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Review Article

Re-Examining Non-Pasteurized Milk Consumption in Human Health and Disease

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ABSTRACT

It was previously believed that raw milk consumption offered no benefits over pasteurized milk and that the risks associated with raw milk were too great to ever reconsider its "reintroduction". This was the stance taken by most government and food agencies. However, recent research has shown that unpasteurized milk can have positive effects on the immune system through the decreased risk of certain types of allergenic diseases and infections. The benefits of raw milk consumption seem to be associated primarily with its whey proteins (and perhaps a few other mechanisms), potentially acting through epigenetic mechanisms and T cells. However, these whey proteins are deactivated or destroyed by heat treatment such as pasteurization, eliminating these benefits. In the past 150 years when dairy farms were becoming industrialized and sanitation theory was minimal, there were few other options to make milk safe without pasteurization. But now, with knowledge and technology, certain testing and hygiene measures can be taken that reduce these safety concerns. It is also now known which pathogens pose the greatest threat to whom and where they often come from in the cold chain. The current methods of dairy production and their role in nutrition need to be re-examined. Allergenic diseases and infections place an undue burden on individuals and thus society and thus raw milk consumption is worthy of renewed research and attention.

INTRODUCTION

Pasteurization is considered "any process, treatment, or combination thereof, that is applied to food to reduce the most resistant microorganism(s) of public health significance to a level that is not likely to present a public health risk under normal conditions of distribution and storage" [1]. Pasteurization kills bacteria through heat, which causes a denaturing of the bacteria's proteins and the melting of membrane lipids, leading to cell death [2]. The CDC, the U.S. Food and Drug Administration, the American Academy of Pediatrics, the American Veterinary Medical Association, and the National Association of State Public Health Veterinarians now all recommend pasteurization for milk consumed by humans [3]. Many high-income countries now mandate milk pasteurization by law to reduce illness: currently, dairy outbreaks only contribute to two to six percent of all food-borne outbreaks in these countries [4]. By comparison, before 1939, almost 25 percent of all foodborne and waterborne diseases were connected to contaminated milk consumption [5].

However, recently there has been a growing trend in high-income countries of the consumption of unpasteurized raw milk. Raw milk is considered, by the European

Union, to be milk that is from a farmed animal's mammary gland that has never been heated to forty degrees Celsius or been put through any type of treatment that has an equivalent effect [5]. The Centers for Disease Control estimates that roughly three percent of the American population consumes raw milk [6]. Undoubtedly, unpasteurized milk can pose dangers to the consumer, and pasteurization was implemented for a reason. However recent research has shown that there can also be some positive effects from the consumption of raw milk and that the consumption of raw milk is on the rise [4].

This narrative review will address the question "How do the benefits of raw milk consumption compare to the limitations and dangers and what are the mechanisms of these benefits?" Current literature was evaluated for the protective effect of raw milk on disease, mainly through prospective cohort studies, reviews, and animal models. Studies looking at raw milk outbreaks and safety data were also examined.

PASTEURIZATION: AN OVERVIEW

The implementation of pasteurization in all its forms begs the question, how did we arrive at this point? Human consumption of dairy has been in practice since the Neolithic period. It was a valuable source of protein and energy. The fact that human evolution began to prevent the downregulation of the lactase gene and how quickly this genetic mutation spread across the world on a comparative scale, highlights the fact that dairy consumption gave a survival and reproduction advantage to humans [7]. Pasteurization has not been around long in contrast to the consumption of dairy by humans and evidence shows that dairy long provided a secure food supply for Europeans [6].

The pasteurization of cow milk was first implemented by the government in 1908 in Chicago mainly due to concerns over tuberculosis being passed from cows to humans. An attempt to identify tuberculosis-free herds was made but became unmanageable. At this time tuberculosis was a major health concern, and around 10 percent of tuberculosis cases were believed to originate from bovine milk consumption. In 1924, what was then the US Public Health Service adopted the Pasteurized Milk Ordinance which outlined the standards for pasteurization and sanitation regarding dairy products that could be voluntarily adopted by the states [8]. Pasteurization was a practice that began in urban environments and worked itself outward, contrary to its origins. Cows were kept in dirty, cramped housing at the beginning of the 1900s, and the lack of scientific knowledge, the lack of refrigeration, the lack of standards for sanitation, and an underappreciation for hygiene all contributed to a potentially dangerous final product [6]. Robert Hartley visited a New York City dairy in 1842 and wrote: "Here, in a stagnant and poisoned atmosphere that is saturated with the hot steam of whiskey slop, and loaded with carbonic acid gas, and other impurities arising from the excrements of hundreds of sickly cattle, they are condemned to live, or rather die on rum-slush. For the space of nine months, they are usually tied to the same spot, from which, if they live so long, they are not permitted to stir, excepting, indeed, they become so diseased as to be utterly useless for the dairy" [6].

The original major method of pasteurization was vat pasteurization which involves heating milk in a large tank for thirty minutes at 145 degrees Fahrenheit. This has been largely replaced by high-temperature short-time (HTST) pasteurization which involves heating milk to 161 degrees Fahrenheit for fifteen seconds. Two other notable methods of pasteurization are ultra pasteurization and ultra-high temperature (UHT), both of which heat the milk to 280 degrees Fahrenheit for two seconds, the latter using completely sterile equipment and packaging which allows it to not be refrigerated [9]. Most countries now set 72 degrees Celsius (HTST) as the minimal pasteurization temperature for safety [10]. UHT pasteurization impacts heat-sensitive milk proteins most strongly, while HTST pasteurization either eliminates or decreases them [7]. LTLT (low temperature/long time) also known as Holder pasteurization (HoP) or vat pasteurization, despite its low temperature (149 F, 30 min), may alter milk's protein even more than HTST or UHT [11].

