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Lactose Intolerance: Clinical Symptoms, Diagnosis and Treatment

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ABSTRACT

This paper discusses the symptoms, diagnosis and treatment of lactase deficiency and the role of lactose in health, as well as presents a compilation of the research to date. When the lactase enzyme lactase is absent or deficient, unhydrolyzed lactose remains in the intestinal lumen and fluid osmotically driven into the intestine, increasing the volume and fluidity of the intestinal contents, allowing undigested lactose to enter the colon and to be fermented by colonic bacteria. The result can be cramping, flatulence, and diarrhea. However, not all individuals with lactose malabsorption experience symptoms. The mainstay of treatment of lactose intolerance is avoidance of all lactose-containing milk and milk-containing products, but it typically is not necessary. Yogurt is an option because the lactose it contains is partially digested by the bacteria present.

INTRODUCTION

Hippocrates first described lactose intolerance around 400 years BC, but its clinical symptoms have been recognized only within the last 60 years [1]. Lactose, the sugar that occurs naturally in milk and most dairy products, is a disaccharide that must be broken down into its component simple sugars (glucose and galactose) by the enzyme lactase, before it can be absorbed in the intestinal tract. Lactose is found only in mammalian milk (7.0 g/100 mL mature human milk, 4.7 g/100 mL in cow's milk) [2,3]. If lactase is low or absent, the undigested lactose moves into the large intestine, where it is fermented by millions of bacteria that reside there. The bacteria then release hydrogen and methane gasses, resulting in gastrointestinal symptoms. The condition, referred to as lactose intolerance, lactose malabsorption or lactase non-persistence, is extremely common and is due to either a relative or an absolute deficiency of the lactase enzyme. However, lactase deficiency is not synonymous with lactose intolerance, which affects individuals to varying degrees. Lactose intolerance is not a disease and not to be confused with cow's milk allergy. Only about 50% of lactase activity is needed for effective digestion of lactose [4,5].

Lactase Deficiency

The lactase enzyme is located in the brush border (microvilli) of the small intestine. The enzyme splits (hydrolyzes) dietary lactose into the monosaccharide's, glucose and galactose, for transport across epithelial cell membranes. When lactase is absent or deficient, unhydrolyzed lactose remains in the intestinal lumen and fluid is osmotically driven into the intestine, increasing the volume and fluidity of the gastrointestinal contents, allowing undigested lactose to enter the colon. The fermentation of lactose by colonic microflora produces lactic acid and hydrogen. In the presence of methanogenic bacteria, hydrogen and carbon dioxide combine together to form methane gas in the colon. Lactase deficiency

does not always translate into lactose intolerance. Only about 50% of lactase activity is needed for effective digestion of lactose [5]. The inability to either partially (hypolactasia) or completely digest lactose (alactasia) can be classified into four types. Lactase deficiency and lactose intolerance are not to be confused with cow's milk allergy, which is an abnormal response by the body's immune system to milk and products containing milk.

- Primary lactase deficiency
- Secondary lactase deficiency
- Developmental lactase deficiency
- Congenital lactase deficiency

Primary Lactase Deficiency

This type of lactase enzyme deficiency is the most common, affecting up to 70% of the world's population; some ethnic and geographic populations are affected more than others. While estimates vary, it's believed that as much as 80% of the African American population is affected, 53% of the Mexican-American population and about 15% of the white population. In Europe, prevalence varies from a low of about 2% in Scandinavia to about 70% in Sicily. Prevalence is about 70%-95% in Africa and is almost 100% in some Asian countries [6]. Lactase deficiency is the result of an autosomal recessive gene, which causes a gradual reduction in the activity of lactase, typically after two years of age and results in a drop below the critical threshold for the digestion of dietary lactose. Humans are the only known mammals that have sustained lactase activity after weaning [7].

Secondary Lactase Deficiency

A deficiency of the lactase enzyme can occur secondary to diseases of, or injury to the small intestine. Common examples include transient loss of lactase following acute gastroenteritis (especially in children) or after surgery involving the small intestine or as a result of chronic diseases, such as celiac disease or Crohn's disease. Generally, as the intestinal mucosa heals and symptoms improve, lactase production increases, but recovery can take months. Lactase is the brush border disaccharides most sensitive to, and the last to recover after, injury or illness [8].

Developmental Lactase Deficiency

This form of lactase deficiency may occur in infants born prematurely, but it typically lasts for a short period of time after birth. Developmental lactase deficiency occurs in premature infants (<34 weeks' gestation) and rapidly improves as the intestinal mucosa in the infant matures [9].

Congenital Lactase Deficiency

Congenital lactase deficiency is a severe, extremely rare gastrointestinal disorder, in which infants are born without the ability to produce the lactase enzyme (alactasia). It is characterized by neonatal-onset of watery diarrhea and failure to thrive [10], neither breastfeeding nor regular formula can be tolerated, as both contain high levels of lactose. Symptoms subside only when a lactose-free formula is provided. The disorder is the result of mutations in the gene coding for the lactase enzyme. Seven different genetic mutations that result in the disorder have been identified in Finland, [11] where the recessive gene is highly prevalent (1/35 are carriers) and the disorder is much more frequent than elsewhere in the world [10-12]. Among those affected, the activities of all other disaccharides remain normal.

Lactose as an important component of the normal diet

It has been suggested that the roles lactose and its derivatives play in the diet are misunderstood, underestimated and undervalued [13]. As a source of energy, lactose provides between 2 and 4 kcal/g, depending on the ingested dose, the combination with meals (solid or liquid) and the degree of intestinal lactase activity present [14]. It is an especially important energy source for infants; constituting about 40% of the total daily energy intake in fully breast-fed infants

[15]. Though it has been studied in detail in animals, there are very few studies that have examined the effect of lactose on growth in children and virtually none in undernourished children [15]. However, increasing lactose content in the diets of weanling piglets increased their food intake and weight gain, especially in very young pigs. Extrapolating these findings to humans would correspond to approximately 6 months of age in an infant [15,16].

Lactose is far more than a source of dietary energy [13]. It is not simply the carbohydrate found in milk best known for the inability of a significant portion of the adult population to digest it. The sugar and its derivatives appear to be valuable ingredients with a wide range of nutritional benefits. The disaccharide has a relatively low sweetening power—about 15-30% that of sucrose—a low glycemic index and prebiotic properties that promote the growth of beneficial bifidobacteria and enhance the absorption of calcium and magnesium [13,14].

These important functions of lactose may be undervalued, in part, because of a large percentage of the world's population has a reduced ability to digest it [13]. However, it is now widely accepted that lactose maldigestion in lactase-deficient populations should not be a reason to discourage or eliminate dairy consumption with its rich lactose content [13].

Therapeutic Effects of Lactose

Undigested Lactose as a Prebiotic: Lactose appears to fit the well-accepted criteria set by Gibson and Roberfroid for what constitutes a prebiotic, [17,18] and it is now clearly established that regular lactose consumption in dairy products influences intestinal microbial flora [19]. It may promote gut health by increasing the growth of non-H₂-producing lactose-fermenting bifidobacteria, which are increased in the presence of undigested lactose [19].

Lactose that escapes digestion not only serves as a substrate for the intestinal flora, favoring the growth of bifidobacteria and lactobacilli, it is also associated with the formation of Short Chain Fatty Acids (SCFA), acetate, propionate and butyrate. These SCFAs can be taken up by epithelial cells or can be used by the microbiota or excreted in the feces [20]. The SCFAs have been demonstrated to have a protective effect in the colon [21,22]. These fatty acids lower the luminal pH and decrease formation of toxic secondary bile acids. Stimulation of sugar-metabolizing enzymes by undigested lactose may depress the formation of toxic bacterial metabolites, such as ammonia, hydrogen, disulphide, phenolic compounds and biogenic amines. Undigested lactose has an effect similar to that of non-digested lactose derivatives, including lactulose, lactitol, lactobionic acid, galacto-oligosaccharides and tagatose [14].

