In the 1950s, milk was hailed as "nature's perfect food" (1). However, American's once idyllic relationship with dairy products has gradually soured over the past 40 years. Although cow's milk continues to be lauded for its high content of calcium, phosphorus, and riboflavin, increasingly diet-conscious consumers have begun to shun whole milk because of its perceived high percentage of saturated fat and cholesterol. Perhaps the greatest strike against the consumption of dairy products, however, has been the scientific discovery of lactose intolerance and the widespread interpretation of this phenomenon within the cultural mainstream. Millions of Americans, convinced that they suffer from a deficiency of the lactase enzyme, restrict themselves to specialty dairy foods, self-medicate with lactase enzymes, or avoid milk products altogether.

While this has led to the development of a multi-million dollar industry in lactase enzymes and low- lactose dairy products; this has also had the unfortunate consequence of discouraging dairy product consumption at a time when nutritionists and health care professionals alike are beginning once again to advocate the beneficial aspects of dairy consumption. Osteoporosis, a disease characterized by low bone density, is increasingly becoming an issue of concern in the aging American population. Calcium has also been implicated as an agent in the prevention of other leading causes of morbidity and mortality such as hypertension and colon cancer (2). The 1994 NIH development conference, "Optimal Calcium Intake" increased recommendations for calcium intake and stated that recent studies show that "the optimal amount of calcium intake may be greater than the amount consumed by most Americans" (3). The authors also concluded that "the preferred source of calcium is through calcium-rich foods such as dairy products" (3).

Yet for many Americans, the ever-present worry of lactose intolerance encourages avoidance of these important, calcium-rich dairy products, and perhaps contributes to a less-than-optimal calcium intake. The average daily calcium intake for women 35-50 years of age in the United States is a mere 540 mg compared to current recommendations of 1,000 mg (4). Another study found that the mean daily consumption of calcium in the United States ranged from 500-600 mg, which compares unfavorably to current recommendations for adults and adolescents that range from 1000-1500 mg (5).

## Origins of the Lactose Intolerance Phenomenon

What is lactose intolerance, and why are Americans so concerned? Lactose, a carbohydrate found only in animal milk and milk derivatives, accounts for up to 30% of the caloric value of whole cow's milk (6). In order for lactose to be digested and absorbed, it must be hydrolyzed by the enzyme lactase, also described as B-D-galactosidase or lactase-phlorizin hydrolase, which is located in the brush border of the small intestine. Lactase hydrolyzes the dietary disaccharide lactose into the two monosaccharides glucose and galactose, which are then absorbed across the intestinal wall and into the blood stream for energy utilization.

If the hydrolysis of lactose in the small intestine is incomplete due to a deficiency or absence of the lactase enzyme, the undigested lactose remains in the gut lumen and is transported to the colon, where it is fermented by naturally occurring colonic bacteria into

fatty acids and various gases. These short-chain fatty acids are absorbed by the intestinal mucosa. The gases produced by fermentation, primarily hydrogen, carbon dioxide, and methane, may be consumed by the bacteria or absorbed across the mucosa into the bloodstream to be ultimately excreted via respiration. Depending on the balance between the production and removal of these fermentation products, gaseous symptoms such as abdominal pain, bloating, and flatulence may develop. When the delivery of lactose exceeds the fermentation ability of the bacteria, excess lactose remaining in the colon may result in osmotic diarrhea.

During infancy in mammals, when milk is the primary form of nourishment, levels of lactase are high except in rare cases of congenital defect. However, as Mendel and Mitchell demonstrated in 1907, levels of lactase are either absent or greatly diminished in adult mammals (7). In the mid-1960s, researchers found that 70% of black adults and 6-12% of Caucasian adults in the Baltimore area were unable to digest test doses of 50 g of lactose given in a water solution (8,9). This sparked rapid investigation into the area of reduced lactase activity with age, which was gradually found to be the genetic norm. Lactase activity appears to be sustained only in a majority of adults of Northern European descent.

