster of the vitamin's absoprtion to a detrimental inhibitor its absorption.

If we synthesize these findings, we could estimate that pasteurization destroys twenty percent of the folate and cuts its absorption in half, suggesting an overall sixty percent loss in folate bioavailability. This should nevertheless be confirmed in a randomized, controlled trial comparing the ability of raw and pasteurized milk to not only provide folate in an absorbable form, but to lower homocysteine levels and maximize the activity of folate-dependent enzymes, which would provide true measures of biological activity.

Vitamin B_6

Heating vitamin B_6 not only destroys some of the vitamin but also produces a compound called phosphorylpyridoxyllysine, which is a conglomeration of the vitamin with the amino acid lysine and acts as an "anti-B_6" compound that interferes with normal B_6 metabolism and aggravates the symptoms of deficiency.[54] This is why the sterilization of milk destroys between one-third and two-thirds of the vitamin, but destroys up to 83 percent of its biological activity.[55] A 1984 review suggested that the formation of this anti-B_6 compound "may account for the unexpected and thus far unexplained epidemic of convulsive seizures observed thirty years ago in infants who were fed nonfortified, heat-sterilized, canned infant formula."[54] HTST pasteurization is gentler than sterilization and destroys only ten percent of the B_6,[56] but in the absence of experimental evidence we could speculate that it destroys at least twenty percent of its biological activity.

Other Vitamins

The contributions of heat-sensitive proteins to the bioavailability of other milk vitamins is not as well understood, but we currently know of several additional interactions between vitamins and milk proteins:

- Beta-lactoglobulin doubles the absorption of vitamin A in rats,[57] and up to half of it is destroyed by pasteurization, as discussed in the section above, "Does Raw Milk Prevent or Treat Asthma?"
- Vitamin D in milk is also bound to proteins that may be heat-sensitive, as discussed above in this section under the subheading, "Milk Minerals."
- Human milk contains a vitamin B_{12}-biding protein called haptocorrin that suppresses the growth of certain bacteria, including a pathogenic, diarrhea-causing strain of *E. coli*,[58] probably by starving it of the vitamin B_{12} that it needs for growth. This protein also increases absorption of the vitamin in a model of the human small intestine.[59] These data suggest that the mammary glands produce the protein in order to ensure efficient absorption of the vitamin and to prevent the growth of pathogenic intestinal bacteria in the infant, and it thus may play a role very similar to that of folate-binding protein. Classic pasteurization destroys half of the B_{12}-binding capacity of human milk, whereas HTST pasteurization destroys forty percent of it.[60] In cow milk, vitamin B_{12} appears to be bound primarily to transcobalamin rather than haptocorrin, and it is likely released from this protein in the human stomach.[61] While pasteurization destroys about ten percent of the B_{12} in milk,[56] then, whether it damages any proteins related to B_{12} utilization in cow milk is currently unclear.

In this section, we have provided not only quantitative estimates of the ability of pasteurization to decrease the biological activity of certain vitamins, but also sufficient proof of principle to show that the effects of pasteurization on a given nutrient must always take into account biological activity. More research is needed to quantify the true effects that pasteurization has on the biological activities of most nutrients.

Does Raw Milk Contain Natural Antimicrobials?

The FDA states that the natural antimicrobial compounds present in milk are not present in high enough concentrations to "kill pathogens and ensure raw milk safety," and that "contrary to raw milk advocates' claims, pasteurization does not completely inactivate these indigenous antimicrobial components." We agree that pasteurization does not completely inactivate them, but it does diminish them and this is reflected in the diminished ability of heat-treated milk to prevent the growth of pathogens, discussed in more detail below. We would also stress that raising cattle on open pasture and with proper standards of cleanliness are essential parts of any strategy aimed at ensuring the safety of raw milk. The natural antimicrobial system present in this wholesome food nevertheless makes an important contribution to its safety.

The FDA provides a substantial amount of data to support its argument that the individual components are not present in sufficient concentrations to be effective – leading one to wonder for what purpose mammals put these compounds into their milk in the first place – but these arguments miss the forest for the trees. There are many interactions between the individual components,[62] so they must be considered together as a system. The antimicrobial activity of milk involves not only probiotic bacteria, but also a whole slew of proteins, many of which have been discovered only recently. These include lactoferrin, lactoperoxidase, lysozyme, xanthine oxidase, RNA-degrading enzymes called ribonucleases, antibodies that function as DNA-degrading enzymes called abzymes, and more recently identified proteins such as angiogenin, lactogenin, and glycolactin. Lactoferrin may not be present in high enough concentrations to exert antimicrobial activity on its own as the FDA suggests, but it synergizes with lysozyme, and some of it is broken down during digestion into fragments with 100 times the antimicrobial potency as the undigested protein. While studying each isolated component on its own may lead to useful mechanistic insights about how these components work, the evidence most relevant to the question at hand comes from studies testing the ability of pathogens to survive in whole, raw milk.