In neonates, lactose may be involved with innate immunity, protecting the neonatal gut against pathogens and in the regulation of the microbiota of the infant, possibly via a synergistic effect of sodium butyrate or phenylbutyrate with lactose in colonic epithelial cells [23]. Since gut bifidobacteria decline with age, milk saccharides may have a life-long role in countering the decline in immune function that occurs with age [24]. Lactose may enhance innate gut immunity not only in early life, but also later in life through synergistic action with SCFA or other carbohydrates [25]. Galactose, produced by hydrolysis of lactose, may also serve as a substrate for cerebroside, ganglioside, and mucoproteins with important neural and immunological roles [25]. Giving 15 g lactose/day to Japanese lactose malabsorbers, resulted in increases in lactobacilli, enterococci and SCFA and decreased clostridia and bacitroids in feces within 6 days, suggesting adaptation to dietary lactose [26].

It has been suggested that studying disease incidence among populations categorized as lactose persistent or lactose non-persistent could offer a unique opportunity to study disease patterns related to lactose and bacterial flora [17]. Lactose may represent the most widely used natural prebiotic, and using digestibility of lactose which varies greatly among and within populations, as a marker could provide insight as to how lactose persistence or non-persistence affects disease pathogenesis. Conversely, the impact of avoidance in lactose-intolerant populations could provide a fresh perspective of

early development and pathogenesis of a number of diseases [17]/ This approach could uncover a potential role of lactose in immunity, i.e., consumption of lactose could exert protective influences on the development of some diseases [17].

Lactose and Mineral Absorption

Although it might seem counterintuitive, malabsorption of lactose enhances mineral absorption, but lactose does not increase calcium absorption in lactose tolerant adults [27]. Under normal dietary conditions, about 30-40% of the calcium in milk and cheese is absorbed in the gut either through vitamin D-dependent transport across the duodenum, facilitated diffusion or under the influence of lactose in the distal small intestine via the paracellular route [28]. Carbohydrates that escape digestion in the ileum and are fermented in the colon enhance the colonic absorption of minerals, particularly calcium and magnesium [29,30]. This positive effect on mineral absorption is attributable to increased mineral solubility and/or enhanced osmotic pressure following fermentation of lactose. Both changes enhance the passive transport of minerals across the epithelial wall [31].

Using a stable isotope technique, [29] researchers showed that a lactose-containing infant formula resulted in a 10.3% greater calcium absorption compared with a lactose-free formula. Calcium absorption, but not zinc absorption, is greater from a lactose-containing, partially hydrolyzed whey-based formula than from a lactose-free formula, even though both formulas provide adequate calcium intakes to meet the needs of infants at calcium concentrations similar to those found in routine lactose-containing infant formulas.

Yogurt specifically has been found to enhance the absorption of other nutrients, such as free fatty acids that affect insulin release, in addition to alleviating lactose malabsorption [32].

Caries

Although lactose has been widely accepted as the least cariogenic of dietary sugars over the years, there have still been questions raised about its caries-causing potential [13]. Lactose is only about 50% as cariogenic as sucrose. There is unequivocal evidence that lactose is cariogenic to teeth when the enamel is exposed to a pure form of the sugar. However, lactose is seldom consumed in pure form and is generally found in dairy products, which seem to have low cariogenic potential and may even have a protective effect [33]. The buffering capacity of milk reduces the cariogenicity of lactose [34].

Lactose is infrequently used as a sugar for sweetening processed foods because it only has 15% of the sweetening power of sucrose. Therefore, studying the cariogenicity of lactose as a pure sugar has little practical significance [33].

Lactose and galactose appear to be less cariogenic than other simple sugars, probably because the acid formation from these sugars in the oral cavity is relatively slow.

Inflammatory Bowel Disease

In inflammatory bowel disease, lactose together with other prebiotics, may promote the maintenance of lactic acid-producing bacteria and prevent the growth of potential pathogens [35]. Lactulose, a pharmaceutical prebiotic derived from lactose, is poorly absorbed (less than 3%) [26] is proven to favorably alter the colonic flora. The similarity of lactose to lactulose has been suggested as a basis for possible benefits of lactose [17]. Lactulose has been shown to have an effect on infections of the gastrointestinal tract, affect surrogate fecal markers of carcinogenesis and has even been proposed for prevention of IBD. But there are few current studies in this area. Studies in these areas using lactose have been lacking [17,37,38,39,40].

Lactose intake, as opposed to glucose and fructose, lactose intake does not appear to be associated with diabetes incidence [41]. Yogurt has a low glycemic index, in part because of the lactose it contains, which has a low-to-medium glycemic index [42]. It has been suggested that yogurt's probiotic effect could modulate glucose metabolism [43]. A recent overview of observational studies

found a 14% lower risk of type 2 diabetes associated with yogurt consumption of 80-125 g/d compared with no yogurt consumption [43]. The American Diabetes Association recommends the use of milk and dairy products because they have a relatively low glycemic index due to dairy protein, in particular casein, as well as lactose, which itself has a low-to-medium glycemic index [44].

Diagnosis and Treatment of Lactose Intolerance

Clinical Symptoms

The excessive production of hydrogen and methane in the intestine leads to bloating, distention of the abdomen, excessive flatulence, and non-specific abdominal pain. In some patients vomiting can occur [1]. The excessive unabsorbed lactose with osmotically driven water, in excess of colonic absorption, can lead to diarrhea in some patients. Conversely, gastrointestinal motility may be decreased, causing constipation in some cases [3]. One study found that 52% of patients do not consciously associate symptoms with the consumption of lactose [45]. Several factors determine the onset of symptoms, such as lactose content of the foods consumed, gut transit time and fermentation capacity of the gut. However, not all patients with lactose malabsorption experience intolerance symptoms. Symptoms seldom occur until lactase activity drops below the 50% of normal and even then not all will be symptomatic [46].

Diagnosis

A subjective diagnosis of lactose intolerance without testing, though widely claimed by members of the general population, proves to be incorrect in 50% of cases [47,48]. Symptoms are often the result of the physiological effects of food intake (of any type) on symptoms in subjects who already suffer from Irritable Bowel Syndrome (IBS), Inflammatory Bowel Disease (IBD) or an intolerance to another food [49-51]. Indeed, patients with IBS appear to be more sensitive to unabsorbed lactose than non-IBS patients [52]. Several methods are available for the diagnosis of lactose malabsorption. The most accurate test for the diagnosis of hypolactasia is an intestinal biopsy to measure the mucosal lactase activity and sucrase-to-lactase ratio [53,54]. However, there is often a poor correlation between lactase levels and symptoms. Moreover, it is unnecessarily invasive for the diagnosis of a relatively benign condition and biopsy results can be influenced by the irregular dissemination of lactase activity throughout the small intestine mucosa [55].

The lactose hydrogen breath test, which is non-invasive and cost effective, is currently considered to be the best diagnostic test for identifying lactose intolerance. After fasting for at least 12 hours, lactose, at a concentration of 1 gm/kg body weight dissolved in a solution with 20% water, is given to the patient [56]. (For a person weighting 68 kg, the lactose dosage would be greater than the amount found in a liter of milk). Breath samples are collected at 20-minute intervals for 2 hours. An increase in breath hydrogen or methane in three consecutive samples confirms the diagnosis of lactose intolerance. (Figure 1) A meta-analysis found that the overall sensitivity for the breath test to be 0.88 and the specificity 0.8557. False negatives may occur, but false positives are less common [58]. However, a consensus conference on the use of the breath test recommended a more physiological test dosage of 20 to 25 grams of lactose [59].

Another available diagnostic test is the Lactose Tolerance Test (LTT) in which the patient typically consumes 50 g of lactose dissolved in water. Blood samples are taken at 15-minute intervals for one hour and tested for plasma glucose concentration. A plasma glucose increase of 1.4 mmol/L or greater indicates lactose intolerance [58]. The digestion of lactose affects blood glucose levels. If blood glucose levels do not increase, it indicates that lactose is not being absorbed.

There also is a genetic test to identify single nucleotide polymorphisms associated with lactase persistence/non-persistence. Genotype CC correlated with hypolactasia, while TT genotype is associated with lactase persistence. Not all those with CC genotype will experience symptoms.

