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How Compatible is Cow's Milk with the Human Immune System?

Mindy Knopfler

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Abstract

Cow's milk has been part of the human diet for at least 8,000 years and provides a rich source of proteins, lipids, vitamins, and minerals. Despite its longstanding importance in human nutrition, questions remain about how compatible cow's milk is with our immune system. Cow's milk allergy (CMA) is the most common form of food allergy in infants and children and cow's milk has been implicated in a number of immune-mediated disorders. Reviewing current research obtained through Google Scholar and Touro's library database on CMA and the potential role of cow's milk in systemic inflammation and autoimmunity reveals a tangle of contradictory findings and competing explanations. While current research does not indicate a significant connection between cow's milk and systemic inflammation in healthy adults or to Rheumatoid Arthritis, it does provide significant, if contested evidence for the role of cow's milk in Type I diabetes, multiple sclerosis, and Behcet's disease. These evolving findings must be considered when we evaluate the current nutritional guidelines on cow's milk.

Introduction

Cow's Milk in the Human Diet:

Humans are the only animals known to consume the milk of another species, a unique behavior that arose during the Neolithic Revolution. The end of the Younger Dryas coincided with a transformation of human subsistence patterns around the world. Populations of hunter-gatherers became more sedentary and experimented with the domestication of plants and animals. The first cattle were domesticated from wild aurochs (*Bos primigenius*) over 10,000 years ago, in regions that are part of present-day Turkey and Pakistan (McTavish et al. 2013). There is disagreement about when cattle were first exploited for milk production. The "secondary products revolution" theory, popular during the 1980s and 1990s, held that Neolithic people did not consume dairy products until the fourth millennium BCE, despite much earlier advances in domestication (Sherratt, 1983; Greenfield et al., 1988). Recent evidence has pushed that date back as far as the 9th millennium BCE, when human beings were still "stock-keeping hunter-cultivators" (Vigne and Helmer, 2007). Residue from pottery shards suggests that milk products were widely consumed in Southwestern Asia and Southeastern Europe by the seventh millennium BCE (Evershed et al. 2008).

Since it was first consumed during the Neolithic period, cow's milk has been an essential dietary staple for numerous populations around the globe and has developed an evolving cultural significance. On the Indian subcontinent, cows have been revered for thousands of years and their milk is used for ritual purification as well as nutrition (Simmons, 1974). Ancient Norse mythology tells of how the first creature, Ymir, was sustained by milk from the sacred cow Auðumbla (Haug, Høstmark, and Harstad 2007). In Medieval Europe, cow's milk was venerated as a spiritual substance, embodying the divine rhythms of nature; during the Renaissance it was celebrated for its taste and health giving properties, with folk remedies citing it as a cure for everything from ulcers to epilepsy (Valenze, 2011). Milk consumption was transformed by two factors in the 19th century: an improved - transportation system, which aided in the delivery

of fresh milk from local farms to cities, and the development of pasteurization, which helped curb the very serious problem of milk-borne disease (Wilson, 1943; Atkins, 1978). These two advances made cow's milk more safe and convenient than ever before and guaranteed its central place in the Western diet. Today cow's milk and dairy products are an almost ubiquitous component of human nutrition, accounting for 14% of the caloric intake in developed countries (Bordoni et al., 2015). Global milk production amounted to an estimated 784 million tons in 2013, or 100 L of milk per year per person (Bordoni et al., 2015). This massive consumption occurs despite the fact that a substantial majority of the world's adult population is deficient in the lactase enzyme and may experience digestion issues with dairy (Lomer et al. 2008).

The Economics of cow's milk in the United States:

Cow's milk is a major economic commodity in the United States. A 2002 survey estimated that the dairy industry accounts for \$140 billion in economic output, \$29 billion in household earnings, and more than 900,000 jobs (Cryan, 2004). The U.S. Department of Agriculture estimates that domestic cow's milk production will reach a record 208.7 billion pounds in 2015 ("Dairy Farmers at the Barricades," 2015).