Numerous studies have shown that pathogens grow more slowly or die more quickly when added to raw milk than when added to heat-treated milk:

- Doyle and Roman inoculated raw and sterilized cow milk with three different strains of *C. jejuni,* kept the samples refrigerated (4 ºC), and observed them for two weeks. Regardless of the specific strain, *C. jejuni* virtually disappeared by eight days in raw milk, but took twice as long to disappear in sterile milk.[63]
- Xiong inoculated raw and HTST pasteurized cow milk with different strains of *C. jejuni* or *C. coli*, kept them refrigerated (4 ºC), and observed them for two weeks. All six strains of *C. jejuni* and three out of six strains of *C. coli* declined in number more rapidly in raw milk than in pasteurized milk. The difference between milks was highly dependent on the specific strain of the organism, and some strains declined 10,000 times as much in raw milk than in pasteurized milk.[64]
- Simms and Mac Rae inoculated raw, HTST pasteurized, and UHT-treated goat milk with *C. jejuni*, kept them at a variety of temperatures, and observed them for 48 hours. At all temperatures, *C. jejuni* disappeared more quickly in raw milk than in heat-treated milk. The organism disappeared the fastest when the samples were kept close to room temperature (20 ºC). At this temperature, *C. jejuni* disappeared by 24 hours in raw milk and by 48 hours in pasteurized milk, but still remained in UHT-treated milk by the end of the study.[65]
- Wang and colleagues inoculated raw milk taken from a local farm and pasteurized milk purchased at a local store with *E. coli* O157:H7, incubated the samples at various temperatures, and observed them for four weeks. When the samples were kept refrigerated (5 ºC), *E. coli* failed to grow in any of them. At all other temperatures, the organism grew more rapidly in pasteurized milk than in raw milk. At room temperature (22 ºC), *E. coli* counts began decreasing in raw milk within two days, but grew rapidly in pasteurized milk through the first week, reaching over 100 times the peak concentration found in raw milk.[66]

These studies clearly show that raw milk contains an active and effective antimicrobial system, and that heat treatment diminishes the efficacy of this system in proportion to the intensity of the heating involved.

What is the Potential Public Health Impact of Raw Milk?

The FDA document contains two sections addressing the relative safety of raw and pasteurized milk. The first is titled "pasteurized milk is safer than raw milk," but the text merely summarizes outbreaks of foodborne illness attributed to raw milk with no attempt to compare them statistically to outbreaks attributed to pasteurized milk. The second is titled "raw milk causes a greater rate of foodborne outbreaks than pasteurized milk," but the text simply acknowledges that the FDA was able to find documentation supporting the claim made in *The Verbal Argument by Mark McAfee* that many outbreaks have been attributed to pasteurized milk. The FDA lists citations for these outbreaks with brief comments, but makes no attempt to compare them statistically to outbreaks attributed to raw milk.

In a third and closely related section, the FDA argues that Hazard Analysis and Critical Control Points (HACCP) plans cannot make raw milk safe because hygienic control and pathogen detection can both fail. As the FDA clearly acknowledged in the previous section, pasteurization can also fail, so without any support for its claim that pasteurized milk is safer than raw milk, its arguments about the potential failures of HACCP plans carry very little meaning. No single program, neither HACCP nor pasteurization nor any other, can banish illness from the face of the earth.

Even if the FDA had attempted to support the claims it made about the relative safety of raw and pasteurized milk, such a comparison would not only be statistically illegitimate for reasons explained below, but would again miss the forest, only this time missing it for just a single tree. The proper way to assess the potential public health impact of raw milk is to compare the totality of its likely benefits to the totality of its likely costs.

To get a sense of what such a calculation might look like, let us take some of the available statistics at face value for a moment before criticizing their limitations. The FDA claims that in 2010 alone raw milk caused 88 illnesses and zero deaths in the United States. The CDC recently estimated that about three percent of the US population drinks raw milk.[26] If everyone in the U.S. were to drink raw milk, we could expect to see just over 2,900 illnesses in a year instead of 88. According to the most recent statistics from the American Lung Association,[67] just fewer than 3,500 people died of asthma in 2007 and an estimated 12.8 million people had at least one asthma attack in 2009. The GABRIELA study found that children who drink raw milk every day are half as likely to have asthma as those who never drink raw milk.[9] If we assume this association represents a cause-and-effect relationship, then we can predict that just over 2,800 additional foodborne illnesses would be the price we would pay to protect 6.4 million people from asthma attacks and to prevent 1,750 asthma-related deaths. These calculations suggest that even if raw milk is every bit as dangerous as the FDA claims it to be, it could still save hundreds of lives every year and improve the lives of millions.