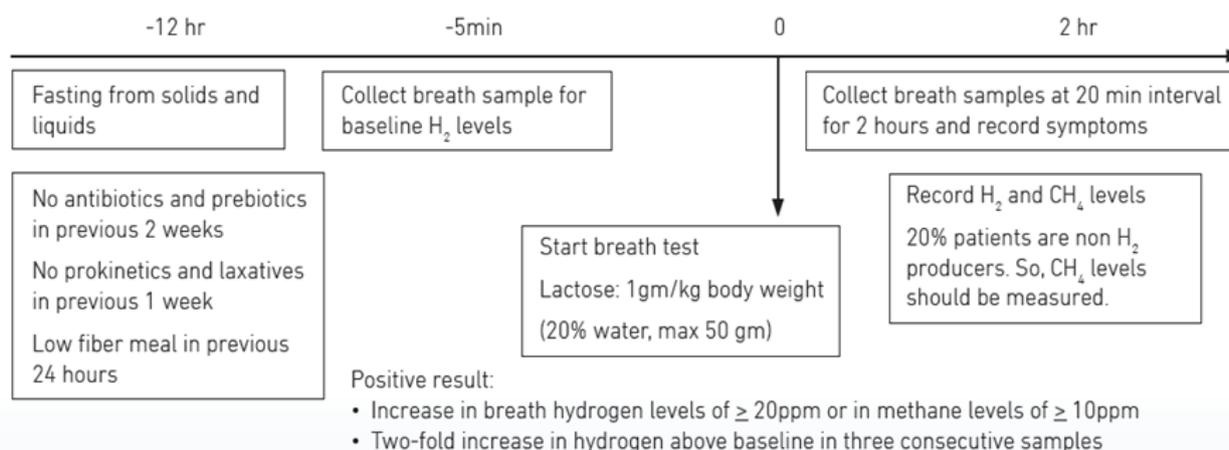


Figure 1.

Figure 1: A meta-analysis found that the overall sensitivity for the breath test to be 0.88 and the specificity 0.8557.

Source: WGO Handbook on Diet and the Gut, 2016.

Treatment

The mainstay of treatment of lactose intolerance is avoidance of all lactose containing milk and milk containing products, but it typically is not necessary. In primary lactose intolerance, lactose-containing foods can be limited for 2-4 weeks to induce remission. After 4 weeks, lactose-containing products can be reintroduced gradually, according to the tolerance of the individual. Yogurt is an option for patients diagnosed with hypolactasia, because lactose is digested by yogurt bacteria, improving absorption compared with other dairy products [60]. Heat treatment of yogurt, however, will reduce the lactase activity of yogurt 10-fold [61]. Patients with mild lactose intolerance may benefit from using lactase enzyme supplements. The incubation of milk with lactase enzymes may also be helpful. It is common for health providers to mistakenly tell patients not to eat any dairy product, which deprives them of a healthful source of protein and the most bioavailable source of calcium. Instead, patients should be instructed about low or no-lactose dairy products.

Preventive strategy to maintain good digestive health

- General hygiene
 - Maintenance of hygiene in food and water
 - Proper washing of hands
- Dietary advice
 - Healthy and well-balanced diet
 - Adequate amount of fiber in the diet
 - Avoidance of processed food

- Low FODMAP diet
- Eating of food slowly
- Avoidance of food that leads to food allergic symptoms
- Drinking of lot of fluids (non-sugar based)
- Maintenance of healthy gut microbiota
 - Probiotics and prebiotics
 - Avoidance of proton pump inhibitors and nonsteroidal anti-inflammatory drugs (NSAIDs)
 - Maintenance of hygiene
- Avoidance of injurious agents to gut
 - Smoking: predisposes to Gastroesophageal reflux
 - Drugs which damages intestinal mucosa, such as NSAIDs
 - Excess and contraindicated use of proton pump inhibitors
 - Avoidance of excess of alcohol
- Maintenance of epithelial integrity
 - Maintenance of healthy microbiome
 - Prevention of GI infections
- Maintenance of enterocytes

In secondary lactose intolerance, lactose is restricted only for a limited duration and can be reintroduced safely after recovery from intestinal damage [55].

Lactose intakes of less than 6 grams (The amount in one-half cup of milk) is unlikely to trigger symptoms among individuals

Source: WGO Handbook on Diet and the Gut, 2016.

Food items that should be avoided	Food items that are allowed
<ul style="list-style-type: none"> • All kinds of milk: whole, low-fat, nonfat, cream, powdered, condensed and evaporated • Chocolate-containing milk • Butter, cottage cheese, ice cream, creamy/cheesy sauces, cream cheeses, soft cheese and mozzarella • Whipped cream • Milk, bread, crackers, and creamer • Muffin, biscuit, waffle, pancake, and cake mixes • Bakery products and desserts that contain the ingredients listed above 	<ul style="list-style-type: none"> • Lactose-free milk and soy milk • Lactose-free dairy and hard cheeses • Yogurts containing live cultures • Kefir • All fruits • All vegetables • All legumes • All cereals • All meat, fish and eggs • All vegetable fats

with primary lactose intolerance [62]. The threshold for lactose-induced symptoms may be doubled when lactose is given with a meal. Twelve to 24 grams of lactose (the amount in 1 to 2 cups of milk, and more than the amount in 2 cups of yogurt) consumed in small amounts throughout the day, during or at the end of a meal, is generally considered to be an amount that is well tolerated, though the threshold for lactose tolerance and symptoms varies widely among individuals [48,63].

Individuals who avoid dairy products because of lactose maldigestion may find that consuming yogurt with live and active cultures, improves lactose digestion, making yogurt a viable dairy option. The European Food Safety Authority (EFSA) reviewed the literature and concluded that live cultures in yogurt (*Lactobacillus delbrueckii* susp. *bulgaricus* and *Streptococcus thermophilus*) in amounts 108 CFU (Colony Forming Units) per gram, improve digestion of lactose present in the yogurt in individuals with lactose maldigestion [64].

Yogurt Research

The following 14 studies were considered pertinent by the European Food Safety Authority when evaluating the validity of the claim that yogurt containing live cultures improves lactose digestion. In 13 of the studies, people with lactose maldigestion whose diets included yogurt containing live starter cultures experienced improved lactose digestion. In the single study that did not demonstrate a beneficial effect on lactose digestion, symptoms nevertheless improved [64].

Kolars JC, Levitt MD, Aouji M, Savaiano DA. Yogurt—an autodigesting source of lactose. *The New England Journal of Medicine*, 1984;310:1-3.

Using the breath hydrogen concentration test, researchers assessed lactose digestion in 10 lactose-intolerant subjects, 20 to 28 years of age, who were given 1 of 5 lactose-containing test meals: 1) Lactose (20 g in 400 mL water), 2) Milk (400 mL containing 18 g lactose), 3) Commercial unflavored yogurt (440 g containing 18 g lactose), 4) Commercial unflavored yogurt (270 g containing 11 g lactose and 5) Lactulose (10 g in 200 mL water). Ingestion of 18 g of lactose from 440 g yogurt resulted in approximately one-third as much hydrogen excretion as a similar amount of lactose in milk or water, indicating significantly better absorption of lactose from yogurt. In addition, significantly fewer subjects reported gastrointestinal symptoms, including diarrhea and flatulence, after consuming yogurt than when milk was consumed (20% vs 80%).

Conclusion: The autodigesting feature of yogurt makes it a well-tolerated source of milk for lactase-deficient persons.

Savaiano DA, AbouElAnouar A, Smith DE, Levitt MD. Lactose malabsorption from yogurt, pasteurized yogurt, sweet acidophilus milk, and cultured milk in lactase-deficient individuals. *The American Journal of Clinical Nutrition* 1984;40:1219-1223.

A study of 9 healthy subjects (20 to 28 years), identified as lactase deficient, were given 410 g of milk, 420 g of sweet acidophilus milk, 465 g of buttermilk, 500 g of yogurt and 500 g of pasteurized yogurt. Each test meal contained 20 g of lactose. Subjects were randomly fed each of the meals, blinded. Breath hydrogen was used to evaluate lactose malabsorption. One-third to one-fifth less hydrogen resulted from yogurt feeding compared with the other test meals. The difference was significant when comparing acidophilus milk, milk, and cultured milk with yogurt and nearly significant when comparing pasteurized yogurt with yogurt. Pasteurization of yogurt eliminated the enhanced digestion of lactose, reduced the inherent lactase activity of the yogurt by 10-fold, and reduced cell counts by 100-fold. Eight of nine subjects fed cultured milk experienced gastrointestinal distress, whereas all subjects fed pasteurized yogurt were symptom free, even though the amount of malabsorbed lactose was similar.