Lactose intolerance is defined as an "inability to tolerate a standard or test dose of lactose without developing diagnostic biochemical changes with or without clinical signs and symptoms of bloating, flatulence, abdominal pain, and diarrhea" (6). The most commonly performed test measures increased breath hydrogen levels, which detects hydrogen produced by the fermentation of unhydrolyzed lactose by colonic bacteria. About 25% of adults in the United States and 75% of adults worldwide are estimated to be deficient in the lactase enzyme.

The scientific community was not alone in exhibiting an interest in lactose intolerance. These discoveries were widely reported in the lay press, along with the enthusiastic, although unproven conclusion that lactase deficiency directly resulted in the inability to digest dairy products. Scrimshaw and Murray described the situation as the "uncritical extrapolation of findings based on the administration of a large dose of lactose in water to the inability to consume milk and milk products without symptoms. In short, lactose intolerance to pharmacologic amounts of the dissolved sugar was often mistakenly equated with intolerance to milk in the diet" (6). It did not take long for members of the business community to capitalize on this newly discovered "need." In 1978, LactAID® began marketing lactase commercially in the form of liquid droplets that could be added to milk to pre-hydrolyze the offending lactose and achieve an advertised decrease in symptoms (10).

There is little doubt that the ingestion of the standard test dose of 50 g of lactose under fasting conditions often causes abdominal pain, diarrhea, bloating, and flatulence in lactase-deficient individuals. The combination of the large test dose — a lactose load equivalent to that found in one liter of milk — and the fasting conditions under which it is presented, which facilitates stomach emptying and increases small bowel transit time, rapidly overwhelms the response mechanisms of the bacterial flora and the ability of the

body to absorb fermentation products, leading to physiologic symptoms. However, there has been considerable controversy as to whether lactase-deficient individuals are affected by much smaller doses of lactose, such as that found in a glass of milk. One early, unblinded study suggested that the majority of people (59% of 44 men with lactose malabsorption) had appreciable symptoms after drinking only 240 ml (8 oz) of milk (11).

Recent Studies

More recent, carefully controlled, studies have called into doubt this and other early experiments that found symptoms after small doses of lactose. A critical 1995 experiment by Suarez, et al investigating the reactions of 30 people with self-described severe lactose intolerance came to a very different conclusion (12). The authors recruited 30 individuals who reported that they consistently had symptoms after ingesting less than 240 ml of milk. After testing the ability of the subjects to digest lactose through a breath hydrogen test, the researchers found that 21 of the subjects were deficient in the lactase enzyme. Surprisingly, the remaining 9 possessed the lactase enzyme. In a randomized, double blind crossover trial, each subject drank 240 ml of a test preparation of 2% milk daily with their usual breakfast for two one-week periods, refrained from consuming additional dairy products, and kept daily dietary and symptom logs. The subjects were given hydrolyzed milk (0 g lactose) for one week, and normal milk (12 g of lactose) sweetened with aspartame to approximate the sweeter taste of hydrolyzed milk. The non-lactose and full-lactose milks were indistinguishable on the basis of taste by independent observers. Suarez et al found that the 240 ml of normal milk was not associated with a significant increase in the severity of bloating, abdominal pain, or flatus. The authors concluded that people frequently misattributed a variety of abdominal symptoms to lactose intolerance, citing the "expectation of many of the subjects before the study that the distress caused by ordinary milk would preclude their completing the study" and reported that lactose-digestive aids or dietary restrictions were not necessary when lactose intake was limited to the equivalent of 240 ml of milk or less per day (12).

