CHAPTER 8

Lactose Intolerance

I. INTRODUCTION

Dairy products are an important source of many nutrients including calcium, high-quality protein, potassium, phosphorus, and riboflavin. Dairy foods are an important part of the diets of children and adults in the United States, Canada, and Europe, as well as in other countries. It has been estimated that up to 75% of the world’s adult population (approximately 25% of American adults), however, have a genetically controlled limited ability to digest lactose, the principle carbohydrate in milk and other dairy foods. This condition is called lactase non-persistence. Limited digestion of lactose can lead to unpleasant gastrointestinal symptoms of varying severity, termed lactose intolerance. However, limited digestion of lactose does not necessarily produce the symptoms of intolerance. Incidence figures greatly overestimate the percentage of those who are lactose intolerant. The estimates are based on studies that employed a 50 gram test dose of lactose, the amount contained in a quart of milk, rather than on an amount usually consumed (12 grams).

All young mammals and human infants (except those with a congenital defect) are born with high levels of the enzyme “lactase” which enables them to digest lactose. Lactase activity declines after weaning in most racial/ethnic groups except most Caucasian North Americans and northern Europeans, so that by approximately 3 to 5 years of age, when the child is consuming a variety of foods, lactase levels are low.

Some have attempted to explain this phenomenon in terms of genetics and evolution. In this culture-historical hypothesis, the selection of a genetic trait (lactase persistence) is influenced by the cultural environment (dairying). A recent analysis supports the hypothesis that lactase persistence is an adaptation to dairying.

The pediatricians Czerny, Finkelstein, and Jacobi who noticed the association between diarrhea and carbohydrate ingestion first described intolerance to milk in 1901. In 1901, the famed biochemist Lafayette B. Mendel published a series of nine papers demonstrating that in most mammals the lactase enzyme reached maximal activity soon after birth; lactase activity then decreased gradually, reaching a
low level after weaning. In 1921, John Howland, in his address to the American Pediatric Society, proposed that milk intolerance in infants and children was due to the lack of the enzyme necessary to hydrolyze lactose. It was not until the mid 1960s that lactose intolerance again attracted the interest of researchers. It was reported that 70% of Black adults, but only 6 to 12% of Caucasian adults studied in Baltimore, were intolerant to the amount of lactose in a quart of milk. As studies were conducted in many populations around the world, it soon became apparent that a marked reduction of lactase activity in early childhood was not uncommon.

Investigators studying lactose intolerance, however, used a large amount of lactose dissolved in water as the test dose. The intolerance symptoms experienced under these experimental conditions has often mistakenly been equated with intolerance to milk in the diet. As a result, the incidence and practical significance of intolerance to milk has been grossly overestimated. Many studies have failed to recognize that cultural and psychosomatic factors as well as biologic mechanisms affect milk intolerance. Researchers investigating lactose intolerance have used a variety of terms to describe the processes involved, making interpretation difficult. Therefore, it is important to carefully define the terms used when comparing the results of research or discussing the topic of lactose indigestion and tolerance. For this reason, a glossary is included at the end of the chapter.

Scientific investigations from many different disciplines, including biochemistry, cultural anthropology, and nutrition have added to our knowledge about lactose digestion. As a result of these studies, we have learned that the ability to digest lactose in adults is most common in northern Europeans and white American ethnic groups; that the trait is genetically transmitted; that the activity of the enzyme cannot be “induced” by continued exposure to lactose, but that adaptation in the colon may improve tolerance to continued milk intake.

Persons who consume less milk and other dairy foods as a result of lactose intolerance generally have lower intakes of calcium and other nutrients supplied by milk, such as vitamin D, riboflavin, potassium, phosphorus, and magnesium. An inadequate calcium intake increases the risk of osteoporosis, hypertension, and perhaps colon cancer (see Section VI on long-term consequences of lactose intolerance). Much is now known about the maldigestion of lactose. Research into the factors involved in lactose digestion has fostered the development of strategies that allow those with low lactase activity to consume dairy products without experiencing unpleasant symptoms.

In this chapter, we will review the current literature on the subject to provide a clear understanding of the biologic mechanisms involved in lactose maldigestion and how individuals can best avoid the unpleasant symptoms which often accompany this condition. Since lactose maldigestion in a majority of non-Caucasian children in this country and developing countries has implications for public health and nutrition policy, we will also review recommendations for including milk in food aid programs and for the treatment of diarrheal disease and malnutrition in children.
II. PHYSIOLOGY OF LACTOSE DIGESTION

Lactose, or milk sugar, is the principle carbohydrate in human and animal milk. Human milk contains an average of 7% lactose, while whole cow’s milk contains 4.8%. Lactose is a disaccharide made up of equal portions of two monosaccharides, glucose and galactose (Figure 8.1). A unique intestinal enzyme, lactase, a beta-galactosidase, is needed to hydrolyze lactose. It breaks the chemical bond between glucose and galactose, freeing them for absorption. Lactase is one of five disaccharidases located on the brush border of the intestinal epithelium. Activity of the lactase enzyme is highest in the proximal ileum and very low in the first portion of the duodenum and in the terminal ileum.

Of all the dietary sugars, lactose is hydrolyzed the most slowly. The hydrolysis of lactose occurs at only half the rate of sucrose hydrolysis. The rate at which lactose is assimilated is dependent on the rate of the hydrolysis. The relative slowness with which lactose is broken down, accompanied by a lack of reserve of the enzyme, helps explain why many people are vulnerable to lactose maldigestion (Figure 8.2). It has been suggested that a faster-than-normal rate of gastric emptying in persons with low lactase activity may also contribute to symptoms of intolerance after milk ingestion. It is thought that when lactose is not hydrolyzed, the osmoreceptors, which lie deeper in the intestinal mucosa than the lactase enzyme, are not stimulated to inhibit gastric emptying.