Conclusions: Yogurt was unique among the products tested in enhancing the digestion of lactose.

Dewit O, Pochart P, Desjeux JF. Breath hydrogen concentration and plasma glucose, insulin and free fatty acid levels after lactose,

milk, fresh or heat yogurt ingestion by healthy young adults with or without lactose malabsorption. *Nutrition* 1988; 4:131-135.

Breath hydrogen excretion, blood glucose, insulin and free fatty acids were measured over 8 hours in 26 young, healthy adults (13 lactose digesters and 13 maldigesters) who received lactose in water, milk or yogurt after an overnight fast. The yogurt contained 3×10^8 CFU/g *S. thermophilus* and 3×10^8 L. *bulgaricus*. In the 13 lactose digesters, BHC remained low over the 8 hours of the test, regardless of the source of the lactose. Among the lactose maldigesters, ingestion of lactose in water, milk or heated yogurt was followed by a rise in BHC after 5 hours. However, ingestion of unheated yogurt resulted in a significant reduction in breath hydrogen concentration compared to when lactose, milk or heated yogurt was consumed.

Conclusion: In adult lactose maldigesters the digestion of lactose in the form of yogurt, is significantly improved compared to lactose in milk. Among those with lactose maldigestion, yogurt eliminated the malabsorption.

Onwulata CI, Rao DR, Vankineni P. Relative efficiency of yogurt, sweet acidophilus milk, hydrolyzed-lactose milk, and a commercial lactase table in alleviating lactose maldigestion. *American Journal of Clinical Nutrition* 1989;49:1233-1237.

Lactose digestion was evaluated in 10 lactose-intolerant subjects consuming one of each of the 5 tests at five weekly intervals: 1) Commercial plan yogurt, 2) Sweet acidophilus milk, 3) Hydrolyzed-lactose milk, 4) 3 Lactase tablets after whole milk consumption and 5) Whole milk. Each provided 18 g lactose, except for the hydrolyzed-lactose milk, which contained 5 g lactose. Lactase activity, as measured by breath hydrogen concentration, was found to be lowest with yogurt consumption.

Conclusion: Yogurt was as effective as lactose-hydrolyzed milk for alleviating gastrointestinal symptoms among lactose-intolerant individuals, but was significantly more effective than commercial lactase consumed along with milk.

Pochart P, Dewit O, Desjeux JF, Bourlioux P. Viable starter culture, beta-galactosidase activity, and lactose in duodenum after yogurt ingestion in lactase-deficient humans. *The American Journal of Clinical Nutrition* 1989;49:828-831.

Ten lactose malabsorbers were intubated before being given fresh or heated yogurt to which polyethylene-glycol and spores of *Bacillus stearothermophilus* had been added as internal standards. In duodenal samples taken after fresh yogurt ingestion, viable starter culture as detected for 60 minutes in 6 of 7 subjects and the ratio of microbial beta-galactosidase activity to *Bacillus stearothermophilus* remained similar during this period to its value in the pre-ingested yogurt. In the two groups ingesting fresh and heated yogurt respectively, ratios of lactose to polyethylene glycol remained similar to pre-ingested values for 90 min and duodenal pH remained less than 5.1. *In vitro*, at pH 5.0 beta-galactosidase activity in yogurt dropped by 80%.

Conclusions: After fresh yogurt ingestion, viable starter culture reaches the duodenum and contains beta-galactosidase activity. However, the buffering capacity of the yogurt that protects bacteria from acidic gastric secretion also prevents microbial beta-galactosidase from hydrolyzing lactose in the duodenum.

Martini MC, Lerebours EC, Lin WJ, Harlander SK, *et al.* Strains and species of lactic acid bacteria in fermented milk (yogurts): effect on *in vivo* lactose digestion. *The American Journal of Clinical Nutrition* 1991;54:1041-1046.

Seven healthy, lactase-deficient subjects (age 23-33), were fed yogurts (Containing mixtures of strains of *Streptococcus salivarius* subsp *thermophilus* and *Lactobacillus delbrueckii* subsp *bulgaricus*) and fermented milks (containing individual species of *S. thermophilus*, *L. bulgaricus*, *L. acidophilus*, or *Bifidobacterium bifidus*). Breath hydrogen was monitored. All yogurts dramatically and similarly improved lactose digestion, regardless of their total beta-galactosidase activity. The response to fermented milks varied from marginal improvement with *B. bifidus* milk to nearly complete lactose digestion with *L. bulgaricus* milk.

Conclusions: Lactose maldigesters more effectively digest lactose in yogurt than in milk, at least in part because of the intrainestinal activity of the microbial beta-galactosidase originating from the yogurt culture. The study demonstrates the importance of strains and specificity of lactic acid bacteria in the production of fermented milks and yogurts. However, pasteurization or similar heat treatment results in increased lactose maldigestion in susceptible individuals. Inadvertent heat damage may also occur during shipping and storage.

Rosado JL, Solomons NW, Allen LH. Lactose digestion from unmodified, low-fat and lactose-hydrolyzed yogurt in adult lactose-maldigesters. *European Journal of Clinical Nutrition* 1992;46:61-67.

To establish the presence of symptoms of lactose maldigestion, subjects were fed a 360 mL glass of whole milk, containing 18 g lactose. The efficiency of lactose digestion was determined by breath hydrogen excretion. Fourteen lactose maldigesters were then tested following consumption of 454 g each of 4 test yogurts: 1) experimental plain yogurt prepared from whole milk treated with a beta-D-galactosidase to hydrolyze 70% of the lactose in milk 2 & 3) two brands of plain yogurt prepared from whole milk and 4) plain yogurt prepared from low-fat milk. The hydrogen breath responses to the two brands of unmodified yogurt and the lactose-hydrolyzed yogurt were significantly less than to whole milk. Despite the finding that lactose maldigestion was slightly greater with the low-fat yogurt, there was no increase in reporting of symptoms of lactose intolerance.

Conclusion: Breath hydrogen concentrations were significantly less with yogurt than with whole milk and there was no therapeutic advantage to consuming prehydrolyzed full-fat yogurt over regular yogurt.

Varela-Moreiras G, Antoine JHM, Riz-Roo B, Varela G. Effects of yogurt and fermented-then-pasteurized milk on lactose absorption in an institutionalized elderly group. *Journal of the American College of Nutrition* 1992;11:168-171.

A group of 53 healthy institutionalized elderly men and women (67-95 years) were evaluated for lactose maldigestion by breath hydrogen concentration after consuming 250 mL semi skimmed milk (1.5%-1.8% milkfat and 11 g lactose). A total of 19 (36%) were identified as malabsorbers. The 19 lactose malabsorbers were given an equivalent amount of lactose in fermented-then-pasteurized yogurt and regular yogurt and asked to record any symptoms experienced after ingestion of the dairy products. Total breath hydrogen over 6 hours following yogurt consumption was significantly lower than for milk consumption. Pasteurized yogurt had an intermediate effect, but it was not significantly different from milk. There was no real difference in reported symptoms, whether the subjects consumed milk or regular yogurt.

Conclusion: A fairly large percentage of elderly adults are lactose maldigesters and yogurt offers a good alternative to milk. After consuming milk, there was little difference in reporting of symptoms between lactose malabsorbers (5%) and lactose absorbers (6%).

Shermak MA, Saavedra JM, Jackson TL, Huang SS, Bayless, TM, Perman JA. Effect of yogurt on symptoms and kinetics of hydrogen production in lactose-malabsorbing children. *American Journal of Clinical Nutrition* 1995;62:1003-1006.

Twenty-three children aged 4-16 were evaluated for lactose malabsorption; fourteen were positively identified and randomly given 3 test meals in a double-blind fashion, every other day over a 5-d period after overnight fasts. The three test meals, containing 12 g lactose each, were 1) low-fat milk 2) yogurt containing active live cultures and 3) pasteurized yogurt. Symptoms and mean breath hydrogen values were recorded for 8 hours. The children experienced significantly fewer symptoms after consuming yogurt with live cultures than after milk, and yogurt was associated with a delayed, slower rate of rise in breath hydrogen concentrations. Pasteurized yogurt had an intermediate effect.

Conclusions: Compared with milk consumption, lactose tolerance was enhanced when yogurt with live cultures was consumed. In children, mechanisms other than enhanced lactose absorption from yogurt, may lead to changes in the kinetics of hydrogen production,

which is associated with improved tolerance.

