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Got milk? Understanding the farm milk effect in allergy and asthma prevention

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Cow's milk is a major component of most of our diets, but concerns about its ingestion have been in and out of public health dialogues for decades. Raw milk has long been associated with numerous foodborne illnesses and outbreaks due to enteric and opportunistic bacteria such as *Brucella*, *Salmonella*, *Listeria monocytogenes*, *Yersinia*, *Campylobactor* species, *Staphylococcus aureus*, and *Escherichia coli* species.[1,2] *Mycobacterium bovis* infection was transmitted to humans following drinking unpasteurized milk from infected cows, causing tuberculosis and scrofula.[3] Pasteurization, in which milk is heated to 161°F for at least 15 seconds and then cooled, was intended to reduce or eliminate the microbial content, thus decreasing the risk for serious bacterial infections and prolonging the shelf life.[4] Since the 1920s, universal pasteurization of milk and milk products has lessened significantly the incidence of these serious infections.[3,5] At the start of the obesity epidemic in the United States in the 1980s, milk was drawn into the public spotlight when the fat in whole milk was considered partly responsible for weight gain and the associated metabolic and cardiovascular complications. When the 1995 US Department of Agriculture guidelines recommended switching from whole milk to reduced-fat milk,[6] consumption of whole milk plummeted in favor of low-fat varieties.

Despite these extensive public health measures, consumer interest in raw, unprocessed whole milk has been rising in recent years,[7,8] boosted by lay organizations endorsing its possible health benefits.[9] Recently, several reports have linked the ingestion of raw milk to atopic disease and asthma prevention.[9–15] Mechanistic studies have implicated greater exposure to

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fatty acids and oligosaccharides in cow's milk, and altered epigenetic regulation and function of several genes and cytokines, particularly in the pregnant mother and young child, related to regulatory T-cell function and allergy.[10,12,16,17] Two articles in this issue of the *Journal*[18,19] now attempt to offer further insight into possible causes of the observed asthma-protective effects of raw milk.

The first article by Brick et al[18] focuses further on effects of milk's fatty acid content and modes of processing on asthma development in the Protection Against Allergy: Study in Rural Environments birth cohort of 5 European countries. Consumption of unprocessed farm milk (overall fat content 4.0%) when compared with shop milk, of high-fat milk (>3.5%) compared with low-fat milk, and of unprocessed compared with boiled milk was associated with lower asthma rates at age 6 years. The protective effect of farm milk when compared with shop milk was more prominent by age 6 years when compared with age 1 year. The protection of high-fat milk trended most robustly among children with FEV_1 above the median or with a positive bronchodilator response.[18] Furthermore, ingestion of higher levels of ω-3 polyunsaturated fatty acids (ω-3-PUFAs), which are present at higher levels in unprocessed farm milk, was associated inversely with asthma and C-reactive protein levels.[18]

Kirchner et al[19] focused more mechanistically on gene regulation and specifically whether microRNA (miRNA) components found in native cow's milk may be responsible for the asthma- or allergy-protective effect. Cow's milk derived from the same batches of native cow's milk was screened after different milk processing procedures that mimicked industrial processing, including separation/centrifugation resulting in a skim milk fraction and a fat fraction, homogenization of whole milk as well as pasteurization, ultra-heat treatment, and heat treatment for extended shelf life of whole milk without homogenization, for differentially expressed miRNAs important to human allergic immune pathways. Differential expression of 52 miRNAs species between pasteurized and ultra-heat treatment milk, and of 25 miRNA species between pasteurized whole milk and raw milk fat samples, was reported. Genes targeted by 3 or more differentially expressed miRNAs with respect to high heat treatment included prostaglandin-endoperoxide synthase 2S (cyclooxygenase-2), a regulator of arachidonic acid–derived eicosanoid synthesis and inflammation whose inhibitory activity can be induced by ω-3-PUFAs, IL-6, IL-13, IFN-γ, and IFNGR1. Signal transducer and activation of transcription 3-targeted miRNAs also were differentially expressed in pasteurized whole milk versus the fat fraction.[19]

Both of these articles have advanced our insights as to the possible mechanisms underlying the asthma-protective factor of farm milk, including implicating higher fat content and ω-3-PUFAs, and the altered activation of allergy genes found in cow's milk with homology to relevant human ones. However, Kirchner et al do not specifically focus on fat content of whole milk, but rather on differences in nonhuman RNA found in the fat fraction in the context of various processing methods. The inexact measures of actual milk consumption over the study period, inattention to asthma phenotypes, and influence of unmeasured confounders, such as early childhood exposure to secondhand cigarette smoke and allergens, may limit the significance and applicability of Brick et al's findings to other populations.

Still, when contextualizing the eventual public health impact of this research, we should realize that the serious risks of raw, unpasteurized milk for foodborne illness caused by bacteria, viruses, and parasites have not necessarily diminished.[1,2] In fact, a 2012 study by Mungai et al[2] actually revealed an increase in raw milk–associated outbreaks with the sale of raw milk. It is also important to recall that according to the World Health Organization, the obesity epidemic is worldwide and has yet to be resolved.[20] The evidence supporting dietary recommendations to reduce dairy-derived saturated fatty acids to curtail obesity has been mixed and arguably unconvincing, including perpetuating the ingestion of other high-fat products.[21,22] Others even have suggested that consumption of reduced-fat milk may increase paradoxically the odds for cardiovascular disease or cancer.[23]

These 2 studies in this month's issue underscore the undoubtedly potential benefits of raw milk with respect to preventing allergic disease. The looming question nonetheless remains whether these prospective benefits are worth the immediate infection risk. Before we completely eschew raw whole milk, more novel research into extracting just the desirable components from raw milk, or developing finer processing methods to selectively remove pathogens while retaining the beneficial effects of raw milk, may be warranted. However, until such research is conducted, present safety concerns still warrant taking heed of policy statements put forth by the American Academy of Pediatrics, along with other national medical associations, the Food and Drug Administration, and the Centers for Disease Control and Prevention, endorsing the consumption of only pasteurized milk and milk products.[5] Although clearly no one would like to see continued perpetuation of childhood and adult obesity or the return of foodborne illnesses, these 2 studies ultimately may yield new paradigms about what may be healthy dietary practices or new research on preparing milk for safe consumption.

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