A. Course of Development of Lactase

In contrast to the other disaccharidases, lactase appears very late in fetal development. It is estimated that at 35 to 38 weeks of gestation lactase levels are approximately 70% of their full-term level. Most studies of lactase development have been conducted in stillborn infants. Because premature infants who survive even for a short time have lactase levels above those of stillborn infants of the same gestational age, it is speculated that feeding might influence the infant’s lactase level after birth.
It is interesting to note that both preterm and term infants in the first few months of life do not completely hydrolyze the lactose in their mother’s milk, as indicated by high breath hydrogen concentrations, though they tolerate and thrive on human milk and formulas that contain lactose.\(^{11,12,13}\)

Klein and colleagues at The Ohio State University measured lactose digestion in 14 preterm infants (26 to 31 weeks of gestation).\(^{11}\) They found that these infants digested <85% of lactose consumed, and an average of 35% was fermented by the colon. Since previous studies conducted by the same group suggested no negative clinical consequences to feeding lactose-containing formulas, the authors concluded that replacement of lactose with other sugars might not be necessary for routine feeding of preterm infants. Lifshitz et al. evaluated lactose digestion in 17 white, normal, breast-fed infants who were 4 to 5 weeks old. Five of the infants (29%) produced large amounts of hydrogen in their breath, indicating that colonic bacteria were fermenting unabsorbed carbohydrate. Three of these infants stopped producing high levels of hydrogen as they grew older; all of them gained weight and grew normally. No glucose appeared in the stools of the infants tested, which indicates that the bacteria fermented the sugars released from lactose. The authors suggest that the fermentation products of unabsorbed lactose may be absorbed in the colon.\(^{13}\) There is evidence that colonic adaptation also occurs in adults with low lactase activity. This will be discussed later in Section 7.

B. Decline of Lactase Expression

A post-weaning decline in lactase activity is not dependent on the absence of lactose in the diet. Many studies have documented that continued lactose consumption does not maintain or enhance lactase. Instead, researchers have concluded that human adult-onset lactase decline is controlled by a single autosomal recessive gene. Researchers using the sucrase/lactase ratio and the lactase/maltase ratio measured in intestinal biopsies, found a trimodal distribution (low, intermediate, and high) of lactase expression. Subjects with a homozygous recessive inheritance pattern had low levels of lactase expression; those who were heterozygous had intermediate levels; those who had a homozygous dominant pattern had high lactase activity.

C. Molecular Regulation

Studies conducted in the fields of molecular and cell biology have provided insight into the gene structure, gene transcription, localization of expression in the small intestine, and biosynthesis of lactase protein. The lactase gene is located on chromosome 2. Differences in the structure of the gene itself, however, are not responsible for differences in lactase expression. Lactase messenger RNA in humans, rats, and rabbits changes coordinately with the amount of enzyme activity, suggesting control of lactase expression at the level of gene transcription.

Researchers in Italy examined lactase activity, biosynthesis, and the levels of messenger RNA (mRNA) in jejunal mucosa of lactase persistent and nonpersistent adults. They concluded that both transcriptional and posttranscriptional factors cause the decline of intestinal lactase. Biosynthesis of prolactase (the precursor of lactase) correlated well with lactase mRNA levels, indicating transcriptional control. A high rate of biosynthesis was the main factor distinguishing those with lactase persistence; the rate was five times higher than in those with non-persistence. These Italian researchers found that posttranscriptional factors (e.g., the routing of prolactase from the endoplasmic reticulum to the brush border membrane, the speed of processing during this routing, or the breakdown of lactase), also influenced lactase levels to some degree. However, they observed wide variability of mRNA level, lactase synthesis, and activity in both lactase persistent and nonpersistent individuals. With such a variety of factors responsible for the decrease in intestinal lactase, it is not surprising, say these researchers, that the time of onset of adult-type hypolactasia can vary widely among various population groups.

The Caco-2 cell line derived from a human colon adenocarcinoma, which expresses hydrolases such as lactase and sucrase-isomaltase, have been used to study the regulation of lactase expression. Studies using Caco-2 cells have demonstrated that biosynthesis of lactase is preceded by a large increase in messenger RNA levels, indicating transcriptional control.

Studies have shown that the decrease in lactase activity is determined by the age of the tissue, not the age of the host. Therefore the pattern for expression is apparently imprinted in the tissue of intestinal epithelum. Several mechanisms for controlling lactase expression have been hypothesized and are currently under investigation.
including regulation by corticoid or thyroid hormones. One promising line of research involves a nuclear factor (NF-LPH1), which binds specifically to the lactose promoter and may be an important regulator of gene transcription.\(^\text{19}\)

**D. Types of Lactase Deficiency**

The absence or decline of intestinal lactase can be described as being *congenital*, *primary*, or *secondary*. Congenital lactase deficiency, or alactasia, is an extremely rare condition in which detectable levels of lactase are absent at birth. An infant with congenital lactase deficiency will have severe diarrheal illness beginning a few days after birth. In addition to measuring breath hydrogen production in these infants, other more aggressive diagnostic procedures such as an intestinal biopsy to measure lactase activity and/or intestinal perfusion study, may be required to rule out other diagnoses.\(^\text{20}\) In congenital lactase deficiency the histology of the small bowel is normal, as is the level of other disaccharidases. Symptoms will resolve if the infant is put on a lactose-free diet. According to recent position paper by the American Academy of Pediatrics, soy protein-based formulas (lactose-free), are appropriate for infants with this form of hereditary lactase deficiency.\(^\text{21}\) Persons with this disorder are unable to tolerate even small amounts of lactose, and will need to follow a lactose-free diet for the rest of their lives.\(^\text{22}\) It is not known whether colonic adaptation might allow a measure of tolerance in these individuals.

In primary lactase deficiency, decline of lactase activity occurs at variable periods after weaning depending on racial/ethnic background (Figure 8.3). In the United States, some degree of lactose maldigestion occurs in an estimated 15% (6% to 19%) of Caucasians, 53% of Mexican Americans, 62% to 100% of Native Americans, 80% of African Americans, and 90% of Asian Americans.\(^\text{2,23}\) Although the standard lactose tolerance test is effective for determining genetic differences in lactase among populations, it tends to overestimate the number of individuals who are intolerant to more physiologic amounts of lactose. Lactase deficiency is seldom total, and whether symptoms of intolerance are experienced depends on the level of lactase activity remaining, the amount of lactose consumed, the adaptation of intestinal flora, and the irritibility of the colon. Primary lactase deficiency or lactase non-persistence is genetically determined and is inherited as an autosomal recessive trait. In contrast, lactase persistence is inherited as an autosomal dominant characteristic.\(^\text{2,7}\)

It is interesting to note that as those who have the ability to digest lactose intermarry with those from a racial/ethnic group that typically does not digest lactose, the rate of maldigestion falls.\(^\text{24}\) For example, though African Americans have an expected rate of lactose maldigestion near 100%, the prevalence has decreased to 70% due to intermixing with white Americans.\(^\text{24}\) The ability of Native Americans to digest lactose has also increased over time. These examples demonstrate the dominant inheritance pattern of the ability to digest lactose.