Pelletier X, Laure-Boussuge S, Donazzolo Y. Hydrogen excretion upon ingestion of dairy products in lactose-intolerance male subjects: Importance of the live flora. *European Journal of Clinical Nutrition* 2001;55:509-512.

A double-blind, randomized, cross-over study tested the breath hydrogen concentration in 24 lactose intolerance men, ranging in age from 21-35, after consuming the following 5 products: 1) milk 2) yogurt (108 CFU/mL) 3) heat-treated yogurt (<15 CFU/mL) 4) yogurt diluted with heat-treated yogurt to provide 106 CFU/mL and 5) yogurt diluted with heat-treated yogurt to provide 108 CFU/mL. At least 3 days were allowed as a wash-out period between two products. For a period of 8 hours after each test providing 25 g lactose, hydrogen excretion was monitored. A significant difference in hydrogen excretion was demonstrated among the products, with yogurt resulting in the least hydrogen excretion. Diluted yogurt resulted in less hydrogen excretion than milk or heat-treated yogurt.

Conclusion: The results demonstrate that ingestion of yogurt with 108 bacteria/mL resulted in lower hydrogen excretion and fewer gastrointestinal complaints than with the other products.

Longer-term Studies

3 days

Marteau P, Flourie B, Pochart P, Chastang C, *et al.* Effect of the microbial lactase (EC 3.2.1.23) activity in yoghurt on the intestinal absorption of lactose: an in vivo study in lactase-deficient humans. *British Journal of Nutrition* 1990;64:71-79.

Eight male and female, lactase-deficient subjects ranging in age from 19 to 27, consumed 18 g of lactose from one of 3 sources for 3 consecutive days. Lactose maldigestion was initially identified by hydrogen breath concentration of the subjects after consuming 50 g lactose in 250 mL water. The 3 lactose test sources were: 1) whole milk (400 mL) 2) yogurt (450 g) and 3) heated yogurt (450 g). On the 4th day, subjects were intubated to collect ileal contents, and lactose, galactose, glucose and lactase were measured. Approximately 20% of the lactase activity contained in yogurt reached the small intestine.

Conclusion: Breath hydrogen concentration is significantly lower after consumption of yogurt and heated yogurt, compared with consumption of milk.

8 days

Lerebours E, N'Djitoyap Ndam C, Lavoine A, Hellot MF, Antoine JM, Colin R. Yogurt and fermented-then-pasteurized milk: effects of short-term and long-term ingestion on lactose absorption and mucosal lactase activity in lactase-deficient subjects. *American Journal of Clinical Nutrition* 1989;49:823-827.

In a double-blind study, sixteen subjects aged 18-26 diagnosed with lactose intolerance were given 125 g of either yogurt or fermented-then-pasteurized milk without living acid bacteria; both provided 18 g lactose/day for 8 days. In all 16 subjects it was confirmed that yogurt enhanced lactose digestion and that the beneficial effect was destroyed by pasteurization. Moreover, long-term digestion did not modify the results of the hydrogen breath tests.

Conclusions: The study demonstrated that enhanced lactase absorption after yogurt consumption, as measured by hydrogen breath tests over 24 hours, does not change over long term ingestion.

15 days or longer

Rizkalla SW, Luo J, Kabir M, Chevalier A, Pacher N, Slama G. Chronic consumption of fresh but not heated yogurt improves breath-hydrogen status and short-chain fatty acid profiles: a controlled study in healthy men with or without lactose maldigestion. *American Journal of Clinical Nutrition* 2000;72:1474-1479.

Two groups of healthy men, 12 with lactose malabsorption and 12 without, aged 20-60, participated in this study. Lactose malabsorption was identified by breath hydrogen concentrations following a 30-g lactose challenge. Subjects were randomly assigned in a crossover design (2 periods of 15 d each, with a 2 week washout

period in between) to 500 g/d of either yogurt containing bacterial cultures or heated yogurt. The daily amount of yogurt was provided as 4 cups of 125 g each, consumed over 3 meals. For those with lactose malabsorption, breath hydrogen at the end of the 15-d yogurt period was significantly lower after the consumption of fresh yogurt, than after consumption of the heated yogurt, and breath hydrogen tended to increase after consumption of heated yogurt.

Conclusion: Among men with lactose malabsorption, regular consumption of yogurt with live bacteria improves malabsorption, even when consumed several times in a day, as assessed by breath hydrogen concentration.

Labayen I, Forga L, Gonzalez A, Lenoir-Wijnkoop I, *et al.* Relationship between lactose digestion, gastrointestinal transit time and symptoms in lactose malabsorbers after dairy consumption. *Alimentary Pharmacology & Therapeutics* 2001;15:543-549.

This double-blind, cross-over study of 22 men and women, who were lactose malabsorbers, examined the effect on breath hydrogen concentration following ingestion of 25 g/d lactose from either 500 g/d yogurt with living bacteria (>108 CFU/g) or heated yogurt (<102 CFU/g) for 15 days. Each period was followed by a 14-day washout period. Lactose digestion was measured by breath hydrogen concentration and gastrointestinal symptoms were self-reported. The breath hydrogen test indicated more effective lactose digestion after yogurt with live bacteria when compared with heat-treated yogurt. Subjects consuming yogurt with live bacteria reported experiencing significantly fewer gastrointestinal symptoms than those consuming heated yogurt.

Conclusions: Lactose malabsorbers digest and tolerate lactose from yogurt that contains live bacteria better than from heated yogurt, in which most of the bacteria have been destroyed. The mechanism responsible for the enhanced lactose digestion and tolerance was attributed to bacterial β -galactosidase in the yogurt with live cultures.

Additional Studies

Several studies published since the 2010 European Food Safety Authority document was released further demonstrate that people with lactose maldigestion whose diets include yogurt containing live starter cultures, experience improved lactose digestion [64]. Additional research has found that dairy foods, such as yogurt, provide difficult-to-replace nutrients, including protein, potassium, magnesium phosphorus, riboflavin, and vitamins A, D, and B12.

Fulgoni VL 3rd, Keast DR, Auestad N, Quann EE. Nutrients from dairy foods are difficult to replace in diets of Americans: food pattern modeling and an analysis of the National Health and Nutrition Examination Survey 2003–2006. *Nutr Res* 2011;10:759–765.

My Pyramid dietary pattern modeling exercises and analyses of data from the National Health and Nutrition Examination Survey 2003-2006 were conducted. The impact of adding or removing 1 serving of dairy, removing all dairy, and replacing dairy with nondairy calcium sources was evaluated. Three to four servings of dairy foods are needed to help individuals meet recommendations for nutrients, including calcium, magnesium and potassium. Replacing dairy with calcium-equivalent foods changes the diet's nutritional profile and affects protein, potassium, magnesium phosphorus, riboflavin, and vitamins A, D, and B12 intakes.

Conclusions: Nondairy calcium replacement foods are not nutritionally equivalent to dairy products. While it is possible to meet calcium recommendations without consuming dairy foods, replacement foods are not nutritionally equivalent to dairy foods.

Madry E, Krasinska B, Wozniwicz M, Walkowiak J. Tolerance of different dairy products in subjects with symptomatic lactose malabsorption due to adult type hypolactasia. *Przegląd Gastroenterologiczny* 2011. 6:310–315.

The aim of the study was to assess the effects of the same dose of lactose consumed by 15 healthy young lactose intolerant adults. All subjects were symptomatic. Hydrogen breath tests were performed on each subject after consuming 400 mL of milk, kefir or yogurt.

Clinical symptoms were then assessed within 12 hours after each product was consumed. While all subjects reported symptoms, the excretion of gases was lower after ingestion of kefir and yogurt compared with milk. Abdominal pain and intestinal rumbling were perceived as more severe after milk consumption and the number of stools was higher and consistency more liquid.

Conclusion: While the findings indicated that young adults with lactose intolerance cannot tolerate a typical dose of dairy products, as assessed by subjective and objective measures, the tolerance of kefir and yogurt was significantly better than that of milk.

Keith JN, Nicholls J, Reed A, Kafer K, Miller GD. The prevalence of self-reported lactose intolerance and the consumption of dairy foods among African America adults are less than expected. *J Natl Med Assoc* 2011;103:36-45.