Inferences of this type, however, are deeply problematic. On the one hand, our estimates of the true prevalence of foodborne illness due to raw milk or any other food are based on data of extremely poor quality mired in bias, and there is every reason to consider the prevalence of illness due to any particular food almost entirely unknown. On the other hand, observational evidence suggesting benefits of raw milk, no matter how biologically plausible, has to be regarded as preliminary until its true benefits can be demonstrated and quantified in randomized trials. Let us consider each of these points in order.

According to the CDC web site, 2008 is the most recent year for which foodborne illness data is finalized. In that year, there were 23,152 cases of foodborne illness reported.[68] Yet the reported illnesses are, by the CDC's estimation, just a tiny smidgeon of the total. In 1999, CDC scientists used an estimate of the overall prevalence of diarrhea and vomiting to calculate that the "true" incidence of foodborne illness is 76 million cases per year.[69] If we are to take the leap of faith required to believe that we can estimate the total prevalence of foodborne illness from these relatively non-specific symptoms, we would have to conclude that only 0.03 percent of all foodborne illnesses are reported and that 99.97 percent go unreported. On the one hand, this would suggest that the true prevalence of foodborne illness attributable to any given food is much higher than what is reported. On the other hand, it would mean that the data associating specific outbreaks with specific foods is such a small sample of the total that even small biases in the reporting or investigation of outbreaks would introduce spurious results of enormous magnitude.

The first randomized, controlled trial was not published until 1948, after pasteurization had already become the favored public health approach for preventing milk-related foodborne illness, but researchers now consider randomization essential for minimizing bias.[70] To date, we have found only one randomized, controlled trial comparing the influence of raw milk on the incidence of infection to that of any other food. Narayanan and colleagues published the results of this trial in the *Lancet* in 1984.[71] The investigators studied 226 low-birth-weight infants born under unhygienic conditions, who were at high risk of infection. They randomly allocated the infants to four groups: one received raw human milk, one received pasteurized human milk, and the other two groups received one or the other of these two treatments with half of the milk replaced by a formula made from pasteurized cow milk. The rate of infection was lowest in the group that received only raw human milk. It was three times higher in the group that received pasteurized human milk and formula, and 50 percent higher in the other two groups. The increased risk of infection only reached statistical significance in the group fed pasteurized milk and formula. The results suggest that raw human milk proved superior in part because it was human milk and in part because it was raw rather than pasteurized.

One of the most remarkable observations in this study is that the investigators were able to culture pathogenic organisms from fifteen percent of the raw milk samples, but the samples of pasteurized milk and formula were sterile. The presence of pathogens was probably so high because many of the mothers were unhealthy and the milk was collected under clean but not aseptic conditions. The trial nevertheless showed that the immune-boosting properties of the unpasteurized milk proved protective despite the presence of pathogens in a substantial minority of the samples.

The epidemiological evidence suggesting that children who drink raw milk have a lower incidence of asthma and allergies is also subject to confounding, just as all epidemiological evidence is. The fifty to eighty percent reduction in allergic diseases found in some of these studies is nevertheless a profoundly intriguing justification for testing the effects of raw milk in randomized trials. If in fact raw milk really possesses any of the supposed dangers that the FDA attributes to it using uncritical analyses of poor-quality, high-bias data, such trials would be able to provide the first real evidence of this. We believe these trials would, on the contrary, demonstrate the health-promoting properties of raw milk, and we believe that high-quality scientific research can only move forward at a rapid pace if the government finally abandons its antagonism towards the producers and consumers of raw milk.

Conclusions

We have herein reviewed evidence that raw milk may protect against asthma and allergies, improve lactose tolerance, and be more easily digested by people with trouble digesting dietary fat. It is richer in minerals than pasteurized milk, its vitamins have greater biological activity, and it contains beneficial bacteria. Raw milk may have the potential to reduce morbidity and mortality from serious diseases such as asthma, and its potential benefits deserve more extensive scientific research. We believe the FDA should encourage this type of research, while promoting consumer choice and freedom of exchange. There is currently no high-quality evidence that can be used to justify the suppression of the rights of farmers and consumers to engage in free exchange on the basis that raw milk is unsafe, and people should be free to consume the foods they believe are most healthy.

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