A large number of studies have been conducted around the world to examine the incidence and age of onset of lactase non-persistence.\(^\text{2}\) Many studies have included wide age ranges of subjects, spanning from the early teens into the 70s, making it difficult to establish a precise relationship between age and prevalence. It appears that the primary reduction in lactase activity occurs in early childhood and
is thought not to progress throughout life. A recent study comparing lactose tolerance between adult (20 to 40 years) and elderly (≥65 years) Asian-Americans confirmed this hypothesis. When fed a challenge dose of 0.5 g lactose/kg body weight, there were no significant differences in breath hydrogen production, flatulence, or fecal β-galactosidase activity between the adult and elderly subjects. Additional studies are needed to confirm these findings in other ethnic populations. Individuals with primary lactase deficiency do not need to avoid all foods containing

Figure 8.3  Lactase activity, age, race, and deficiencies. (From Ferguson, A., Allergy, 50(20 Suppl.), 32, 1995. With permission).
lactose. By using the management strategies outlined later in this chapter, a variety of dairy foods may be comfortably included in the diet.

Secondary lactase deficiency is a temporary condition, caused by any environmental factors that injure the intestinal mucosa where lactase is expressed. It can occur at any age. The most important causes of secondary lactase deficiency are infectious diarrheal disease, the parasites giardia and ascaria, inflammatory bowel disease such as Crohn’s disease, celiac disease, allergy to milk protein, gastrointestinal surgery, radiation treatment, and certain medications such as aspirin, non-steroidal anti-inflammatory drugs, and antibiotics. Secondary lactase deficiency is reversed upon correction of the causative factor.

When diarrhea is of infectious origin, loss of lactase activity may persist for a long time if the diarrhea is recurrent. In severe protein-calorie malnutrition, such as kwashiorkor, lactase activity is reduced along with all other enzyme activity. Lactose tolerance increases quickly as nutritional status improves. In children who developed a lactase deficiency secondary to cancer chemotherapy treatments, yogurt proved a useful dietary supplement. diets

Diet therapy for secondary lactose intolerance involves restricting or eliminating lactose-containing foods depending upon the tolerance of the patient. Since tolerance varies between patients, the diet is administered on a trial-and-error basis. Consultation with a nutrition professional will help prevent nutritional deficiencies during treatment of the underlying disease. Patients may need to restrict all lactose-containing foods temporarily or use lactose-hydrolyzed products. A recent commentary on dairy sensitivity in patients with inflammatory bowel disease (IBD), states that patients with either ulcerative colitis or Crohn’s disease often avoid dairy products more than they need to because they have incorrect perceptions, and receive arbitrary advice from physicians and authors of popular diet books. Since dairy products are an important source of calcium and other nutrients, the author recommends testing IBD patients for lactose malabsorption using the breath-hydrogen test before recommending the elimination of dairy foods or the use of lactose-reduced products. In a study of 161 IBD patients, those with diagnosed lactose maldigestion (29%) did not have significantly different gastrointestinal symptoms or improvement/worsening of their condition than those who digested lactose. Most of the patients felt, however, that identifying lactose maldigestion helped them to gain awareness of food-symptom relationships.

Manufacturers of candy, confections, and bakery products, such as pancakes, waffles, and toaster pastries use lactose as an ingredient. Its limited sweetness, solubility, crystallization, and browning properties make it ideal for use in these products. Other non-dairy foods that may contain lactose include shakes and instant breakfast mixes, coffee whiteners, commercial breakfast and baby cereals, cake mixes, mayonnaise, salad dressings, luncheon meats, sausage, and frankfurters. If intolerance is severe, patients may need to check ingredient labels and avoid products with the following ingredients: milk, lactose, milk solids, whey, curds, nonfat milk powder, and nonfat milk solids. Medication and vitamin labels should be checked as well, since some contain lactose as a carrier. Some dairy foods, such as Cheddar cheese, have a relatively low lactose content. See the table, Lactose Content of Dairy Products included at the end of this chapter.
E. Lactose Malabsorption

It is estimated that of the lactose that remains unhydrolyzed in the small intestine, approximately 1% is absorbed by passive diffusion into the bloodstream, which is then excreted into the urine unmetabolized. As the remainder of unabsorbed lactose reaches the jejunum, it exerts an osmotic effect, causing water and sodium to be secreted into the intestinal lumen. Transit of the contents of the small bowel accelerates. Significant amounts of lactose may then enter the colon, where it is fermented by colonic bacteria. The majority of the undigested lactose reaching the colon is metabolized to short chain organic acids, and hydrogen, methane, and carbon dioxide gases. Some of the organic acids are absorbed into the bloodstream, while some may be excreted in the feces, resulting in acidic stools (Figure 8.4).  

III. SYMPTOMS

Lactose intolerance refers to gastrointestinal symptoms associated with the incomplete digestion of lactose. The presence of fermentation products in the colon may produce a variety of symptoms including abdominal discomfort, cramps or distention; nausea; flatulence; or diarrhea. Symptoms resulting from lactose malabsorption may be more pronounced in women than in men, according to a study...
conducted recently in Germany.\textsuperscript{31} The women in the study, who were diagnosed as maldigesters by a breath-hydrogen test, had lower breath hydrogen concentrations after ingestion of 50 g of lactose and complained of more abdominal pain, gas, and distension than did their male counterparts. Another recent controlled trial of lactose maldigesters, however, demonstrated no gender differences in lactose digestion or tolerance (unpublished data per personal communication: Dennis Savaiano).

Individuals with an allergy to cow’s milk protein may experience symptoms similar to those of lactose intolerance. Therefore it is important to make the distinction between these two very different sensitivities involving the ingestion of milk (Table 8.1).