It does, however, seem that according to research, pasteurization eradicates the anti-allergenic and anti-infective properties of raw milk [7,12]. This is believed to be through the damaging of certain whey proteins by heat. These whey proteins appear to be the major contributors to raw milk's protective effects [13]. There are numerous other beneficial components contained within raw milk that could be affected by pasteurization, such as beneficial microbes, fats, microsome, and maternal cells, but the research on these remains less conclusive [14,15]. The exact mechanism of the whey proteins

remains to be elucidated, but epigenetics is believed to play a role [16].

Homogenization, also worth mentioning, is a common step in milk processing. It is when milk is pumped into a high-pressure setting through super thin pipes, which reduces the size of the fat globules and reduces fat separation in the final milk product [17]. This is usually done after pasteurization (Michigan State Extension). Milk fats are present in the solution as milk fat globules. These MFGs are secreted from the epithelial cells and allow the fat portion to be emulsified in the milk. They are made up of a triglyceride core surrounded by a complex membrane that includes numerous proteins [18,19]. The disrupted milk fat globular membrane releases bioactive components when homogenized, so this may potentially alter the effects of the milk on the immune system [20]. The reduced fat globule size caused by homogenization also increases the surface area of these remaining fat droplets [17]. This then causes some whey and casein proteins to be presented at the droplet surface which were not before. Certain caseins and membrane proteins can be bioactivity beneficial, potentially being anticarcinogenic or hypotensive, and some can be harmful. However, Michalski found that there is no association between milk allergy, lactose intolerance, or type 1 diabetes and homogenization, and homogenized milk may be more digestible [21].

DANGERS OF RAW MILK

The safety argument of raw milk is ongoing, and often not very clear. Food outbreaks are inherently hard to trace, and many go unreported. Any food can be associated with illness. This includes both raw and pasteurized milk. And often when there are reports of outbreaks related to raw milk, there is no context given [6]. A recent analysis by Langer et al. discovered that unpasteurized dairy products once equated to the amount consumed by the general public, are 150 times more likely to cause an outbreak or an outbreak-associated illness of any kind. However, the breakdown between raw milk and raw milk products was not distinguished by this number which is a significant factor [22]. There is also a distinction that needs to be recognized between the black market and amateur producers of raw milk who are selling it under the table without proper training and who are not producing a food quality product and those who follow hygienic standards and have been trained. These under-the-table sales even further confuse the safety data on raw milk consumption and need to be recognized as a factor [6]. However unpasteurized dairy still makes up a greater percentage of dairy food outbreaks than pasteurized products [23]. However, that is not to say that pasteurized dairy is without risks, in 1985, 168,000 people were sickened with *Salmonella* from pasteurized milk, and in 2007 *Listeria* from pasteurized milk killed three people. The investigation after these deaths concluded that the pasteurization methods were 'adequate' [6]. Neither pasteurized nor unpasteurized milk can ever be 100% safe [24]. However, it needs to be acknowledged that despite the current increasing trend in raw milk consumption, there are still risks to unpasteurized milk consumption. But to say that the data on the true dangers of unpasteurized milk are confusing is an understatement [23].

As previously mentioned, safety data, specifically raw milk safety data, can be vague. Klerk and Robinson's study found that per million capita, there were 0.61 unpasteurized milk outbreaks and that in the USA there were 0.015 deaths per million capita from unpasteurized milk between 2000 and 2018 which equates to roughly four deaths. The current data on disease outbreaks linked to raw milk consumption have been attempted to be organized by researchers including Klerk & Robinson to highlight some of these threats posed by the recent increase in consumption. Data between 2000 and 2018 from North America, Europe, New Zealand, Australia, and Japan were analyzed for food-borne outbreaks linked to unpasteurized milk consumption and found that there were 343 recorded outbreaks and 7 recorded deaths in the last 18 years (2022). However, contrary to Klerk and Robinson, Langer et., al found that not a single death from the consumption of unpasteurized fluid milk was reported for thirteen years, between 1993 and 2006. This seems to indicate a contradiction to the earlier study of Langer et al., or there was a jump in raw milk deaths. [22]. This needs further research and elucidation. To put this in context, the CDC states that roughly 3,000 individuals die every year from food-borne illnesses [25].

Sebastianski et al. looked at disease outbreaks linked to both pasteurized and unpasteurized dairy products in the U.S. and Canada between 2007 and 2020. They found that although

there were more outbreaks associated with unpasteurized dairy, hospitalizations and deaths were proportionally greater in the pasteurized dairy outbreaks, with *Listeria monocytogenes* being the major cause. There were five deaths among the 530 cases of unpasteurized milk-associated illness. Three were due to *Listeriosis*, one due to *E. coli O157:H7*, and one death was a *Campylobacter jejuni* gastroenteritis infection linked to a chronic medical problem. It does seem however that hospitalization is more often caused by consuming raw unpasteurized cheese products rather than raw fluid milk (2022). This is probably due to Listeria, which is one of the more threatening illnesses that can be present in dairy, causing diarrhea, flu-like symptoms, miscarriages, and meningitis [4]. Regarding pasteurized milk there were 284 illnesses with 134 hospitalizations and 17 deaths. Among the deaths, fifteen were due to *Listeriosis monocytogenes*, one to *Yersinia enterocolitica*, and one to *Clostridium botulinum* [23]. The seriousness of an illness also needs to be taken into consideration when looking at outbreak data, as some food outbreaks result in hospitalization or deaths, and others result in rather mild illnesses. Not all infectious organisms are equal.