Chemistry and Nutrition of Cow's Milk:

Cow's milk is complex mixture of lipids, proteins, bioactive peptides (e.g. immunoglobulin, cytokines, and enzymes), amino acids, vitamins and minerals. The sugars (primarily lactose) and most minerals are dissolved in solution, the lipids are emulsified in globules, and the proteins are suspended in colloidal dispersions (Huang et al. 2007). About 80% of the proteins in cow's milk are caseins, which form complexes with calcium and phosphate (Huang et al. 2007). Although the composition of cow's milk can vary with the age, breed, nutrition, and stage of lactation of the cow, on average, a cup of milk (244 grams) provides 146 calories, 7.9 grams of fat (4.6 saturated), 7.9 grams of protein, 276 milligrams of calcium, 349 milligrams of potassium, 222 milligrams

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of phosphorous, 249 IU of Vitamin A, and 97.6 IU of Vitamin D (USDA, 2015). cow's milk is an important dietary source of the cis9, trans 11 isomer of conjugated linoleic acid and glutathione (Huang et al., 2012).

Allergy, Autoimmunity, and the Hypothetical Role of "Leaky Gut"

The human immune system is an enormously complex collection of structures and processes that protects the body against harm by pathogens. Immunity operates at a number of levels. The skin and mucosal membranes are the first line of protection, acting as a physical and chemical barrier to invaders. The second level of defense is the innate immune system, in which macrophages and neutrophils of the innate immune system provide a robust, but non-specific defense against pathogens, including the cytokine-mediated inflammatory response. Finally, the adaptive immune system provides a targeted response to specific pathogens. It is divided into humoral immunity, mediated by B lymphocytes and their antibodies, and cell-mediated immunity, mediated by T lymphocytes. (Hall, 2016)

Allergy refers to an inappropriate immune response to a harmless substance. Most allergies are mediated by the IgE antibody, which is secreted by B-cells in response to antigens binding mast cells and basophils until a second exposure. Autoimmunity refers to an immune response against the body's own cells and tissues. There are two classical models for the pathogenesis of autoimmune disorders (Fasano, 2012). According to the "molecular mimicry" model, certain microbial antigens resemble self-antigens to a degree that the immune system cross-reacts with the latter and targets them for destruction. In the "bystander effect" model, microbes directly damage tissues, leading to the exposure of internal self-antigens that the immune system interprets as foreign. These two models are continuously being expanded and revised with ongoing research and may represent complementary descriptions of the multifaceted phenomenon of autoimmunity. A third, more tentative hypothesis involving the gut is presented below.

The role of the gut in immune disorders is a fascinating new area of research. While we often think of the skin as great primary barrier of our immune system, the intestines are actually the largest surface in the body, amounting to an area more than 200 times greater than the skin (Hollander 1999). Maintaining a proper balance between immune tolerance and sensitivity over this vast surface area is an exceedingly complicated task, and the failure of such regulation is associated with allergy and various forms of autoimmunity (Dejaco et al. 2006; Vitaliti et al. 2012). cow's milk is often the first foreign substance that an infant's gut will encounter and the first serious challenge to immune homeostasis in the intestines. Some researchers have suggested

that there is a group of individuals who are especially prone to immune complications from food antigens, due to excessive permeability of the intestines and abnormal microbiota (Perrier, C and Corthésy, 2010; Fasano 2012). These individuals, the theory goes, are not only at a greater risk for conventional food allergies but may also find that various foods which are well tolerated by the general populations contribute to immune dysfunction. While some promising research has been conducted into the contributions of intestinal barrier dysfunction to immune-mediated disorders (De Kort, et al. 2011), and excessive intestinal permeability is particularly well attested in the pathogenesis of celiac disease (Hollander, 1999), the general role of "leaky gut" in autoimmunity remains ill-defined and controversial. While this paper does not intend to assess the validity of this hypothesis, a growing body of research on diet, allergy, and immune disorders suggests the need for an evolving paradigm of the role of the gut in autoimmunity.

Purpose:

This paper will review current research on cow's milk and the human immune system. It will begin by exploring the prevalence, natural history, and immunopathogenesis of cow milk allergies (CMA). It will then examine research on the possible contributions of cow's milk to systemic inflammation in people without clinically defined CMA. Finally, it will assess the possible link between the consumption of cow's milk and a number of immune-mediated disorders. All research into the role of cow's milk in non-immune-mediated disorders, including lactose intolerance, has been excluded. The discussion will examine the factors affecting research into the health of cow's milk and assess nutritional guidelines in light of current findings.

Methods

All research articles for this paper were obtained by searching Google Scholar and Touro's Library Database.