<table>
<thead>
<tr>
<th>Milk Allergy</th>
<th>Lactose Intolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cause</td>
<td>Abnormal immune response to ingestion of cow’s milk protein</td>
</tr>
<tr>
<td>Age of Onset Symptoms</td>
<td>Usually in infancy</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain, vomiting, diarrhea, nasal congestion, skin rash</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Food elimination and challenge; RAST blood test</td>
</tr>
<tr>
<td>Dairy Food Use/Avoidance</td>
<td>Eliminate cow’s milk protein from the diet for a time</td>
</tr>
</tbody>
</table>

In milk allergy, gastrointestinal symptoms may predominate, but other symptoms involving the respiratory tract and skin, such as rhinitis and atopic dermatitis, are also common. Cow’s milk allergy usually occurs within the first four months of life in bottle-fed infants, though it may in rare instances be first detected in adolescence or adulthood. The incidence of cow’s milk allergy as determined by double-blind studies is quite low, in the range of 1 to 3% of infants and children in the first two years of life. Most children with milk allergy outgrow it by age 2-3 years as a result of maturation of the gastrointestinal and immune system.\textsuperscript{31} This is the reverse of the time-course of lactose intolerance, which may begin to appear at this age in some individuals.\textsuperscript{2}

IV. DIAGNOSIS

Dietary exclusion of lactose is the diagnostic method used by most physicians when they suspect lactose intolerance.\textsuperscript{29} There are several reasons why this is an unsatisfactory approach. Most importantly, this approach is highly inaccurate. Several double-blinded studies have shown that many patients who believe they are intolerant to milk and milk products continue to report symptoms when lactose is removed from the diet.\textsuperscript{34-39} In addition, exclusion diets usually involve removing only dairy products from the diet and have several drawbacks, whether used by a
physician or for self-diagnosis. Excluding dairy foods from the diet for an arbitrary amount of time could result in nutritional shortcomings. If all foods containing lactose are not removed from the diet, symptoms may continue, leading the client to believe lactose was not the cause of the symptoms. Or the reverse could be true; removal of lactose from the diet may happen to coincide with resolution of the symptoms from a totally unrelated cause, thus perpetuating unnecessary dietary restrictions. In addition, self-diagnosis could delay treatment for another more serious gastrointestinal problem. If symptoms are chronic, a physician should be consulted, and an objective test for lactose maldigestion conducted.

Both direct and indirect methods are available to diagnose lactase deficiency. It is possible to directly assay the lactase activity in the small bowel by taking an intestinal biopsy. Researchers have used this method to identify populations with primary lactase deficiency. The procedure is invasive and time-consuming, and may not yield accurate results when intestinal injury is involved. This is because intestinal lesions may affect only a small area that may be missed during the biopsy. Symptoms of intolerance do not correlate as well with mucosal lactase activity as they do with the breath hydrogen test, an indirect measure of lactose maldigestion.\(^7\)

Indirect methods for diagnosing lactose maldigestion include the lactose tolerance test, a stool acidity test, and the breath hydrogen (\(H_2\)) test. The lactose tolerance test, which measures the rise in blood glucose after a dose of lactose, is performed in a manner similar to that of the glucose tolerance test used for the diagnosis of diabetes mellitus. A relatively large dose of lactose is required to separate digesters from maldigesters. Typically, an aqueous solution of 50 g of lactose is consumed. In persons who weigh more than 25 kg, a dose of 100 g may be required.\(^20\) Blood is drawn before lactose ingestion, then at intervals of 30, 60, 90, and 120 minutes thereafter.\(^29\) Failure of blood glucose to rise 20 mg/dl from baseline, in the presence of symptoms, indicates lactase deficiency. Even though the lactose tolerance test (actually, a test for lactose maldigestion) is positive, smaller amounts of lactose may be tolerated.\(^22\) This method is mildly invasive, since several blood samplings are involved, and results correlate poorly with actual mucosal lactase levels. Since the rate of gastric emptying slows the rate at which glucose enters the bloodstream, individuals with delayed gastric emptying will have a false-positive test.\(^20\) Results will be questionable if used with diabetic patients or those with malabsorption syndromes.

Testing stool samples for acidity and reducing sugars has been used for years to assess whether infants and young children are absorbing lactose. The test, however, requires the presence of lactose in the diet and availability of fresh stool. The test is not sensitive enough to exclude lactose intolerance, but can be used to confirm the results of another test.\(^29\)

The breath hydrogen (\(H_2\)) test has become the “gold standard,” or method of choice, for diagnosing lactose maldigestion. The test is noninvasive, inexpensive, and can easily be performed on children and adults. The results of this test are reported to correlate well with lactase activity in mucosal biopsy specimens.\(^40\) When lactose or any other dietary sugar is not completely absorbed, the unabsorbed portion is fermented by colonic bacteria, forming hydrogen (as well as methane in some
individuals and CO\textsubscript{2}), some of which is absorbed into the portal circulation and exhaled in breath.\textsuperscript{7}

Test protocol requires the patient to report after an overnight fast, where a baseline breath sample is taken. Historically, the patients were given a 20\% aqueous solution of 2 g of lactose per kg of body weight (10 to 50 g) to drink. Fifty grams of lactose is the amount contained in one quart of milk. The solution may be diluted to 10\% in infants younger than 6 months or in adults when severe lactose intolerance is suspected. Breath samples are taken every 30 min for 3 hours; samples are collected in test tubes, and hydrogen in breath is analyzed by gas chromatography. An increase in breath hydrogen of >10 to 20 ppm above the baseline value indicates fermentation of unabsorbed carbohydrate, and is positive for lactose maldigestion.\textsuperscript{29}

Even though a rise in breath hydrogen of 10 ppm above baseline indicates the presence of incompletely absorbed lactose in the colon (more than can be accounted for by variability of the technique), many investigators recommend that a rise of 20 ppm be used as the criteria for judging lactose digestion as "abnormal."\textsuperscript{20} This criteria is often used because it correlates with less than a 20 mg/dl rise in blood glucose following a 50 g dose of aqueous lactose. However, this rationale has been questioned, because using the >20 ppm criteria unnecessarily limits the sensitivity of the breath hydrogen test to that of the lactose tolerance test, especially when the dose of lactose given is less than 50 g.\textsuperscript{41}

Hydrogen production is proportional to the lactose dose. Therefore, when the dose of lactose given is small (10 to 12 g), the criteria of >10 ppm above baseline is diagnostic of lactose maldigestion. Patients with a breath hydrogen rise of only 10 ppm are less likely to experience intolerance symptoms than those with a higher rise.\textsuperscript{42} The lactose dose used for the test may also be administered in the form of milk, infant formula, or yogurt (not with active cultures). Lactose doses in the range of usual intakes (10 to 12 g) can be used, since the test can determine the maldigestion of as little as 2 g of carbohydrate.\textsuperscript{7} When the hydrogen breath test is used for research purposes, many investigators collect samples for 8 hours. This increases the sensitivity of the test when lower doses of lactose are administered. While the breath hydrogen test has the capability of measuring absorption of the amount of lactose in usual milk intakes, the protocol historically used pharmacological doses.