ORGANISMS

Mycobacterium tuberculosis, the infectious agent of what is typically known as just tuberculosis or TB is believed to have given rise to the strain associated with cattle, *Mycobacterium bovis*, with raw milk being a common source in the early twentieth century. This strain can be zoonotic. Children under the age of five were particularly susceptible to this disease and roughly six percent of tuberculosis deaths in Great Britain before any type of control were believed to be due to *M. bovis*. In 1917 in the United States *M. bovis* from cattle is estimated to have killed 15,000 people. TB is now able to be prevented, treated, and cured, yet it is still a major killer today. Tuberculosis was one of the major original reasons for pasteurization in Chicago in the first place. When tuberculin is used to test for Bovine TB (bTB) in control/eradication programs TB is rarely now seen as a disease [26]. A TB vaccine is now given to infants in certain countries which prevents TB outside of the lungs [27]. Most cases of non-lung TB were due to infected milk [26]. Although in the Western developed world, Tuberculosis from milk is rarely a concern, other organisms from dairy can still pose a threat to human health [4].

Pasteurization removes the organisms that potentially cause harmful infections such as tuberculosis, brucellosis, diphtheria, scarlet fever, and Q-fever. It also kills bacteria like *Salmonella, Listeria, Yersinia, Campylobacter, Staphylococcus aureus,* and *Escherichia coli O157:H7* which are some of the most common pathogenic food organisms considered today [28]. Together these organisms plus a few others accounted for 304 outbreaks between the years 2000 and 2018. The three major pathogenic bacteria that pose a major risk in modern unpasteurized milk outbreak data are *Campylobacter spp.* (accounting for 67.8% of outbreaks), *E. coli* (12.4%) and *Salmonella spp.* (9.3%). [4]. *Listeria Monocytogenes* will also be looked at specifically due to the threat it poses in terms of hospitalization and death [23].

Campylobacter is a gram-negative rod bacterium that is one of the most common causes of bacterial diarrhea illness in the United States. It is also the most common cause of foodborne illness associated with raw milk, being the agent responsible for just shy of 70 percent of cases. [4]. The typically considered pathogenic species are *Campylobacter jejuni* and *Campylobacter coli* with C. *jejuni* making up almost 90% of reported cases. Gastroenteritis is the most common illness associated with *Campylobacter*. Symptoms typically begin two to five days after ingesting the bacteria and resolve by themselves within five to seven days. However, complications can occur, though rarely, that include extraintestinal infections in the immunocompromised and potentially Guillain Barr syndrome and irritable bowel disease. Domestic and wild birds are the number one reservoir of *Campylobacter*. Infection occurs through the fecal-oral route and can come from undercooked poultry, unclean water, and unpasteurized milk. Cases are typically more sporadic rather than outbreak-associated [29]. Between the years 2000 and 2018, *Campylobacter* spp. was the single most common associated agent with foodborne outbreaks associated with raw milk, making up 67.8% of outbreaks that were cultured. *Campylobacter* spp. needs only a very small amount to cause infection, it also cannot multiply in milk, which makes the cold chain an irrelevant protection mechanism for this particular bacterium [4]. The reach of *Campylobacter spp.* goes far beyond simply the consumption of

unpasteurized dairy, as some global estimates believe it may be the number one cause of diarrheal-prompted visits to outpatient clinics for children under five [30]. A systematic review and meta-analysis (using Stata) was performed by Christidis et al. [31] to determine the prevalence and amount of Campylobacter spp. in raw milk samples. Studies that isolated the pathogenic species of campylobacter (C. *jejuni* and C. *coli*) found a prevalence of 0.75%. Only two of the studies looked at Campylobacter levels, with approximately 0.16 ± 0.3 and 0.047 per ml. It is interesting to note that in samples from Finland, New Zealand, Switzerland, goats, sheep, laboratory or government sources, and retail raw milk sources the 95% CI estimated for the prevalence value was zero (2016). According to this study, the consumption of raw milk is considered risky, because even though the prevalence of Campylobacter is low, it is sometimes present and with regards to raw milk nothing is being done to inactivate it, due to a lack of heat treatment. *Campylobacter* accounted for one death from unpasteurized milk consumption between 2007 and 2020 [23].

Escherichia coli is a gram-negative bacterium that is often a part of normal intestinal flora. However, certain subtypes are known to cause severe illness in humans. *Escherichia coli O157:H7* is a Shiga toxin-producing *Escherichia coli* serotype (STEC) [32]. It is zoonotic and can be found in the gastrointestinal tract of cattle, sheep, goats, deer, moose, swine, horses, dogs, cats, pigeons, chickens, and turkeys. Human STEC infections, however, are typically derived from cattle manure contamination. It can cause diarrhea, hemorrhagic colitis, and hemolytic-uremic syndrome (HUS), which typically occurs in children [33] Symptoms usually emerge three to four days after exposure, and recovery is usually within five to seven days. If HUS occurs it usually begins seven days after the first symptoms, once the diarrhea begins to improve [34]. Very small amounts of this bacterium can cause illness and are typically linked to contaminated produce, undercooked beef, and unpasteurized dairy. The CDC reported 3,127 cases of STEC in the United States in 2019 [32]. *E. coli* accounts for roughly 12.4% of cultured raw dairy-associated outbreaks [4]. However, *E. coli* can survive the pasteurization process. For this reason, refrigeration is important, specifically maintaining a temperature below seven degrees Celsius. The cold chain plays a major role in the potential of disease in the consumer. When the milk falls out of this temperature range, rapid pathogenic growth can occur [4]. *E. coli O157:H7* accounted for one death from unpasteurized milk consumption between 2007 and 2020 [23].