An online survey of African Americans (2016 adults) and a comparison sample of the general population (1084 adults) found that African Americans were more likely to eat fewer dairy foods, to experience discomfort after consuming dairy foods (49%) and to believe they were lactose intolerant (24%) compared with the general population.

Conclusions: Dairy foods, calcium and vitamin D intake among African Americans, as well as the general population, are below recommendations. However, self-diagnosed lactose intolerance is less common than previously reported.

Madry E, Krasinska B, Wozniwicz M, Drzymala-Cryz S, *et al.* Yogurt-a potential strategy for overcoming lactose intolerance: the significance of the dose. *Przegląd Gastroenterologiczny* 2012;7:81-86.

The purpose of the study was to determine the dose of lactose that is tolerated by 10 healthy, lactose-intolerant young adults in a single serving of yogurt. The hydrogen breath test was performed 5 hours after a load of 400, 200 and 100 ml of yogurt. Clinical symptoms were assessed for 12 hours after consumption of the yogurt. Ingestion of 400 ml of yogurt resulted in abnormal hydrogen breath tests and symptoms in all subjects. Symptoms were more severe than observed after a load of 200 ml of yogurt. Consumption of 200 ml of yogurt resulted in abnormal breath test results in two of the subjects while the test dose of 100 ml caused borderline hydrogen excretion in one subject. None of the subjects consuming 100 ml of yogurt reported gastrointestinal symptoms.

Conclusions: Based on observed symptoms, young adults with lactose intolerance may tolerate up to 200 ml of yogurt served in a single meal. However, based on hydrogen breath test results, the maximum dose per meal should not exceed 100 ml.

de Vrese M, Laue C, Offick B, Soeth E, *et al.* A combination of acid lactase from *Aspergillus oryzae* and yogurt bacteria improves lactose digestion in lactose maldigesters synergistically: A randomized, controlled, double-blind cross-over trial. *Clinical Nutrition* 2015;34:394-399.

A randomized, placebo-controlled, double-blind, 5-arm crossover study of 24 lactose malabsorbers investigated whether different lactase preparations and freeze-dried yogurt culture affect gastrointestinal lactose digestion after consuming 12.5 g of lactose. Hydrogen breath tests were administered over 6 hours. Symptoms of lactose intolerance (Excess gas production, abdominal pain, diarrhea or nausea) were assessed using validated questionnaires. Both the higher dose lactase and the combination preparation significantly reduced symptoms and was associated with hydrogen exhalation.

Conclusions: The combined administration of freeze-dried yogurt cultures and acid lactase increased lactose digestion more than either freeze-dried yogurt cultures or acid lactase alone.

Casellas F, Aparici A, Perez MJ, Rodriguez P. Perception of lactose intolerance impairs health-related quality of life. *European Journal of Clinical Nutrition* 2016;70:1068-1072.

A 3-year prospective, cross-sectional study was performed in 580 patients referred for a lactose hydrogen breath test. Patients were asked about their subjective opinion relative to their lactose tolerance and completed a questionnaire regarding their symptoms.

A 50-g lactose breath test was performed. Fifty-six percent considered themselves to be lactose intolerant and that perception was associated with avoidance of dairy consumption. Patient-reported, health-related quality of life was measured. Self-perception of intolerance was associated with avoidance of dairy consumption and lower health-related quality-of-life measures.

Conclusion: Subjective perception of lactose intolerance affects the decision to avoid dairy more than objective malabsorption. Both self-perception of lactose intolerance and objective malabsorption were associated with poorer perceived quality of life.

Zingone F, Bucci C, Iovino P, Ciacci C. Consumption of milk and dairy products: Facts and figures. *Nutrition* 2017;33:322-325.

Individuals in Campania, Italy, aged 18 to 75 (1173) answered an online questionnaire regarding their average consumption of milk and dairy products. The study found that 22.2% of responders do not drink milk and 18.1% drink lactose-free milk, mainly due to gastrointestinal symptoms. The majority avoided milk without consulting a doctor or undergoing a breath test for lactose intolerance.

Conclusions: The decision to avoid milk is often based on personal perception and "alternative" food intolerance tests, rather than a standardized test.

Hertzler SR, Clancy SM. Kefir improves lactose digestion and tolerance in adults with lactose maldigestion. *Journal of the American Dietetic Association* 2003;103:582-587.

Kefir typically has a larger and more diverse range of microorganisms in its starter culture than yogurt. The kefir used in this study contained the following cultures: *Streptococcus lactis*, *Lactobacillus plantarum*, *Streptococcus cremoris*, *Lactobacillus casei*, *Streptococcus diacetylactis*, *Saccharomyces florentinus* and *Leuconostoc cremoris*. This was the first study to evaluate lactose digestion from kefir in adults with lactose maldigestion. In this randomized study, 15 subjects with lactose maldigestion were fed test meals consisting of 20 g lactose portions of milk (2% reduced fat), plain and raspberry flavored kefir, and plain and raspberry flavored yogurt, each following an overnight fast (12 hours). Breath hydrogen was tested and lactose intolerance symptoms were monitored hourly for 8 hours after each test meal. Improved lactose digestion from kefir was accompanied by a concomitant improvement in flatus symptom that was comparable with the improvement observed between the flavored and plain yogurt. The breath hydrogen response to the flavored yogurt was higher than for plain yogurt. An even greater difference was observed between the flavored and plain kefirs.

Conclusions: The study demonstrated that plain kefir improves lactose digestion just as well as plain yogurt.

Review Articles

Several review articles have concluded that misconceptions and incorrect self-diagnosis of lactose intolerance are widespread and that, if counseled appropriately, most people with hypolactasia can tolerate some lactose-containing foods, such as yogurt containing live, active cultures, confirming the findings of the overwhelming majority of clinical trials.

Swagerty DL, Walling AD, Klein RM. Lactose intolerance. *American Family Physician* 2002;65:1845-1850.

Persons with lactose intolerance are unable to digest significant amounts of lactose because of a genetically inadequate amount of the enzyme lactase. Symptoms include abdominal pain and bloating, excessive flatus, and watery stools following the ingestion of foods containing lactose. A sizable number of adults believe they are lactose intolerant, but do not actually have impaired lactose digestion, and some persons with lactase deficiency can tolerate moderate amounts of ingested lactose.

Harrington LK, Mayberry JF. A re-appraisal of lactose intolerance. *International Journal of Clinical Practice* 2008;62:1541-1546.

The terminology relating to lactose intolerance (lactose maldigestion, lactose malabsorption, lactose intolerance) is confusing for clinicians and researchers. Clinicians need to ensure

that these problematic terms do not cause diagnostic mistakes and inappropriate treatment. Researchers should be aware of inconsistent terminology in studies and resultant problems with the interpretation of the results.

Lomer MC, Parkes GC, Sanderson JD. Review article: lactose intolerance in clinical practice-myths and realities. *Aliment Pharmacol Ther* 2008;27:93-103.

Several nutritional and genetic factors influence the development of lactose intolerance. For this review, PubMed was searched using the terms, lactose, lactase and diet to find original research and reviews. Relevant articles and clinical experience provided the basis for this review. The lactase gene has been identified. The "wild-type" gene, characterized lactase non-persistence, often leading to lactose intolerance. Two genetic polymorphisms responsible for lactase persistence have been identified. Their distribution is concentrated in northern Europeans. If given appropriate advice, most people with hypolactasia can tolerate some lactose-containing foods.

Heaney RP. Dairy intake, dietary adequacy, and lactose intolerance. *Adv Nutr* 2013; 4:151-156.

Despite recommendations to consume 3 servings of dairy per day, dairy intake remains well below recommendations. Many health professionals are unaware of the benefits of calcium and are unduly concerned about lactose intolerance. Diets low in dairy foods contribute to chronic disease in industrialized nations. While dairy is often avoided because of lactose intolerance, or perceived lactose intolerance, it can be easily managed without eliminating dairy from the diet. Health professionals need to understand that lactose intolerance should not be a barrier to improving nutrient intakes.

Silanikove N, Leitner G, Merin U. The interrelationships between lactose intolerance and the modern dairy industry: global perspectives in evolutionary and historical backgrounds. *Nutrients* 2015;7:7312-7331.