A small percentage of people (2 to 20\%) do not have colonic flora which ferment lactose; this can lead to false negative results. This situation is uncommon and may be the result of the use of an antibiotic before the test.\textsuperscript{29} Smoking prior to the test may lead to a false-positive result.\textsuperscript{7}

The breath hydrogen test is also useful in diagnosing an underlying condition, such as bacterial overgrowth, which can cause secondary lactose intolerance. The bacterial overgrowth in the small bowel can be treated with antibiotic therapy and the secondary lactose maldigestion is managed with a lactose-controlled diet.\textsuperscript{29} Lactose maldigestion eventually resolves with the treatment of the underlying condition. In children less than 5 years of age, an abnormal breath hydrogen test indicates an abnormal intestinal mucosa and lactose maldigestion secondary to another problem.\textsuperscript{43}
Patients can now easily perform the breath hydrogen test at home using commercially available kits. Breath samples in vacutainers can be mailed to a central laboratory for analysis.  

V. RELATIONSHIP BETWEEN LACTOSE MALDIGESTION, INTOLERANCE, AND MILK INTOLERANCE

A. Dose Dependence

Controlled studies have shown that consuming one cup of milk (240 ml) or its lactose equivalent (12 g) at a time produces little or no intolerance symptoms in adults with primary lactase deficiency. The vast majority of those with low lactase levels can tolerate ingestion of 12 g of lactose, particularly if consumed with a meal or other foods. Hertzler et al. found that individuals with lactase non-persistence could tolerate up to 6 g of lactose under fasting conditions when consumed in water. When the lactose dose is 50 g vs. 12 g, a much higher percentage of those with hypolactasia experience intolerance symptoms. A group of American Indians studied by Newcomer in 1978 illustrates this phenomenon. Less than 20% of the subjects experienced symptoms when the lactose dose was between 0 and 18 g. However, 88% were symptomatic to a dose of 50 g (Figure 8.5).

Therefore the term lactose intolerance should only be used when referring to the symptomatic response to a defined lactose load. For example, an individual might be tolerant to 12 g of lactose, but be intolerant to 24 g. Determination of the presence and severity of symptoms is somewhat subjective, and may be influenced by factors other than the presence of lactose. Lactose maldigestion, on the other hand, is...
determined by an objective test, such as the breath hydrogen test. Both the objective
determination of maldigestion and the subjective determination of intolerance are
needed to develop a dietary strategy. Those with limited lactose digestion may or
may not experience intolerance symptoms.

B. Milk Intolerance

Milk intolerance due to lactose is characterized by at least one clinical sign of
intolerance experienced a few hours after ingestion of a known quantity of milk or
milk-containing products. When the prevalence of milk intolerance is being evalu-
ated rather than lactose maldigestion, several factors, such as the amount and form
in which lactose is given, whether it is consumed with a meal, and whether the study
is double-blinded, may influence the results.

Johnson et al. evaluated the relationship between maldigestion and intolerance
in 164 African American adolescents and adults. Objective testing with the breath
hydrogen test revealed that 50% of the subjects maldigested and were intolerant to
25 g of lactose, the amount in 2 cups of milk (480 ml); 86% of this group experienced
symptoms of lactose intolerance. Eight percent of the subjects were maldigesters,
but tolerant; 15% were digesters but intolerant; and 27% were digesters and tolerant
(Table 8.2). This study further confirms what others have observed, that there is a
complex relationship between lactose maldigestion, lactose intolerance, and milk
intolerance.

It is important that studies evaluating lactose tolerance (or other food tolerance)
be double blind. This means that neither the subject nor the investigator knows
whether the test solution contains lactose or a placebo. Unblinded studies may
overestimate intolerance due to expectations of the subjects or the researcher. Lactose
is often given in water for tolerance testing, and can be easily distinguished from a
solution of glucose and galactose. When different levels of lactose are tested in milk,
it is important to give the same volume of milk. When tolerance to milk is compared
to that of lactose-hydrolyzed milk, an artificial sweetener should be added to the
milk so that subjects cannot distinguish a taste difference between products. Subjects

<p>| Table 8.2 Outcome of Lactose-Tolerance Breath-Hydrogen Study in 164 Volunteers. All Volunteers Claimed to be Intolerant of a Cup (240 mL) of Milk |</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>Classification</th>
<th>Symptoms*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Maldigesters, intolerant</td>
<td>+</td>
<td>82 (50)</td>
</tr>
<tr>
<td>2</td>
<td>Maldigesters, tolerance</td>
<td>–</td>
<td>13 (8)</td>
</tr>
<tr>
<td>3</td>
<td>Digesters, intolerant</td>
<td>+</td>
<td>25 (15)</td>
</tr>
<tr>
<td>4</td>
<td>Digesters, tolerant</td>
<td>–</td>
<td>44 (27)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>164 (100)</td>
</tr>
</tbody>
</table>

* Symptoms: abdominal fullness, cramps, flatulence, burbo-
ygmi, nausea, vomiting, diarrhea.

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who are aware that the solution they are drinking contains lactose or that the volumes are being increased, sometimes experience symptoms they wouldn’t have otherwise. Newcomer states that if all the studies evaluating tolerance were blinded, the percentage of subjects intolerant to 12 g of lactose would be only 10-15%. Results of recent double-blind, randomized, crossover trials indicate that most individuals with primary lactase deficiency can tolerate one cup (240 ml) of milk with a meal or two cups (480 ml) if consumed in divided doses with breakfast and dinner. Most recently, the same investigators found that women with limited lactose digestion can eat a dairy-rich diet that includes milk, yogurt, and cheese, supplying about 1500 mg of calcium per day, without major impediment.