Listeria monocytogenes is specifically known to be harbored by cheeses [4], but it can be present in milk as well. However, pasteurization does not always protect consumers from *Listeria*. It has emerged as one of the primary pathogens in pasteurized dairy products and often comes from contamination post-pasteurization. It can come from soil, animals, or plant matter. It is most dangerous in the fact that it is highly virulent and poses a significant risk to pregnant women and the immunocompromised. Some surmise that the increased use of biological response modifiers has made infection from *Listeria* more common [23]. A quantitative microbial risk assessment estimated *Listeria* deaths from pasteurized milk per year 18 [35]. Sampedro et al. [36] analyzed the public health impact and completed a risk assessment on *Listeria* in common foodstuffs. Ready-to-eat foodstuffs were the most common sources of infection, as cooking destroys the bacteria. The susceptible immune compromised population was at up to a ten thousand times higher risk than the general population. Deli meats were responsible for 90 percent of cases, followed by salads at roughly four percent, and soft cheese and seafood at one percent. Up to 98 percent of cases were in the increased-risk population. Removing product lots with one colony forming unit (CFU) per gram of final product or greater reduced infection cases by up to 100 percent (2022). This data could perhaps be applied to raw milk consumption. *Listeria* accounted for three deaths from unpasteurized dairy consumption between 2007 and 2020 [23].

Salmonella is one of the most important causes of foodborne illness. The European Centre for Disease Prevention and Control (ECDC) reported that *Salmonella* had the second highest number of infectious cases of a foodborne bacterium at roughly ninety thousand. *Salmonella* is a gram-negative bacterium that moves using a flagellum. It is contracted through the feces of an infected individual or animal. Symptoms can include everything from gastroenteritis to abdominal cramps, bloody diarrhea, fever, myalgia, headache, nausea, and vomiting. Most cases of salmonella are linked to the

consumption of poultry, pork, and egg products [37]. However, *Salmonella spp*. Are also known to be agents of foodborne illness through unpasteurized milk [4]. Touching animals or other sources in the environment can also spread the bacterium. Symptoms usually begin six hours to six days after the initial infection and can last four to seven days. Antibiotics are typically not needed as salmonella resolves by itself, yet antibiotic resistance is increasing. However, in cases of severe illness antibiotics might be prescribed. 1.35 million illnesses, 26,500 hospitalizations, and 420 deaths are estimated to occur each year by the CDC [38].

WHERE IT IS LEGAL

Some European countries such as Italy and Germany have specific scenarios in which the sale of raw milk to the consumer is allowed [10]. Germany sells raw milk for consumption commercially, but it is legally controlled and certified for this purpose [17]. This milk is called 'Vorzugsmilch' and follows strict hygienic guidelines. It is certified Grade A and follows strict Hazard Analysis Critical Control Point (HACCP) standards [39]. Italy has allowed the sale of raw milk from specialized vending machines spread throughout the country since 2004. Usually located near town centers, the milk in these refrigerated machines is required to come with a boil warning for consumers after multiple cases of hemolytic uremia were identified and then deemed necessary by the Italian Ministry of Health. The burden of safety lies very much with the consumer in these cases as it is up to them to boil it, and many ignore the warning [40]. In the United States, the legal sale of raw milk comes down to the state legislators. In 15 states the sale of raw milk is allowed commercially, in 13 states the sale directly from farms is legal and in 24 states the sale of raw milk is outright illegal [41]. With multiple countries in the European Union and about half the states allowing the sale of raw milk, it seems that it is a doable and practical achievement with manageable risks. There is also a distinction that needs to be recognized between the black market and amateur producers of raw milk who are selling it under the table without proper training and who are not producing a food quality product and those who follow hygienic standards and have been trained. These under-the-table sales even further confuse the safety data on raw milk consumption and need to be recognized as a factor [6].

A GROWING TREND

Despite the implementation of these rules and requirements by authorities, consumers have begun purposely seeking out unpasteurized milk for numerous reasons in recent decades. Consumer beliefs on why they consume raw milk include a higher nutritional content, being easier to digest, improved taste, helping to prevent asthma and allergies, less of an impact on the environment, and supporting local farmers. The desire to boost the local economy and to preserve the environment are reasonable reasons for raw milk consumption and should not be underplayed. It is also believed that culture, such as the consumption of raw milk during upbringing, plays a major role. It is notable that most consumption also takes place in households and on farms rather than through public distribution or marketing [4,5]. Interestingly, Bovbjerg et al. [42] further analyzed the beliefs of consumers of raw milk in a meta-analysis and found that taste was the number one reason for raw milk consumption at 72.4 percent, and second to that was perceived health benefits at 67.2 percent. Notably, 67.9 percent of consumers also reported distrust of governmental food safety recommendations (2018). The raw milk movement originated with consumers and farmers who sought to bring back traditional farming methods. Consumers of raw milk come to appreciate the nature of an operation due to the fact they are often buying directly from farmers. Juxtaposed to this is the fact that effective large-scale distribution seems to require sterilization such as pasteurization [6].

BENEFITS

It was once believed by certain researchers that raw milk consumption was not involved in any protective effects on allergy and asthma [8]. Today, even certain government agencies, such as the Washington State Department of Health, declare "there are no health benefits from drinking raw milk that cannot be obtained from drinking pasteurized milk" [43]. However, the benefits of raw milk consumption are now supported by numerous research articles. The nutrient content itself does not differ much between unpasteurized and pasteurized milk [8]. However, there do seem to be certain factors in raw milk that decrease the incidence of allergenic diseases [17].