Another recent double-blinded study by Hertzler, et al looked directly at bacterial fermentation levels as well as reported symptoms under fasting conditions (13). Hertzler et al found that lactase-deficient individuals had only slightly increased breath hydrogen levels at a 6 g dose of lactose, indicating that bacterial fermentation did not occur until this level of lactose was reached. Furthermore, even though lactose was maldigested at this 6 g load, intolerance symptoms were not significantly different at this level of lactose from that observed with a 0 g lactose load, leading the researchers to conclude that lactose maldigestion does not necessarily result in the development of symptoms. The authors reported that "Lactose maldigesters should be able to tolerate foods containing small amounts of lactose, such as hard cheeses (which generally contain less than 2 g lactose per serving) and small servings of milk (120 ml = 6 g lactose)" (13). The researchers noted that although maldigestion and intolerance symptoms increased after consumption of lactose doses of 12 g or greater, these larger doses of lactose may still be well tolerated, particularly if consumed with other foods as in the Suarez study.

Still another recent study by Vesa et al found that there was no difference in the severity of reported symptoms between test doses of 200 ml of fat-free, lactose-free milk to which 0.5, 1.5, and 7 g of lactose had been added (14). In their randomized crossover, double-blinded study of 29 lactose maldigesters and 15 lactose digesters, subjects drank test milks after an overnight fast and recorded symptoms. The authors found no difference in the severity of reported symptoms between the test milks and the lactose-free milk in the group of maldigesters. One third of the lactose maldigesters did not experience symptoms from any of the test doses. From this, the researchers concluded that gastrointestinal symptoms in most lactose maldigesters are not induced by lactose when small amounts are included in the diet. Interestingly, a greater proportion of subjects experienced symptoms on the lactose-free milk than on either the 0.5 g or the 1.0 g lactose-loaded milks. The authors suggested that this might be the result of cultural or psychological influences: "[An] explanation is that the lactose-free milk was less sweet than the other milks. Because most lactose-intolerant subjects…are familiar with the sweet taste of lactose-hydrolyzed milk, which they tolerate well, the less sweet taste of the lactose-free milk may have influenced their symptoms" (14). The subjects' misperception of the less sweet, lactose-free milk as ordinary, lactose-containing milk may have biased their symptoms accordingly.

It seems apparent, at least from these carefully-controlled double-blind studies, that low levels of lactose (equivalent to that found in a glass of milk) presents few, if any, physiologic symptoms. Yet the publicity surrounding lactose intolerance has made consumers aware of the phenomenon, and the demand for low-lactose and lactose-free products has greatly increased in recent years (14). This possibly cultural sensitivity to lactose products is made even more apparent by the large percentage of individuals discovered in studies who consider themselves to be severely lactose intolerant despite their retention of the lactase enzyme and their ability to digest lactose. In their non-blinded study, Rosado et al investigated gastrointestinal symptoms after the oral ingestion of 360 ml of milk in 25 adults who claimed to be milk intolerant. Most of their subjects experienced some of their customary discomfort during the study. However, the degree of discomfort was similar for the 9 (36%) who proved to be true lactose maldigestors and the 16 (64%) who had flat breath hydrogen responses, indicating the retention of the ability to digest lactose (15). In other words, some subjects who were able to digest lactose, responded with the same subjective response as the lactase-deficient individuals.

## Explaining the Discrepancy: Psychological and Cultural Aspects of Lactose Intolerance

How can this discrepancy between patients' claims and the results of double-blinded trials be reconciled? An editorial accompanying the Vesa et al article posits one explanation. The authors observe that irritable bowel syndrome (IBS), a relatively common condition thought to be the result of disordered gastrointestinal motility or enteric nervous system dysfunction, by definition has no identifiable anatomical or biological abnormality to explain the typical bloating, pain, and bowel movement abnormalities. Lactose intolerance differs from IBS only in that it has an identifiable cause, namely the low levels of lactase. The authors write:

Humans abhor the existence of unexplained symptoms and IBS patients have an overwhelming desire to attribute their symptoms to an identifiable etiologic factor, usually some dietary intolerance. Although most patients are confident that they can identify the foods that aggravate their problem, it is not clear that this confidence is justified. Patients tend to focus on foods that have received extensive publicity as causes of abdominal distress, e.g., dairy products (lactose) (16).