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Lactose Dose (g) Breath Hydrogen Test</th>
<th>Lactose Digesters</th>
<th>Lactose Maldigesters</th>
<th>Milk Products Tested</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suarez et al.</td>
<td>30 self-described, LI racially mixed adults</td>
<td>15 g</td>
<td>30%</td>
<td>70%</td>
<td>One cup of milk (12 g lactose) with breakfast</td>
<td>All tolerant</td>
</tr>
<tr>
<td>Suarez et al.</td>
<td>49 self-described, LI racially mixed adults</td>
<td>15 g</td>
<td>31%</td>
<td>69%</td>
<td>Two cups of milk/day consumed in divided doses with breakfast and dinner</td>
<td>All tolerant</td>
</tr>
<tr>
<td>Suarez et al.</td>
<td>62 female racially mixed adults</td>
<td>15 g</td>
<td>50%</td>
<td>50%</td>
<td>One cup of milk at breakfast, 1 cup of milk, 1 ounce of cheese and 8 ounces of yogurt at lunch, and 1 cup of milk and 1 ounce of cheese at dinner.</td>
<td>All tolerant – increased flatus frequency rated &quot;trivial&quot; in maldigesters</td>
</tr>
</tbody>
</table>

Suarez et al. measured gastrointestinal symptoms in 30 subjects who described themselves as intolerant to very small amounts of milk, such as the amount used on cereal or in coffee. Of the 30 subjects, 21 (70%) were lactose maldigesters based on breath hydrogen concentrations after intake of 15 g of lactose, whereas 9 (30%) were lactose digesters. Both groups then participated in a randomized, double-blind, crossover trial in which they received either one cup of 2% milk (lactose-containing) or lactose-hydrolyzed milk every day with breakfast for one week. Since hydrolysis of the milk increases the sweetness, aspartame was added to the regular milk so that the sensory characteristics of the two milks were indistinguishable. The symptoms reported by both maldigesting and digesting subjects after consumption of one cup of milk (240 ml) were minimal, and were not significantly different than those...
reported after consumption of lactose-free milk. The researchers concluded that lactose-digestive aids are not necessary when lactose intake is limited to the equivalent of 240 ml of milk or less a day.\textsuperscript{34}

The same researchers conducted a similar trial to test tolerance to two cups of milk daily (i.e., the average amount usually consumed).\textsuperscript{35} A secondary goal of the study was to determine whether psychological factors play a role in a subject's perception of intolerance (this will be discussed in more detail in the next section). Two groups of lactose maldigesters (confirmed by a breath hydrogen test to 15 g of lactose), participated in the study: those who believed they were markedly intolerant to lactose (symptomatic) and those who believed that lactose did not induce symptoms (asymptomatic). Participants received either one cup of 2\% milk (lactose-containing) or one cup of lactose-hydrolyzed milk with breakfast and another at dinner for one week. After a seven-day washout period, study participants switched to the opposite treatment. Both symptomatic and asymptomatic lactose maldigesters reported only minimal symptoms following intake of regular or lactose-free milk. These findings indicate that most self-described lactose intolerant subjects can readily tolerate two cups of milk daily if this milk is ingested in divided doses with breakfast and dinner.\textsuperscript{35}

In a subsequent randomized, double-blind, crossover design study, Suarez and colleagues at the University of Minnesota, tested whether lactose maldigesting pre- and postmenopausal women could tolerate a dairy-rich diet providing approximately 1500 mg of calcium/day, the amount recommended by an Expert Panel of the National Institutes of Health to prevent osteoporosis.\textsuperscript{49} The intake of dairy products was spread out over the day, and a variety of dairy products were used. The participants (50\% maldigesters and 50\% digesters per the breath hydrogen test) were randomly assigned to one of two dietary regimens for one week, then switched to the other (1) 240ml of 1\% fat milk with breakfast and dinner, plus one serving (30 g) of a hard cheese at lunch and dinner, and 8 ounces of low fat, strawberry flavored yogurt at lunch; or (2) a similar regimen using lactose-hydrolyzed milk and yogurt. The dairy products provided about 1300 mg of calcium per day; it was assumed that the remainder of the diet would provide about 200 mg of calcium daily. Lactose maldigesters who consumed the dairy-rich diet experienced a significantly greater frequency of small flatus, but no differences in bloating, abdominal pain, nausea, fullness, or diarrhea, than when they consumed lactose-hydrolyzed products.

The above findings indicate that primary lactase deficiency need not be an obstacle to meeting calcium needs with milk and milk products. It has been confirmed with double-blind trials that lactose maldigesters can tolerate the amount of lactose in approximately 3 to 4 servings of milk and milk products, which provides the amount of calcium recommended by the expert panel of the National Institutes of Health (i.e., 1000 to 1500 mg) or the National Academy of Sciences for American adults (i.e., 1000 to 1200 mg).\textsuperscript{50}

\textbf{C. Subjective Factors Affecting Milk Tolerance}

Some individuals, whether or not they are able to digest lactose, experience intolerance symptoms to whatever placebo is used in double-blind studies. This
phenomenon complicates the diagnostic process, making it difficult for clinicians to accurately assess their patient’s condition. Tolerance to milk is sometimes affected by factors unrelated to its lactose content, such as psychological factors or cultural attitudes toward milk.

A discussion of studies observing this phenomenon may help illustrate the complexity of the problem. Haverberg et al., in a double-blind trial, evaluated tolerance to 240 ml and 480 ml of a lactose-free and lactose-containing chocolate dairy drink in a group of 110 healthy Boston teenagers, 14 to 19 years of age. Theoretically, symptoms due to lactose should occur only in those with limited lactose digestion in response to a lactose-containing beverage. However, 40% of those identified as lactose digesters per a breath-hydrogen test, and 31% of maldigesters reported symptoms after consuming the lactose-free beverage or after both the lactose-containing and the lactose-free beverage. Suspecting that perhaps the large number of false-positive results were because too much emphasis had been placed on reporting symptoms, the researchers conducted a follow-up study in a similar population of high school students using a simplified questionnaire that placed less emphasis on possible symptoms.