Allergenic diseases are on the rise in the world. Diseases such as atopic dermatitis, allergic rhinitis, and allergic asthma have

vastly increased in the last thirty years. The World Health Organization puts the number of people suffering from these diseases at 235 million, making them some of the most common chronic diseases [44]. Some researchers put asthma rates alone at 334 million people worldwide [45]. It had been previously shown that those raised on a farm suffered lower rates of allergenic diseases. Although initially believed to possibly just be an effect of general immune exposure, Brick et al. [10] conducted a very important meta-analysis establishing that raw milk consumption could be a factor that exerts a protective effect against allergenic diseases. What was very notable was the fact that this effect can theoretically be translated to individuals who consume raw milk even if they do not live on a farm (2020).

Due to the dangers of the consumption of raw milk, which has a chance, albeit rare, of causing life-threatening infections, it cannot be considered truly ethical to attempt interventional studies, particularly in young children. Thankfully, however, there are numerous study group cohorts available throughout Western and Central Europe that are examining allergenic diseases, respiratory infections, and their associations with farm life. Data often includes the consumption of raw milk, and isolates it for its singular effect, while also examining other farm life factors. These studies include the Allergy and Endotoxin Study (ALEX), Prevention of Allergy Risk Factors for Sensitization in Children Related to Farming and Anthroposophic Lifestyle (PARISFAL), Protection Against Allergy Study in Rural Environments (PASTURE) and Multidisciplinary Study to Identify the Genetic and Environmental Causes of Asthma in the European Community (GABRIELA). Observational studies, however, can only go so far. There is a new experimental study underway, the Milk Against Respiratory Tract Infections and Asthma trial (MARHTA) which may help to define a connection. This trial will use minimally processed full cream milk against typical UHT shop milk. Outcomes recorded include asthma, respiratory infections, wheezing, inflammation, atopic sensitization, and eczema. The details of this "minimal processing" are not elucidated and the parallel remains to be seen between this milk and raw farm milk [10].

Loss et al., using the GABRIELA study group, analyzed the protective effect of raw milk consumption on asthma and atopy (defined in this study as a positive test result for IgE antibodies towards *Dermatopagoides pteronyssinus*, cat, birch, or grass mix; allergy was defined as a positive fx5 test towards fish, cow's milk, eggs, peanut, soybean, and wheat flour). Unique amongst these studies, Loss et. al. also sought to determine the specific milk constituent responsible for the associations. Questionnaires were used about lifestyle and farm habits, including the consumption of raw milk. Serum samples were provided to assess IgE levels and milk samples were collected at the homes of the participants to analyze. Bacterial counts, whey proteins, and fat content were also assessed. This association with objective measurements using multiple regression analysis was a first. Raw milk consumption was inversely associated with asthma, atopy, and hay fever, independent of other farm exposures (2011). The bacterial content of milk and the fat content of milk were not associated with these benefits, contrary to the hypothesis of other research [15]. Increased levels of the whey proteins bovine serum albumin (BSA), alpha-lactalbumin, and beta-lactalbumin levels were all inversely associated with asthma but not atopy. Transforming growth factor-beta levels were not associated with less atopy in this study, yet the TGF-B content in breast milk has been associated with reduced allergies in infants [12].

Further research by Loss et al. looked at how unprocessed cow's milk consumption is protective for infants from respiratory infections. The data used for this was obtained from the PASTURE birth cohort (the prospective birth cohort Protection against Allergy—Study in a Rural Environment). Women from these studies were recruited from multiple Western European countries including Austria, Finland, France, Germany, and Switzerland. Lifestyle and parental background questionnaires were taken during the third trimester and the infant's two-month and 12-month birthmarks. In comparison to ultra-heated milk (UHT), raw milk from the farm was inversely associated with rhinitis, respiratory tract infections, otitis, and fever. C-reactive protein was also inversely associated with raw farm milk consumption. Loss et al. showed that the consumption of raw cow's milk at an early age was able to decrease respiratory infections by 30 percent (2015).

Worth mentioning as well is lactose intolerance. Lactose intolerance is a very common occurrence, presenting in roughly 75 percent of the worldwide population. There is a potential ability of unpasteurized milk to cause an improvement in the

gastrointestinal symptoms associated with lactose intolerance. Unpasteurized milk contains beneficial bacteria including *Lactobacillus acidophilus*. This species produces lactase enzymes. Raw milk has been shown to increase *Lactobacillus* species in the gut microbiome [4]. A single study was done to see if the consumption of raw milk could improve the symptoms of lactose intolerance. No improvement was found using hydrogen breath tests and reported symptoms. However, this study used only 16 participants and within a time frame of just five days went from no milk consumption to 24 ounces, all consumed within just one setting [46]. Further research into the amount of time needed to establish a residence of *Lactobacillus acidophilus* sourced from raw milk, in the intestinal tract, could be useful here.

MECHANISMS

The exact role of the vast array of components in bovine milk and how they may specifically benefit the human immune system are not entirely understood [12]. Most research conducted thus far points towards whey proteins, that have not been damaged by heat, causing the immune effects of raw milk. Healthy T-cell differentiation appears to be the main mechanism [13]. Abbring et al. looked at the ability of eight-day raw milk exposure, versus pasteurized milk exposure, on C3H/HeOuJ mice, to reduce the allergic response to five weeks of ovalbumin sensitization. Histone acetylation of T cell genes was initially driven by raw milk but then shown to be modulated after ovalbumin allergen stimulation compared to pasteurized milk. This showed that raw milk induces initial reactions that resolve but prepare the mice for future potential allergen stimulation. This study points towards an epigenetic mechanism of allergy tolerance through raw milk (2019). However, Loss et al., as mentioned earlier, did not find any correlation between the levels of any specific whey proteins and atopy, though atopy was significantly decreased by raw milk consumption (2019).