Literature Review

Definition, Prevalence, and Natural History of Cow's Milk Allergy (CMA):

Cow's milk allergy (CMA) is an adverse immune reaction to one or more components of cow's milk. CMA is the most common food allergy in infancy and childhood, occurring in 2%-3% of children in the developed world, (Ahrens et al., 2012). It is typically classified into IgE-mediated allergies and non-IgE-mediated allergies; the former are more common and almost always resolve during childhood and the latter persist in a small percentage of adults (Crittenden and Bennett, 2005). One study of over 4,000 children with IgE-mediated CMA found total resolution to be 19% by age 4 years, 42% by age 8 years, 64% by age 12 years, and 79% by 16 years (Skripak, et al., 2007). CMA can cause a range of reactions, including diarrhea and vomiting,

loss of blood into the intestines, respiratory tract infection, and anaphylaxis (Freier and Kletter, 1970). A study of food allergies in Britain during the 1990s found that CMA accounted for greatest number of fatalities (Macdougall et al., 2002). Some of the symptoms of CMA may initially be confused with lactose intolerance or Hirschsprung's disease (Kubota et al. 2006). In order to make the diagnosis a physician must observe "a definite disappearance of symptoms after elimination of cow's milk from the diet, recurrence of identical symptoms after one cow's milk challenge, disappearance of symptoms after re-elimination of cow's milk, and exclusion of lactose intolerance and coincidental infections" (Sprikkelman et al. 2000).

Immunopathogenesis of CMA:

Research into the immunopathogenesis of CMA is ongoing and its mechanisms are not fully understood. The major allergic components of milk have been identified as four proteins in the casein fraction (as1-, as2-, b-and k-casein) and two proteins in the whey family, although there is great heterogeneity among the allergenic epitopes of these proteins (Ahrens et al., 2012). The mechanisms of CMA are typically classified into IgE-mediated and non-IgE-mediated.

IgE-mediated CMA occurs in two stages (Vitaliti et al. 2012; Brandtzaeg 2001; Beyer et al. 2002). When an allergic child first consumes cow's milk, the immune system undergoes a process of "sensibilization." First, antigen-presenting cells (APCs) consume milk particles and display allergenic fragments on their surfaces. Then 2 T helper (Th2) cells, which are insufficiently regulated by the immune system in CMA, come into contact with the allergen fragments and become activated. The Th2 cells in turn activate B cells, which produce large amounts of antigen-specific IgE. IgE antibodies against cow's milk proteins are then secreted and bind to the surface of mast cells and basophiles. After this immune arsenal has been built up and the child again consumes cow's milk, the allergy moves to its "activation" phase. IgE associated with mast cells bind allergenic epitopes on milk proteins, triggering an intracellular cascade that culminates in the release of histamine, platelet activating factor, and other inflammatory mediators. Chatchatee et al. (2001) found that the presence or absence of two binding regions IgE (AA 69-78 and AA 173-194) can be used to predict whether an allergy will resolve in early childhood or persist.

Although many cases of CMA involve an IgE-mediated mechanism there are also many cases that do not present circulating IgE specific for cow's milk proteins. The immunopathogenesis of non-IgE-mediated CMA is more obscure and a number of mechanisms have been proposed. One theory suggests the reaction is mediated by Th1 cells, host immunity effectors that typically act against intracellular bacteria and protozoa and have

already been implicated in Type-I Diabetes (Lee et al., 2010; Zhu and Paul, 2008). Another theory points to interactions between T lymphocytes, mast cells, and neurons (Lee et al. 2010). Some individuals with CMA demonstrate both IgE-mediated and non-IgE-mediated reactions.

Research has implicated the dysfunction of Tregs, a subpopulation of T cells that modulate the immune system and maintain tolerance to self-antigens in both IgE-mediated and non-IgE-mediated reactions. The body must maintain a delicate balance between mucosal tolerance and hypersensitivity: too great a tolerance will allow dangerous antigens to accumulate in the body and too great a sensitivity will lead to indiscriminate immunization against harmless foreign particles. Tregs help to regulate this balance by secreting "tolerogenic cytokines" such as TGF-beta 1 and IL-10. The resolution of CMA in children has been associated with the development of Treg cells. For example, Karlsson et al. (2004) gave milk to 21 children who had been following an elimination diet for at least two months and found that those who had outgrown the allergy had higher levels of circulating CD4(+)CD25(+) T cells.

Looking Beyond CMA:

The prevalence of CMA is well established and research has increasingly shed light on its mechanisms, but what about the impact of cow's milk on the immune systems of people without clinically defined CMA? In some quarters dairy has been accused of having "pro-inflammatory" properties and implicated as a cause or aggravating factor in a number of immune-mediated conditions. Some health resources have advised that people cut out dairy entirely. The rest of this paper will examine some of the research on these claims about cow's milk and the immune system.