This time, 29% of the lactose digesters reported symptoms that apparently were due to an unidentified cause other than lactose. One criticism of these studies is that since chocolate has been shown to improve tolerance to lactose, the addition of chocolate to the dairy drinks (used to make the drinks similar in taste) may have affected the level of symptoms reported. Healthy elderly lactose digesters and maldigesters following a similar protocol to that of Haverberg, reported symptoms with the same degree of frequency to a lactose-containing drink as to a lactose-free drink. The authors concluded that the symptoms were either psychosomatic or were the result of other physiologic causes.

Johnson et al. tested for milk tolerance a subgroup of 45 African American subjects who had confirmed lactose maldigestion and intolerance to 25 g of aqueous lactose. Subjects were given either 315 ml of lactose-containing milk or lactose-hydrolyzed milk alternately on three different days in a double-blind test. One third of the subjects experienced symptoms of intolerance to both types of milk, indicating that their symptoms were not due to lactose. The authors conclude that social and cultural habits and attitudes also affect tolerance to milk drinking.

Two recent studies by Suarez et al. discussed earlier also illustrate this phenomenon. In a study testing tolerance to one cup of milk served with breakfast, the researchers recruited subjects who reported severe lactose intolerance and who said they consistently experienced symptoms after consuming less than 240 ml of milk. Surprisingly, approximately one third (9 out of 30) of the subjects who claimed intolerance were able to digest lactose per the breath-hydrogen test. The authors concluded that people who identify themselves as severely lactose intolerant may mistakenly attribute a variety of abdominal symptoms to lactose intolerance.

Similarly, in a second study designed to test tolerance to two cups of milk, approximately a third (31%) of recruited subjects (of mixed ethnic background) who claimed severe intolerance, were able to digest lactose as measured by the breath-hydrogen test. This group was not included in the subsequent milk trial, but was included with the other subjects in a psychological assessment, using the Minnesota Multiphasic Personality Inventory. The lactase deficient subjects who complained
of symptoms, demonstrated a high level of psychasthenia (incapacity to resist irrational phobias, obsessions, and compulsions), but no correlations with any clinical psychological conditions (e.g., depression, hypochondriasis, paranoia) in response to the personality inventory. However, since these individuals also failed to respond candidly to the test (they tended to exaggerate, minimize, or conceal information), the researchers question the validity of these findings.

These studies further emphasize the need for objective testing for those complaining of gastrointestinal symptoms after drinking milk, since it appears that a significant portion of the population mistakenly attribute their symptoms to lactose.

D. Lactose Tolerance During Pregnancy

Pregnant women need to consume at least three servings of Milk Group foods to obtain the 1000 mg of calcium/day recommended by the National Academy of Sciences. Women with limited lactose digestion may be encouraged to discover that their tolerance to lactose-containing milk and milk products may improve during pregnancy.

For example, Villar and colleagues demonstrated that 44% of women who maldigested 360 ml of milk (18 g of lactose) before the 15th week of gestation, were able to digest that amount of lactose by the end of their pregnancy. Average breath hydrogen (an indication that undigested lactose is being metabolized by colonic bacteria) decreased by more than half over this time period.

Some researchers hypothesize that slower intestinal transit time during pregnancy improves tolerance to lactose. For example, investigators compared lactose maldigestion and symptoms of intolerance between pregnant African American women and nonpregnant controls. The pregnant women reported fewer symptoms than the nonpregnant women after drinking 8 ounces of 1% milk, although their ability to digest lactose did not change. The authors suggest that the improved tolerance was most likely due to slower intestinal transit time. They explain that because the rise in breath hydrogen in response to ingested lactose occurs approximately an hour later in pregnant versus nonpregnant women, breath hydrogen should be measured over a longer time period. This may be why earlier studies showed improved digestion. Whether actual digestion improves or not, it is clear from these studies that women may enjoy improved tolerance to milk and milk products while they are pregnant.

VI. LONG-TERM CONSEQUENCES OF LACTOSE INTOLERANCE

A. Lactose Digestion and Calcium/Nutrient Absorption

Studies conducted in the 1970s and 1980s in both animals and humans failed to provide any evidence that the maldigestion of lactose impaired the absorption of any other nutrient. Nutrients studied include protein, fat, vitamins A and C, calcium, magnesium, copper, manganese, and zinc. In a review of this information, Leichter concluded that “if the unabsorbed lactose has some effect on the absorption of other nutrients it is doubtful whether this effect has significant nutritional consequences
in healthy lactose intolerant adults who consume milk and milk products in moderate amounts.54

Because some portion of the lactose consumed passes undigested into the colon, those with limited lactose digestion obtain slightly less energy from milk and milk products than do lactose digesters. Part of the unabsorbed lactose is converted by fermentation into volatile fatty acids which are a source of energy and may help maintain the health of intestinal cells.2 The small amount of energy lost seems to be of no practical significance.

While the presence of lactose stimulates the intestinal absorption of calcium in laboratory animals55 and in human infants,56 there is no evidence that it improves calcium absorption in adults.57 Conversely, limited digestion and absorption of lactose does not appear to decrease calcium absorption. A review of research in this area concludes “the bulk of the evidence indicates a favorable or neutral effect of lactose on Calcium absorption in both lactose digesters and maldigesters.”2

Tremaine and colleagues investigated how lactose might influence the absorption of calcium from milk in adults with and without lactase deficiency.58 Using a double-isotope method, the researchers compared calcium absorption between lactose-containing milk and hydrolyzed milk in both lactase-deficient and -sufficient adults. The subjects with lactase deficiency absorbed calcium equally well from lactose-containing or lactose-hydrolyzed milk. Mean calcium absorption was greater in lactase-deficient subjects, presumably due to a lower calcium intake. Decreased calcium intake is known to cause an increase in calcium absorption, although calcium intake was not verified by diet history in this study. Horowitz et al. found no relationship between lactose and calcium absorption when an oral dose of 5 μ Ci of radioactive calcium chloride (20 mg of calcium) was measured in serum an hour later in 46 postmenopausal women with osteoporosis.59 Roughly half of all subjects, whether or not they were lactose maldigesters, had below normal absorption of calcium. Griessen and colleagues also studied what influence lactase deficiency might have on calcium absorption.60 Using a double-isotope technique, they compared calcium absorption in young adult lactase-deficient and -sufficient males from two commercial milks, one containing lactose and the other containing glucose. They then compared absorption between lactose-containing milk and water. Results demonstrated that all subjects absorbed calcium equally well from milk and from water. Glucose, when substituted for lactose in milk, did not improve calcium absorption. Lactase-deficient subjects absorbed calcium from the lactose-containing milk better than did the lactase-sufficient subjects. The authors did not attribute the increase to lower calcium status of the lactase-deficient group, since calcium intake of all subjects was normalized prior to the beginning of the study. The authors conclude that avoidance of dairy foods, rather than calcium malabsorption, is most likely the cause of increased risk of osteoporosis in lactase-deficient individuals.