Researchers from multiple European Institutions sought to elucidate the role of T regulatory cells in the protective effects of farm exposure for asthma and atopy. 298 children of four and a half years of age were included in this study. 149 were farm children and 149 were controls. Questions that determined farm exposures were given to parents. The Allergy Screen Test Panel for Atopy was used to determine serum IgE levels from samples in these children after stimulation. Treg cells were significantly increased in farm children after peripheral blood mononuclear cell (PBMC) stimulation. Children exposed to raw milk also showed a significantly higher level of FOXP3 demethylation. Treg cells were also significantly negatively associated with asthma as diagnosed by a doctor. These in vivo associations with raw milk and the FOXP3 gene and Treg cells are a first in research in this area [47].

Researchers at the Swiss Tropical and Public Health Institute, Basel, Switzerland collaborated with the PASTURE study group to conduct this multicenter trial. 1133 pregnant women were recruited from Austria, France, Finland, Germany, and Switzerland. The goal was to see how the expression of immunity genes was altered by prenatal and early-life exposures. mRNA expression of multiple genes involving toll-like receptors (TLR) and CD14 were measured at birth and one year in infants whose mothers had farm exposures. Specific environmental exposure was surveyed using questionnaires. Polymorphisms in innate receptor genes were compared to the gene expression of innate immunity receptors through ANOVA and regression analysis. Raw milk consumption had the strongest association with the mRNA expression of these innate immunity receptors. How this study shows a change in gene expression of innate immunity receptors, directly related to raw milk consumption in humans is unique [16].

Some of the other whey proteins with potential allergy-protective effects in raw bovine milk include immunoglobulin g antibodies, which can form immune complexes with allergens promote oral tolerance, and suppress IgE activation of mast cells and basophils (as well as binding to RSV). Lactoferrin can destabilize bacterial cell walls scavenge free iron, and promote bifidobacterial and lactobacillus, which in turn can increase short-chain fatty acids. Transforming growth factor beta enhances epithelial barrier function, Treg cell differentiation, and IgA class switching. Interleukin 10 inhibits the function of antigen-presenting cells eosinophil function and mast cell and Th2 cell activation. Alkaline phosphatase may work by preventing some of the toxic effects of lipopolysaccharide (LPS). Osteopontin modulates Th1 and Th2 responses, but it does not seem damaged by heat [13].

The bacteria and fat portion of raw milk are also of interest regarding allergenic effects, but the research on their effect is

less consistent. Loss et al., found no correlation between asthma and atopy of the bacteria and fat component (2011), while Sozanska speculated that the effect on CD14 through consumption of raw milk could be through a microbiota influence (2019). Bielie et al. [48] found that the inverse association between the consumption of farm milk and allergenic diseases is through CD14 mechanisms. However, this milk was only defined as farm milk and not raw or unpasteurized milk (2007). Abbring et al. discovered that alkaline phosphatase (ALP), which interestingly enough is often used as a marker by countries to determine if milk has been pasteurized, signified by its deactivation, when added back to pasteurized milk, restored the protective effects on allergic reactions to food. This was accompanied by a restoration of a microbial shift towards butyrate-producing bacteria such as *Clostridiales* and a decrease in inflammatory *Proteobacteria* by the raw milk (2019).

Brick et al., [] found that the significantly higher omega-three fatty acid content found in raw versus shop milk did indeed contribute to the asthma protective effects (2016). As the live microbial community of raw milk is further researched, the maternal live cell community is also receiving some interest. Bode et al. investigated how live maternal cells in milk (which include stem cells) affect the infant (2014). Regarding the live cell portion, the species from which the milk is sourced can be significant, with goat milk containing nearly one billion cells per liter of raw milk and cow's milk containing less than a tenth of those maternal cells. These cells include epithelial cells, lymphocytes, neutrophils, and macrophages. Lymphocytes in human milk and sow milk have also been shown to contribute to the immune defenses of newborns [49].

ALTERNATIVES TO PASTEURIZATION

Pasteurization is not the only safety control measure that has been implemented since the 1900's. Other methods to reduce possible contamination and improve milk for human consumption include a focus on herd health and extreme attention to milking practices [4]. Vorzugsmilch (VZM), as previously mentioned, is a German federally regulated program established in the 1930s and is still in existence today. It provides raw milk to consumers following strict hygienic standards to control zoonotic diseases. Testing is done to make sure the strict controls are working. Standard plate counts and coliform counts are done, to check for human contamination. Somatic cell counts and *staphylococcus aureus* are measured to check for udder health; and *Campylobacter, E. coli, L. monocytogenes,* and *Salmonella* are measured to check for zoonotic risks. Following these strict hygiene management techniques, VZM farms' raw milk has shown a comparable zoonotic risk to pasteurized milk [24]. De Klerk and Robinson stated that ". . . it has been demonstrated in Germany that it is feasible to produce raw milk with the same hygiene level as pasteurized milk, resulting in the possible equalization of the microbial risk" (2022). Abbring et al. also note that when raw milk is produced under strict microbiological and hygienic standards the risks are indeed low (2019). This data could point towards a possible alternative to pasteurization, keeping milk safe in the future, but also raw.