Milk and dairy products have provided important, almost irreplaceable, nutritional advantages in different cultures over the course of 10,000 years of human development. A National Nutrition Survey (NHANES) carried out during 2001-2002 in the US, found that adequate intake of calcium by adolescents (9-18 years of age) cannot be met with dairy-free diets, while still meeting other nutrient recommendations. The recent spread of milk usage in countries, such as China and Japan in which the vast majority of the population is lactose intolerant, is a vivid example of the realization by the population, health care professionals, and public opinion leaders in these countries regarding the importance of milk as a source of essential nutrients. To accommodate those who are lactose intolerant, it is recommended that food producers using milk and milk-derived products be required to specify the content of lactose in their products along with nutrition information.

Szilagyl A, Galiatsatos, Xue X. Systematic review and meta-analysis of lactose digestion, its impact on intolerance and nutritional effect of dairy food restriction in inflammatory bowel diseases. *Nutrition Journal* 2016.15:67.

The role of dairy foods in Inflammatory Bowel Disease (IBD) has been controversial and confounded by the phenotypic divide of lactase status in the adult population. In this review and meta-analysis it was concluded that lactose maldigestion in IBD is dependent on ethnic make-up of the population. Lactose intolerance symptoms depend on several parameters beside lactose maldigestion. There is emerging suggestive evidence that dairy foods may actually decrease risk of IBD and restriction may negatively impact bone and nutrient intake.

Together, these studies and reviews clearly establish that a significant improvement in lactose digestion from yogurt among lactose maldigesters occurs when they consume yogurt containing live active cultures (≥ 108 CFU), whether in a single day or over a period as long as 2 weeks. They also show that reporting or lack of reporting of gastrointestinal symptoms is not an accurate indication of the presence of lactose malabsorption.

Heine RG, AlRefaee F, Bachina P, De Leon JC, Geng L, Gong S,

Madraza JA, Ngamphaiboon J, Ong C, Rogacion JM. Lactose intolerance and gastrointestinal cow's milk allergy in infants and children—common misconceptions revisited. *World Allergy Org J* 2017;10:41 DOI 10.1186/s40413-017-0173-0.

There is ongoing confusion between lactose intolerance and cow's milk allergy, which results in misdiagnosis and unnecessary dietary restrictions that have a negative nutritional impact on dietary intake. This confusion can lead to a delayed diagnosis of cow's milk allergy. Primary lactose intolerance in children under 5 years of age is uncommon, even in areas of the world where there exists a high prevalence of primary hypolactasia. Contrary to common belief, most infants with cow's milk allergy can tolerate dietary lactose. In fact, the addition of lactose to extensively hydrolyzed formula can be beneficial in the treatment of formula-fed infants with cow's milk allergy, as a result of prebiotic effects.

Study Findings

Several studies, dating back to 1984, demonstrate the positive effects the consumption of yogurt with live cultures has on lactose digestion. The best quality studies have measured breath hydrogen concentrations. Only a few studies have examined lactose digestion after a long period of yogurt consumption; most evaluated lactose digestion after a single dose.

Yogurt made with the live starter cultures *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus* has been shown to improve digestion of lactose in individuals with lactose maldigestion. On the basis of the available research, the European Food Safety Authority (EFSA) approved the health claim, "Live yoghurt cultures in yoghurt improve digestion of lactose in yoghurt in individuals with lactose maldigestion."64 Yogurt contains approximately 31% less lactose per serving than milk; Greek yogurt contains even less and the lactose that is present in yogurt is more easily digested than from other dairy sources of lactose due the presence of lactase-producing bacteria [3].

CONCLUSIONS

Lactose intolerance is not a disease and is not to be confused with a dairy allergy. Self-diagnosis of lactose intolerance is often inaccurate and is likely to result in avoidance of nutrient-dense dairy foods. Twelve to 24 grams of lactose (the amount in 1 to 2 cups of milk, and more than the amount in 2 cups of plain yogurt) consumed in small amounts throughout the day, during or at the end of a meal, is generally well tolerated, though the threshold for lactose tolerance varies widely among individuals. Yogurt may present a more easily digestible alternative to milk, mainly because of the presence of lactase-producing live bacteria.

The probiotic qualities of yogurt are now recognized by the EFSA claim. Individuals who avoid dairy products because of lactose maldigestion may lack important nutrients in their diets, especially calcium. Yogurt is a nutrient-rich food and with its live and active cultures, improves lactose digestion, making yogurt a viable dairy option. In addition to improving lactose digestion, yogurt has a low glycemic index and consumption is associated with a reduced risk of diabetes.

BIBLIOGRAPHY

- Matthews SB, Waud JP, Roberts AG, Campbell AK. Systemic lactose intolerance: a new perspective on an old problem. *Postgrad Med J*. 2005;81(953):167-173.
- Solomons NW. Fermentation, fermented foods and lactose intolerance. *Eur J Clin Nutr*. 2002;56 Suppl 4:S50-55.
- Lomer MC, Parkes GC, Sanderson JD. Review article: lactose intolerance in clinical practice--myths and realities. *Aliment Pharmacol Ther*. 2008;27(2):93-103.
- Swallow DM. Genetics of lactase persistence and lactose intolerance. *Annu Rev Genet*. 2003;37:197-219.
- Luyt D, Ball H, Makwana N, et al. BSACI guideline for the diagnosis and management of cow's milk allergy. *Clin Exp Allergy*. 2014;44(5):642-672.
- Lember M. Hypolactasia: a common enzyme deficiency leading to lactose malabsorption and intolerance. *Pol Arch Med Wewn*. 2012;122 Suppl 1:60-64.
- Szilagyi A. Adult lactose digestion status and effects on disease. *Can J Gastroenterol Hepatol*. 2015;29(3):149-156.
- Vandenplas Y. Lactose intolerance. *Asia Pac J Clin Nutr*. 2015;24 Suppl 1:S9-13.
- Bhatnagar S, Aggarwal R. Lactose intolerance. *BMJ*. 2007;334(7608):1331-1332.
- Fazeli W, Kaczmarek S, Kirschstein M, Santer R. A novel mutation within the lactase gene (LCT): the first report of congenital lactase deficiency diagnosed in Central Europe. *BMC Gastroenterol*. 2015;15:90.
- Diekmann L, Pfeiffer K, Naim HY. Congenital lactose intolerance is triggered by severe mutations on both alleles of the lactase gene. *BMC Gastroenterol*. 2015;15:36.
- Torniainen S, Savilahti E, Jarvela I. [Congenital lactase deficiency—a more common disease than previously thought?]. *Duodecim*. 2009;125(7):766-770.
- M G. Forward—Nutrition and health aspects of lactose and its derivatives: State of the science. *International Dairy Journal*. 2012;22:87.
- Schaafsma G. Lactose and lactose derivatives as bioactive ingredients in human nutrition. *International Dairy Journal*. 2012;22:458-465.
- Grenov B, Briend A, Sangild PT, et al. Undernourished Children and Milk Lactose. *Food Nutr Bull*. 2016;37(1):85-99.
- Sangild PT. Gut responses to enteral nutrition in preterm infants and animals. *Exp Biol Med (Maywood)*. 2006;231(11):1695-1711.
- Szilagyi A. Redefining lactose as a conditional prebiotic. *Can J Gastroenterol*. 2004;18(3):163-167.
- Gibson GR, Roberfroid MB. Dietary modulation of the human colonic microbiota: introducing the concept of prebiotics. *J Nutr*. 1995;125(6):1401-1412.
- Strocchi A, Corazza G, Ellis CJ, Gasbarrini G, Levitt MD. Detection of malabsorption of low doses of carbohydrate: accuracy of various breath H2 criteria. *Gastroenterology*. 1993;105(5):1404-1410.
- Probiotics. Rijeka, Croatia: InTech; 2012.
- Wong JM, de Souza R, Kendall CW, Emam A, Jenkins DJ. Colonic health: fermentation and short chain fatty acids. *J Clin Gastroenterol*. 2006;40(3):235-243.
- Morrison DJ, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes*. 2016;7(3):189-200.
- Cederlund A, Kai-Larsen Y, Printz G, et al. Lactose in human breast milk an inducer of innate immunity with implications for a role in intestinal homeostasis. *PLoS One*. 2013;8(1):e53876.
- Vulevic J, Juric A, Walton GE, et al. Influence of galacto-oligosaccharide mixture (B-GOS) on gut microbiota, immune parameters and metabonomics in elderly persons. *Br J Nutr*. 2015;114(4):586-595.
- Lukito W, Malik SG, Surono IS, Wahlqvist ML. From 'lactose intolerance' to 'lactose nutrition'. *Asia Pac J Clin Nutr*. 2015;24 Suppl 1:S1-8.
- Ito M, Kimura M. Influence of lactose on faecal microflora in lactose maldigesters. *Microb Ecol Health Dis*. 1993;6:73-76.
- Zittermann A, Bock P, Drummer C, Scheld K, Heer M, Stehle P. Lactose does not enhance calcium bioavailability in lactose-tolerant, healthy adults. *Am J Clin Nutr*. 2000;71(4):931-936.
- Caroli A, Poli A, Ricotta D, Banfi G, Cocchi D. Invited review: Dairy intake and bone health: a viewpoint from the state of the art. *J*