Cow's milk and Systemic Inflammation:

Systemic inflammation is caused by the release of pro-inflammatory cytokines from immune-related cells and the chronic activation of the innate immune system. It is a risk factor for atherosclerosis, metabolic syndrome, type 2 diabetes, cardiovascular diseases, and other conditions (Labonte et al. 2013). The causes of systemic inflammation are notoriously difficult to isolate, and there has been disagreement over whether cow's milk-based dairy can contribute to systemic inflammation in healthy adults.

Although some epidemiological studies have found a correlation between dairy consumption and biomarkers of inflammation, the overwhelming majority of controlled studies have found a neutral or anti-inflammatory effect (Bordoni et al. 2015). Nestel et al. (2012) looked at four different full-fat dairy foods and found that they did not increase eight circulating biomarkers

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related to inflammation. Schmid et al. (2015) found no significant difference in inflammatory markers after subjects ate a high-fat dairy and high-fat non-dairy meal. Several studies have even reported an inverse correlation between dairy consumption and inflammation. Panagiotakos et al. (2010) looked at the concentrations of the inflammatory factors CRP, IL-6, and TNF- α in individuals consuming more than 14 servings of dairy products a week and found them to be 29%, 9%, and 20% lower than those in individuals consuming less than 8 servings a week. Esmailzadeh and Azadbakht (2010) studied 486 healthy women aged 40-60 years found that subjects on a low-fat dairy diet had lower circulating levels of IL-6 and sVCAM-1 than the control. Labonte, et al. (2013) conducted a meta-analysis of 9 studies and found no significant relationship between dairy consumption and systemic inflammation. Finally, Bordoni et al. (2015) conducted the largest meta-study to date (52 human studies) and found that the consumption of dairy products is generally associated with anti-inflammatory effects in humans. Of particular note was that none of the studies using low-fat dairy products indicated a pro-inflammatory response. Taken together, these findings suggest that the association between cow's milk and systemic inflammation in healthy adults is largely unfounded.

Cow's milk and Immune-Mediated Diabetes:

Diabetes mellitus type 1 (T1D) is a form of diabetes mellitus that results when T-cell-mediated autoimmunity destroys the insulin-producing beta cells of the pancreas. Although this form of diabetes has a strong genetic basis, it is also influenced by environment. The precise environmental triggers of T1D are a matter of ongoing research and debate, with some suggesting the role of particular antigens (Knip and Simell, 2012). The literature appears to be split on the question of whether cow's milk has a role in the pathogenesis of T1D.

The controversy began in 1984, when Borch-Johnsen et al. suggested there was an inverse-correlation between T1D and the duration of breast-feeding. Although some subsequent studies cast doubt on this link, researchers began to explore early exposure to cow's milk (as opposed to discontinued feeding by human milk) as a possible cause. Following this hypothesis, Scott (1990) looked at consumption of milk per-capita and found a significant positive correlation between consumption of unfermented milk protein and incidence of T1D in data from various countries. More precise epidemiological studies soon followed, such as a study of 690 T1D children in Finland, which found that children were 1.5 times more likely to develop T1D if they were exposed cow's milk early in life (Virtanen et al. 1993). The first meta-analyses showed a modest, but significant increase of diabetes in children who were exposed to cow's milk before the age of 3 months (Gerstein, 1994; Norris & Scott, 1996). Some recent studies have expanded on these findings. Kinip et al.

(2010) reported on the Trial to Reduce IDDM in the Genetically at Risk (TRIGR), in which Finnish researchers assigned 230 infants to drink either conventional cow's milk-based formula or a dairy-free alternative. Ten years later, children who were fed the non-dairy alternative exhibited 50-60% fewer markers of β -cell autoimmunity. Villagrán-García et al. (2015) studied 150 children and found that those who began drinking cow's milk in early childhood were four times more likely to have T1D, one of the most dramatic results yet reported.

Several mechanisms have been proposed for a possible link between a child's early exposure to cow's milk and T1D. One theory suggests that cow's milk proteins may mimic autoantigens of the pancreas beta cells, leading to the autoimmune destruction of these cells (Kolb & Pozzilli, 1999). Another suggests that early exposure to cow's milk leads to elevated antibodies against bovine insulin and subsequent immunization against human insulin (Vaarala et al., 1999). A more recent proposal involves beta-lactoglobulin, a whey protein found in cow's milk but not in human milk, and glycodelin, a near-homologue that regulates T-cells. According to this theory, some infants produce antibodies against beta-lactoglobulin, which cross-react with glycodelin and allow autoreactive T-cells to proliferate (Goldfarb, 2008).