Alternatively, the Raw Milk Institute is a not-for-profit institution founded in 2011 by those from the raw milk industry in the state of California. This organization teaches farmers how to produce safe raw milk and protect them from zoonotic organisms. The goal is to provide consumers with a safe option for raw milk. The institute gives guidelines for farmers to set up their risk management system. Often used is a 'Test-and-Hold' system, where the milk is not sold until it has been held and tested for coliform bacteria and standard plate counts. These are checked daily and allow evaluation for any fecal contamination or pathogen growth. The values these farmers hold themselves to for bacteria levels regularly fall well below the limits set by the European Union and even the United States standards for post-pasteurized milk [24]. A third example of an existing system for the possibility of the consumption of raw milk by numerous consumers includes the British Herd Share Association, which is a non-profit society based in Canada. In Canada, raw milk is completely illegal. However, herd shares, are an arrangement in which consumers own a proportion of the dairy herd and can consume an equitable amount of products to their proportionate share. This allows fresh raw farm milk consumption to be a possibility for those who do not own cows or a farm. This milk is regularly tested and matches the same level of hygiene as the Raw Milk Institute's milk and tests negative for the four major pathogenic bacteria, *VTEC, Listeria, Salmonella, and Campylobacter* [24].

Other potential mechanisms of hygiene besides sanitary practices include Pulsed electric field treatment, UV light, Ultrasound, Cold Plasma Treatment, Micro fluidization, Infrared Spectroscopy, Membrane Microfiltration, Nitrate and Lysozyme addition, and high-pressure processing (HPP) also known as Pascalisation. But these new technologies and mechanisms could also leave consumers with milk whey proteins negatively affected in new unforeseen ways. HPP does appear to denature milk whey proteins including beta-lactoglobulin. Countries such as Germany have shown that raw unpasteurized milk can be produced with a similar level of hygiene as pasteurized milk by following stricter hygiene standards, perhaps this is the least complicated and ideal avenue [4,5].

CONCLUSION

This review highlights that raw milk does hold some potential in positively modulating some immune-related outcomes and warrants further study. Whey proteins that are undamaged by heat also appear to hold potential in positively modulating allergenic and infectious diseases. These proteins likely work through the regulation of CD14 function and CD4+ cell activation as well as through more complex epigenetic mechanisms. Given that allergenic diseases are a growing problem and pose a large burden economically on the healthcare system, the intersection of unpasteurized milk and whey protein deserves additional attention. Moreover, this review highlights the diminished safety concerns associated with raw unpasteurized milk due, in part, to improvements in sanitation, refrigeration, and the overall awareness of microbes and their sources. Milk safety should be re-evaluated and the risks that remain should be targets for further mitigation by alternative practices that do not include pasteurization allowing for retention of native protein structures which may influence a variety of health outcomes.

REFERENCES

1. Nate Anderson (n.d.). Overview of FDA Regulations and Process Validation Considerations. United States Department of Agriculture.
2. Bozoglu TF, Erkmen O. (2016). Food Microbiology: Principles into Practice. John Wiley & Sons.
3. Centers for Disease Control and Prevention. (2022). Food Safety. Legal Status of the Sale of Raw Milk and Outbreaks* Linked to Raw Milk, by State. 2013–2018.
4. de Klerk JN, Robinson PA. (2022). Drivers and hazards of consumption of unpasteurized bovine milk and milk products in high-income countries. PeerJ. 10: e13426.
5. Alegbeleye OO, Guimarães JD, Cruz AG, Sant'Ana AS. (2018). Hazards of a 'healthy' trend? An appraisal of the risks of raw milk consumption and the potential of novel treatment technologies to serve as alternatives to pasteurization. Trends in Food Science & Technology. 82: 148-166.
6. Heckman JR. (2019). Securing fresh food from fertile soil, challenges to the organic and raw milk movements. Renewable Agriculture and Food Systems. 34: 472-485.
7. Loss G, Depner M, Ulfman LH, van Neerven RJ, Hose AJ, et al. PASTURE study group (2015). Consumption of unprocessed cow's milk protects infants from common respiratory infections. The Journal of Allergy and Clinical Immunology. 135: 56-62.
8. Lucey JA. (2015). Raw milk consumption: risks and benefits. Nutrition Today. 50: 189.
9. International Dairy Foods Association. (n.d.). Pasteurization.
10. Brick T, Hettinga K, Kirchner B, Pfaffl MW, Ege MJ. (2020). The beneficial effect of farm milk consumption on asthma, allergies, and infections: from meta-analysis of evidence to clinical trial. The Journal of Allergy and Clinical Immunology: In Practice. 8: 878-889.
11. Chen D, Li X, Zhao X, Qin Y, Wang J, Wang C. (2019). Comparative proteomics of goat milk during heated processing. Food chemistry. 275: 504–514.
12. Loss G, Apprich S, Waser M, Kneifel W, Genuneit J, et al. GABRIELA study group (2011). The protective effect of farm milk consumption on childhood asthma and atopy: the GABRIELA study. The Journal of Allergy and Clinical Immunology. 128: 766-773.e4.
13. Abbring S, Hols G, Garssen J, van Esch B. (2019). Raw cow's milk consumption and allergic diseases - The potential role of bioactive whey proteins. European Journal of Pharmacology, 843: 55-65.
14. Bode L, McGuire M, Rodriguez JM, Geddes DT, Hassiotou F, et al. (2014). It's alive: microbes and cells in human milk and their potential benefits to mother and infant. Advances in Nutrition. 5: 571–573.