- Dairy Sci. 2011;94(11):5249-5262.
29. Griffin IJ, Davila PM, Abrams SA. Non-digestible oligosaccharides and calcium absorption in girls with adequate calcium intakes. *Br J Nutr.* 2002;87 Suppl 2:S187-191.
 30. Scholz-Ahrens KE, Schaafsma G, van den Heuvel EG, Schrezenmeir J. Effects of prebiotics on mineral metabolism. *Am J Clin Nutr.* 2001;73(2 Suppl):459S-464S.
 31. Schaafsma G. Bioavailability of calcium and magnesium. *Eur J Clin Nutr.* 1997;51 Suppl 1:S13-16.
 32. Dewit O, Pochart P, Desjeux JF. Breath hydrogen concentration and plasma glucose, insulin and free fatty acid levels after lactose, milk, fresh or heated yogurt ingestion by healthy young adults with or without lactose malabsorption. *Nutrition.* 1988;4:131-135.
 33. Aimutis WR. Lactose cariogenicity with an emphasis on childhood dental caries. *International Dairy Journal.* 2012;22:152-158.
 34. Schaafsma G. Lactose and lactose derivatives as bioactive ingredients in human nutrition. *International Dairy Journal.* 2008;18:458-465.
 35. Szilagyi A. Review article: lactose--a potential prebiotic. *Aliment Pharmacol Ther.* 2002;16(9):1591-1602.
 36. National Institutes of Health. Lactulose. <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=7d39b21b-aafc-4d7b-9034-58263a24fba6&type=display>. Accessed October 11, 2018.
 37. Levine MM, Hornick RB. Lactulose therapy in *Shigella* carrier state and acute dysentery. *Antimicrob Agents Chemother.* 1975;8(5):581-584.
 38. Bovee-Oudenhoven IM, Termont DS, Heidt PJ, Van der Meer R. Increasing the intestinal resistance of rats to the invasive pathogen *Salmonella enteritidis*: additive effects of dietary lactulose and calcium. *Gut.* 1997;40(4):497-504.
 39. van Berge Henegouwen GP, van der Werf SD, Ruben AT. Effect of long term lactulose ingestion on secondary bile salt metabolism in man: potential protective effect of lactulose in colonic carcinogenesis. *Gut.* 1987;28(6):675-680.
 40. Liao W, Cui XS, Jin XY, Floren CH. Lactulose--a potential drug for the treatment of inflammatory bowel disease. *Med Hypotheses.* 1994;43(4):234-238.
 41. Ahmadi-Abhari S, Luben RN, Powell N, et al. Dietary intake of carbohydrates and risk of type 2 diabetes: the European Prospective Investigation into Cancer-Norfolk study. *Br J Nutr.* 2014;111(2):342-352.
 42. Wolever TM. Yogurt Is a Low-Glycemic Index Food. *J Nutr.* 2017;147(7):1462S-1467S.
 43. Salas-Salvado J, Guasch-Ferre M, Diaz-Lopez A, Babio N. Yogurt and Diabetes: Overview of Recent Observational Studies. *J Nutr.* 2017;147(7):1452S-1461S.
 44. Visioli F, Strata A. Milk, dairy products, and their functional effects in humans: a narrative review of recent evidence. *Adv Nutr.* 2014;5(2):131-143.
 45. Tolliver BA, Herrera JL, DiPalma JA. Evaluation of patients who meet clinical criteria for irritable bowel syndrome. *Am J Gastroenterol.* 1994;89(2):176-178.
 46. Deng Y, Misselwitz B, Dai N, Fox M. Lactose Intolerance in Adults: Biological Mechanism and Dietary Management. *Nutrients.* 2015;7(9):8020-8035.
 47. Nicklas TA, Qu H, Hughes SO, et al. Self-perceived lactose intolerance results in lower intakes of calcium and dairy foods and is associated with hypertension and diabetes in adults. *Am J Clin Nutr.* 2011;94(1):191-198.
 48. Suarez FL, Savaiano DA, Levitt MD. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med.* 1995;333(1):1-4.
 49. Eadala P, Matthews SB, Waud JP, Green JT, Campbell AK. Association of lactose sensitivity with inflammatory bowel disease--demonstrated by analysis of genetic polymorphism, breath gases and symptoms. *Aliment Pharmacol Ther.* 2011;34(7):735-746.
 50. Yang J, Fox M, Cong Y, et al. Lactose intolerance in irritable bowel syndrome patients with diarrhoea: the roles of anxiety, activation of the innate mucosal immune system and visceral sensitivity. *Aliment Pharmacol Ther.* 2014;39(3):302-311.
 51. Misselwitz B, Pohl D, Fruhauf H, Fried M, Vavricka SR, Fox M. Lactose malabsorption and intolerance: pathogenesis, diagnosis and treatment. *United European Gastroenterol J.* 2013;1(3):151-159.
 52. Bayless TM, Brown E, Paige DM. Lactase Non-persistence and Lactose Intolerance. *Curr Gastroenterol Rep.* 2017;19(5):23.
 53. Shaw AD, Davies GJ. Lactose intolerance: problems in diagnosis and treatment. *J Clin Gastroenterol.* 1999;28(3):208-216.
 54. Lebenthal E, Antonowicz I, Shwachman H. Correlation of lactase activity, lactose tolerance and milk consumption in different age groups. *Am J Clin Nutr.* 1975;28(6):595-600.
 55. Usai-Satta P, Scarpa M, Oppia F, Cabras F. Lactose malabsorption and intolerance: What should be the best clinical management? *World J Gastrointest Pharmacol Ther.* 2012;3(3):29-33.
 56. Hovde O, Farup PG. A comparison of diagnostic tests for lactose malabsorption--which one is the best? *BMC Gastroenterol.* 2009;9:82.
 57. Marton A, Xue X, Szilagyi A. Meta-analysis: the diagnostic accuracy of lactose breath hydrogen or lactose tolerance tests for predicting the North European lactase polymorphism C/T-13910. *Aliment Pharmacol Ther.* 2012;35(4):429-440.
 58. Di Rienzo T, D'Angelo G, D'Aversa F, et al. Lactose intolerance: from diagnosis to correct management. *Eur Rev Med Pharmacol Sci.* 2013;17 Suppl 2:18-25.
 59. Gasbarrini A, Corazza GR, Gasbarrini G, et al. Methodology and indications of H₂-breath testing in gastrointestinal diseases: the Rome Consensus Conference. *Aliment Pharmacol Ther.* 2009;29 Suppl 1:1-49.
 60. Savaiano DA. Lactose digestion from yogurt: mechanism and relevance. *Am J Clin Nutr.* 2014;99(5 Suppl):1251S-1255S.
 61. Kolars JC, Levitt MD, Aouji M, Savaiano DA. Yogurt--an autodigesting source of lactose. *N Engl J Med.* 1984;310(1):1-3.
 62. Heaney RP. Dairy intake, dietary adequacy, and lactose intolerance. *Adv Nutr.* 2013;4(2):151-156.
 63. Suchy FJ, Brannon PM, Carpenter TO, et al. National Institutes of Health Consensus Development Conference: lactose intolerance and health. *Ann Intern Med.* 2010;152(12):792-796.
 64. European Food Safety Authority. Scientific opinion on the substantiation of health claims related to live yoghurt cultures and improved lactose digestion (ID 1143,2976) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal.* 2010;8(10):1763-1781.