Although some epidemiological studies have supported a link between cow's milk and T1D, and a number of plausible mechanisms have been proposed, there is also conflicting evidence. For example, Savilahti and Saarinen (2009) found that infants who were exposed to cow's milk very early in life were actually slightly less likely to develop T1D before age 8 (although the discrepancy disappeared by age 11.5). Karlsson et al. (2001) studied 30 children with T1D and 18 healthy, age-matched children and found no difference in their Th1- and Th2-like immune response to cow's milk proteins, suggesting that cow's milk antigens do not have a significant role pathogenesis. Some researchers have argued that the existence of populations in which there is a high level of dairy consumption and a low rate of T1D disproves any connection (e.g. Iceland and Zealand), although these discrepancies have also been explained by the fact that protein content can vary by region (Thorsdottir, 2000). Some have suggested that only cow's milk with A1-type casein is contributing factor to T1D (Laugensen and Elliot, 2003), while others argue that the apparent differences between A1-type and A2-type milk are really due to differences in sun-exposure and vitamin D production (Merriman, 2009). Ultimately, the relationship of cow's milk and T1D remains a matter of debate, despite some epidemiological evidence supporting a causal link and the elaboration of a number of plausible mechanisms.

Cow's milk and Multiple Sclerosis:

Multiple sclerosis (MS) is a chronic inflammatory disease in

which the myelin sheaths that insulate the central nervous system are damaged. A connection between cow's milk and multiple sclerosis (MS) has long been debated. One of the first large scale studies on the question was Malosse et al. (1992), which examined the relationship between MS prevalence and dairy product consumption in 27 countries and 29 populations all over the world. The study found there was strong correlation between MS prevalence and the consumption of liquid cow's milk, but not between MS and more processed forms of dairy, like cheese. Some researchers have proposed that molecular mimicry between CNS myelin antigens and cow's milk proteins could explain the relationship. According to this theory, the IgE targeted to the cow's milk proteins cross-react with the myelin and lead to damage of the nerve cells (Ahrens et al., 2012). It has been suggested that the failure of T cells to regulate auto-reactive CD4+ and CD8+ cells has a role in the disease (Viglietta et al., 2004). Given the possible role of autoreactive T cells in MS, the mechanism proposed by Goldfarb (2008) for T1D may also be plausible here. Particularly interesting in this respect are studies linking the autoimmunity of T1D and MS (Winer et al., 2001).

Some studies have questioned the link between cow's milk and MS. Ramagopalan et al. (2010) examined 6638 cases of MS in Canada and found no significant difference in the percentage who reported childhood CMA, an odd finding if there is a significant cross-reaction between cow's milk proteins and myelin. Ashtari et al. (2012) examined 48 healthy subjects and 48 subjects with MS and found no difference in the detection of cow's milk-specific IgE. Given these contradictory results, the role of cow's milk in MS remains uncertain.

Cow's milk and Bectet's Disease:

Bectet's disease (BD) is characterized by chronic, immune-mediated inflammation of the blood vessels, leading to skin rashes and lesions, optic atrophy, and ulcers of the mouth and genitals. Although the etiology of the disease is not fully known, there is strong evidence for the role of Th17 cells, adaptive immune cells that are also associated with MS and RA (Hatemi et al. 2012).

Research on cow's milk as a factor in Bectet's disease is currently very limited. Triolo et al. (2002) cited promising research on the relationship between cow's milk and immune-mediated conditions like T1D and MS as a basis for examining the role of cow's milk in BD. First, the study cultured lymphocytes from 16 patients with BD and eight normal controls in the presence of β -casein, β -lactoglobulin, and a number of controls. ELISA revealed that when cultured with milk proteins lymphocytes from BD subjects produced significantly more IFN γ , a cytokine associated with auto-inflammation, than lymphocytes from the controls. Then the study used ELISA to analyze the serum antibody

levels of 46 patients with BD and 37 healthy controls and found significantly higher levels of anti- β -casein and anti- β -lactoglobulin antibodies in the subjects with BD.