Findings that lactase malabsorbers complain more frequently of abdominal symptoms during both treatment and control periods than control subjects suggests that subjects who believe themselves to be intolerant to small doses of lactose may in reality have an underlying symptomatic state such as IBS which they misattribute to lactose intolerance. The authors continue, "Intolerance to lactose is probably the most commonly implicated dietary cause of nonspecific abdominal symptoms that would, in the absence of lactose malabsorption, be attributed to IBS. The enormous publicity concerning lactose intolerance in lay publications has led to the self-diagnosis of this problem by a sizable fraction of the US population" (16).

"Proof" that lactose products are to blame may be established by patients via a temporal linkage between lactose ingestion and subsequent symptoms of bloating, gas, abdominal pain, or diarrhea. The widespread use of dairy products often allows for the ingestion of at least some lactose containing products before a symptomatic period. An apparent reduction in symptoms following the restriction of lactose products or the use of lactose digestive aids may provide conclusive evidence that the lactose-containing product is the offender. However, as Suarez and Levitt comment "the nonspecific symptoms of abdominal bloating and distention characteristic of IBS are very susceptible to the placebo effect associated with dietary manipulations or medications" (16).

Extrapolation from observations concerning the symptoms induced by the standard test dose of 50 g of lactose has led to the common belief that lactose, regardless of the dosage, is a potential cause of abdominal symptoms in susceptible individuals. This concept was supported by early, unblinded studies, which suggested that small doses of lactose, such as the amount in a cup of milk, caused symptoms in the majority of lactose maladigesters. However, more recent controlled studies using double-blinded techniques seem to provide conclusive evidence that small amounts of lactose up to the amount found in 240 ml of milk (12 g), if taken with other foods under normal dietary conditions, results in no apparent ill effects. Unfortunately, common misperceptions and advertising by the lactase-supplement companies may be encouraging Americans to avoid important dairy products and to attribute common indigestion symptoms to lactose intolerance.

These entrenched cultural perceptions may be difficult to correct. The market for reduced-lactose and lactose-free products continues to expand, in part as a result of vigorous advertising on the part of LactAID® and other manufacturers who currently market lactase tablets, lactase drops, and lactose-free or lactose-reduced milk, ice cream, cottage cheese, and hard cheeses. In 1996, LactAID® lactase tablets alone reached $350 million in gross sales (10). Newsletters and cookbooks extol the virtues of low-lactose diets and provide support for lactose-intolerant individuals, information on lactose-free

products, and low-lactose recipes. Although a brief flurry of publicity in the lay press surrounded the publication of the 1995 Suarez et al article, even physicians appeared to be largely unconvinced at the time, as the resulting commentary demonstrated. Two years later, the article seems to have been largely forgotten by the general public, except in Internet support groups where it continues to receive blistering anecdotal criticism. The more recent papers by Hertzler et al and Vesa et al have received little, if any, attention in the lay press.

In spite of the health benefits of increased calcium intake, individuals who believe themselves to be lactose intolerant have had little incentive to alter their opinions. Psychologically and emotionally, it is difficult to manage pain and discomfort, particularly if the cause is unknown. The belief, even if unfounded, that their gastrointestinal symptoms are the result of offending dairy products may perhaps give sufferers some degree of control over their disease. Irritable bowel syndrome patients may even derive actual benefit from managing their symptoms by avoiding lactose, even if the underlying cause is not lactase-deficiency, through the well studied placebo phenomenon.

Notwithstanding scientific evidence to the contrary, "the concept that modest doses of lactose can be tolerated with negligible symptoms is anathema to most individuals who perceive themselves to be lactose intolerant. Despite results of controlled studies to the contrary, these individuals adamantly maintain that small amounts of lactose cause symptoms" (16). Perhaps the most fascinating lessons that can be learned from this controversy lie not within the question of lactase deficiency and milk tolerance, but rather in observations concerning the cultural impact of scientific discovery and the mind-body connection between health and behavior.

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