15. Sozańska B. (2019). Raw Cow's Milk and Its Protective Effect on Allergies and Asthma. Nutrients. 11: 469.
16. Loss G, Bitter S, Wohlgensinger J, Frei R, Roduit C, PASTURE study group, et al. (2012). Prenatal and early-life exposures alter expression of innate immunity genes: the PASTURE cohort study. The Journal of Allergy and Clinical Immunology. 130: 523-530.e9.
17. Abbring S, Wolf J, Ayechu-Muruzabal V, Diks MAP, Alhamwe BA, et al. (2019). Raw Cow's Milk Reduces Allergic Symptoms in a Murine Model for Food Allergy-A Potential Role For Epigenetic Modifications. Nutrients. 11: 1721.
18. Dos Santos Morais R, Gaiani C, Borges F, Burgain J. (2020). Interactions microbe-matrix in dairy products.
19. Chai C, Oh S, Imm JY. (2022). Roles of Milk Fat Globule Membrane on Fat Digestion and Infant Nutrition. Food science of animal resources. 42: 351–371.
20. Michalski MC, Januel C. (2006). Does homogenization affect the human health properties of cow's milk?. Trends in Food Science & Technology. 17: 423-437.
21. Michalski MC. (2007). On the supposed influence of milk homogenization on the risk of CVD, diabetes and allergy. The British journal of nutrition. 97: 598–610.
22. Langer AJ, Ayers T, Grass J, Lynch M, Angulo FJ, et al. (2012). Nonpasteurized dairy products, disease outbreaks, and state laws-United States, 1993-2006. Emerging infectious diseases. 18: 385-391.
23. Sebastianski M, Bridger NA, Featherstone RM, Robinson JL. (2022). Disease outbreaks linked to pasteurized and unpasteurized dairy products in Canada and the United States: a systematic review. Canadian Journal of Public Health = Revue Canadienne de Sante Publique, 113: 569–578.
24. Berge AC, Baars T. (2020). Raw milk producers with high levels of hygiene and safety. Epidemiology and Infection. 148: e14.
25. Centers for Disease Control and Prevention. (2018, November 5). Estimates of Foodborne Illness in the United States.
26. Good M, Bakker D, Duignan A, Collins DM. (2018). The history of in vivo tuberculin testing in bovines: tuberculosis, a "One Health" issue. Frontiers in Veterinary Science. 5: 59.
27. World Health Organization. (2023, April 21). Tuberculosis.
28. Dida K. (2021). Advances in Dairy Research (Pasteurization). Annals of Biological Sciences.
29. Fitzgerald C. (2015). Campylobacter. Clinics in Laboratory Medicine. 35: 289-298.
30. Lanata CF, Mendoza W, Black RF. 2002. Improving diarrhoea estimates. Geneva: World Health Organization.
31. Christidis T, Pintar KDM, Butler AJ, Nesbitt A, Thomas MK, et al. (2016). Campylobacter spp. prevalence and levels in raw milk: a systematic review and meta-analysis. Journal of food protection. 79: 1775-1783.
32. Mueller M, Tainter CR. (2023). Escherichia coli Infection. [Updated 2023 Jul 13]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. multiple-drug-resistant Salmonella Enteritis from raw milk. J. Am. Med. Assoc.
33. Samuel Mohammed Chekabab, Judith Paquin-Veillette, Charles M. Dozois, Josée Harel. (2013). The ecological habitat and transmission of Escherichia coli O157:H7, FEMS Microbiology Letters. 341: 1-12.
34. Centers for Disease Control and Prevention. (2014). E. coli (Escherichia coli).
35. Stasiewicz MJ, Martin N, Laue S, Gröhn YT, Boor KJ, et al. (2014). Responding to bioterror concerns by increasing milk pasteurization temperature would increase estimated annual deaths from listeriosis. Journal of food protection. 77: 696-712.
36. Sampedro F, Pérez-Rodríguez F, Servadio JL, Gummalla S, Hedberg CW. (2022). Quantitative risk assessment model to investigate the public health impact of varying Listeria monocytogenes allowable levels in different food commodities: A retrospective analysis. International Journal of Food Microbiology. 383: 109932.
37. Ehuwa O, Jaiswal AK, Jaiswal S. (2021). Salmonella, Food Safety and Food Handling Practices. Foods. 10: 907.
38. Centers for Disease Control and Prevention. (2023). Salmonella.

39. Baars T. (2013). Milk consumption, raw and general, in the discussion on health or hazard. Journal of Nutritional Ecology and Food Research. 1: 91-107.
40. Tremonte P, Tipaldi L, Succi M, Pannella G, Falasca L, et al. (2014). Raw milk from vending machines: Effects of boiling, microwave treatment, and refrigeration on microbiological quality. Journal of Dairy Science. 97: 3314-3320.
41. Centers for Disease Control and Prevention. (2022, January 28). Raw Milk Questions and Answers.
42. Bovbjerg ML, Waite-Cusic JG, Häse CC, Poulsen KP. (2018). Knowledge, attitudes and practices regarding raw milk consumption in the Pacific Northwest. Food Protection Trends. 38: 104-110.
43. Washington State Department of Health. (n.d.). Raw Milk.
44. Julia V, Macia L, Dombrowicz D. (2015). The impact of diet on asthma and allergic diseases. Nature Reviews Immunology. 15: 308-322.
45. Enilari O, Sinha S. (2019). The global impact of asthma in adult populations. Annals of Global Health. 85.
46. Mummah S, Oelrich B, Hope J, Vu Q, Gardner CD. (2014). Effect of raw milk on lactose intolerance: a randomized controlled pilot study. The Annals of Family Medicine. 12: 134-141.
47. Lluis A, Depner M, Gaugler B, Saas P, Casaca VI, et al. (2014). Protection Against Allergy: Study in Rural Environments Study Group (2014). Increased regulatory T-cell numbers are associated with farm milk exposure and lower atopic sensitization and asthma in childhood. The Journal of Allergy and Clinical Immunology. 133: 551–559.
48. Bieli C, Eder W, Frei R, Lauener R, Martinez FD, et al. (2007). A polymorphism in CD14 modifies the effect of farm milk consumption on allergic diseases and CD14 gene expression. The Journal of allergy and clinical immunology. 120: 1308-1315.
49. Boutinaud M, Jammes H. (2002). Potential uses of milk epithelial cells: a review. Reproduction Nutrition Development. 42: 133-147.