These results suggest some correlation between BD and sensitivity to milk proteins, but do not define a causal order. The authors suggest that milk proteins may damage the gut and lead to immune dysfunction and offer two possible mechanisms. First, the caseins in cow's milk may give rise to peptides that mimic opiates and bind T cells and macrophages, disrupting their function. Second, molecular mimicry between cow's milk proteins and self-proteins may lead to damaging cross-reactivity. These mechanisms are only speculative however, and there has been little research on the relationship between cow's milk and BD. The rarity of BD (approximately 0.1-7.5 /100,000 in Europe and the USA) makes epidemiological studies difficult to conduct (Zouboulis, 1999).

Cow's milk and Rheumatoid Arthritis:

Rheumatoid arthritis (RA) is a chronic inflammatory disorder that primarily affects the small joints in the hands and feet, leading to swelling, pain, and loss of mobility. cow's milk has sometimes been cited as a contributing factor to RA. Although dairy has been identified as an aggravating factor in individual cases of RA (Panush et al. 1986; Panush, 1990), larger studies have failed to find a connection between the disease and the consumption of cow's milk. Panush et al. (1983), for example, studied 11 subjects on a dairy-free diet and 15 subjects on a placebo diet and found no significant differences in rheumatologic or immunologic findings. The literature on diet-therapy for RA is not extensive and tends to dispute any connection between cow's milk and RA; however, there are indications that dairy may be an aggravating factor in a small percentage of cases.

Discussion

The Challenges of Studying cow's milk:

Determining the impact of cow's milk on the immune system is complicated by a number of factors. Allergic and autoimmune reactions are multifaceted and reflect a confluence of individual biochemistry, genetics, and environmental influences that is not fully understood. Milk itself is a complex mixture with numerous bioactive components, and its composition can vary by region. Moreover, the consumption of cow's milk is always part of a large, multivariable diet, making it hard to rule out confounding factors. Any interpretation of the evidence must be cautious given the enormous complexity of the variables.

Current Nutritional Guidelines for cow's milk:

The 2010 dietary guidelines authored jointly by the Department of Agriculture and the U.S. Department of Health and Human Services stress the importance of cow's milk and cow's milk-products as part of a healthy diet. The guidelines recommend 3 cups

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per day of fat-free or low-fat milk and milk products for adults and children over 9, 2.5 cups per day for children ages 4-8, and 2 cups for children ages 2 -3.

Assessment of Results:

Cow's milk is a vital staple of American nutrition, economy, and culture. This does not diminish the importance of continued research into the effects of cow's milk on human health. CMA is the most common form of allergy in childhood and can lead to serious complications. Beyond clinical CMA, cow's milk may impact the immune system in subtle, unexpected ways. Upon reviewing the evidence, there is no strong indication that cow's milk is a contributing factor to systemic inflammation in healthy adults or to RA. However, there is some significant, but contested evidence that it plays a role in the pathogenesis of T1D, MS, and Behcet disease. Currently, there is much we do not know. One theme emerging from the literature is the difficulty of drawing conclusions from epidemiological studies. Some epidemiological studies reveal a striking correlation between cow's milk and various immune disorders while others yield conflicting results. While prospective cohort studies offer obvious advantages over retrospective studies, they can still yield opposing findings, as evidenced by the large disagreement between Savilahti and Saarinen (2009) and Knip et al. (2010) over whether cow's milk is a risk factor for T1D. Such discrepancies suggest the need for further research and meta-analysis.

Additional Considerations and Conclusions:

The results are too messy and speculative to write off cow's milk as a "dangerous" food or to clear it of all suspicion. They do underscore the fact that we do not yet know enough about the bioactivity of cow's milk to rule out the possibility of detrimental effects on immune function. This uncertainty is compounded by recent findings that link cow's milk to prostate cancer and Parkinson's (Chen et al., 2007; Mandair et al., 2014). Numerous studies have questioned the traditional belief that consuming cow's milk improves bone health and some have even found that it increases risk of fracture (Michaëlsson K. et al. 2014; Feskanich et al. 2014). Although many of these findings are still questionable, taken together they may warrant a reconsideration of current guidelines, especially when people in developed nations generally can obtain calcium and other vital nutrients from alternative sources. Given the important place that cow's milk has held in human nutrition and culture for thousands of years, and the vital role it plays in the contemporary American economy, any shift in thinking about dairy might be difficult to achieve. Nevertheless, it is important to evaluate the evolving body of evidence without cultural or economic bias and arrive at nutritional guidelines on the basis of sound science alone.

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