B. Effect on Milk Consumption and Nutritional Status

Lactose intolerance is one factor that may influence milk consumption. Data from most studies, but not all,61 suggest that individuals with primary lactose deficiency consume less milk than those who digest lactose normally.39,54,62 For example,
in a study conducted at the University of Connecticut, subjects with a history of milk intolerance consumed significantly less milk than the control subjects. The adult subjects consumed an 8-ounce serving (240 ml) of milk less than 1 to 3 times per month, while the lactose tolerant control group consumed an average of 1 to 2 servings of milk per day.\textsuperscript{62} Finkenstedt et al. observed that lactose maldigestion affected milk intake in middle aged women. The daily intake of calcium from milk was significantly lower in those women with osteoporosis (125 mg/d) vs. controls (252 mg/d), more of whom were lactose maldigesters. Because of this finding, the investigators suggest that lactose maldigestion be considered a risk factor for osteoporosis.\textsuperscript{63}

Interestingly, decreased milk intake as a result of lactose intolerance is not always a deliberate or conscious decision. Horowitz et al. found that even though only 5\% of the lactose maldigesters he studied reported a history of milk intolerance, they drank significantly less milk (<1 cup/day) than those who digested milk normally (2 cups/day).\textsuperscript{59} Newcomer observed a similar phenomenon.\textsuperscript{64} Subjects diagnosed as lactose maldigesters by the breath-hydrogen test were not aware of milk intolerance, yet their intake of milk and calcium was significantly lower than that of lactose digesting subjects. He suggested that perhaps these subjects had decreased their milk intake during childhood as a result of lactose intolerance, but had forgotten that they had done so.\textsuperscript{64}

Recent studies demonstrate that a low calcium intake and/or low milk intake results in a low intake of other milk-related nutrients both in adults and teenagers.\textsuperscript{65,66,67} Young adult women who had low calcium intakes also had low intakes of protein and 9 other vitamins and minerals.\textsuperscript{65} A majority of those nutrients found low in the diets of these women, vitamin A, riboflavin, folate, vitamin B_{12}, vitamin B_{6}, phosphorus, and magnesium, are provided by milk. Similarly, a recent study revealed that teenagers (13 to 18 years) who drank milk had higher intakes of vitamin A, riboflavin, folate, vitamin B_{12}, vitamin B_{6}, calcium, magnesium, and potassium than those who did not drink milk.\textsuperscript{66} In another study, adults were asked to increase their calcium intake to 1500 mg/day primarily by increasing dairy food intake. Those who increased their dairy food intake also increased their intake of other milk-related nutrients when compared to those who received a calcium supplement (1000 mg/day) or a placebo.\textsuperscript{67} During the 12-week experimental period, the group consuming extra dairy foods did not experience weight gain or any change in plasma lipid or lipoprotein concentrations. The authors observed that “a diet which consistently excludes or limits dairy foods will not only provide less calcium, but may also limit those nutrients that track with calcium in foods.”\textsuperscript{67} In an accompanying editorial, Dr. Robert Heaney states that this study reminds us of the value of food sources of calcium and that “recommended calcium intakes can feasibly be achieved from food sources alone.”\textsuperscript{68}

Therefore, it is important from a nutritional standpoint to encourage those with lactose intolerance to employ the dietary strategies available for including adequate amounts of dairy foods in the diet. Those with limited lactose digestion do not necessarily dislike dairy foods.\textsuperscript{69} Populations with a high incidence of lactose mal-digestion often have a positive attitude toward milk and consume moderate amounts without complaint.\textsuperscript{2} Teens with lactose intolerance should especially be encouraged
to maintain calcium and dairy food intake, since it is now believed that maximizing bone mass attained before age 30 is the most effective way to prevent osteoporosis later in life.  

C. Risk of Osteoporosis/Chronic Disease

Low calcium intake has been implicated in the etiology of several chronic diseases, such as osteoporosis, hypertension, and possibly some types of cancer. As discussed previously, those with limited lactose digestion tend to have lower calcium and dairy food intakes.

Lactose maldigestion when accompanied by low calcium intake has been suggested as a risk factor for osteoporosis. Studies conducted in the 1970s and 1980s reported a higher prevalence of lactose maldigestion among women with osteoporosis than in those without metabolic bone disease. Recent research links lactose intolerance (report of symptoms) with low dairy food/calcium intake and low bone density in perimenopausal and postmenopausal women, and with increased osteoporotic fractures in both women and men.

In a study conducted among 57 postmenopausal Italian women, those who maldigested and were symptomatic to 20 g of aqueous lactose had significantly lower calcium intakes and bone mineral density than those who were maldigesters and asymptomatic. Researchers in Finland investigated the relationship between self-reported lactose intolerance, calcium intake, and bone mineral density in 2025 women aged 48 to 59 who participated in the Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study. Mean dairy calcium intake was significantly lower (558 vs. 828 mg/d) and mean bone density of the spine and hip were 2.8% lower in women who reported lactose intolerance than in other women. Dairy calcium intake was an independent predictor of bone mineral density of the hip. These results suggest that perimenopausal bone density is reduced in women who report lactose intolerance, and is possibly due to reduced calcium intake. The same researchers studied all 11,619 women age 38 to 57 years, who were enrolled in the OSTPRE trial to test whether long-term low calcium intake in premenopausal women decreases bone strength differentially in weight-bearing bones. Similar to the previous trial, mean dairy calcium intake was significantly lower in women who reported lactose intolerance than in other women (570 vs. 850 mg/d), while the risk of fracture of the tibia and metatarsal was higher (odds ratio of 3.31 and 2.84, respectively). Fractures of the wrist, ankle, and rib, however, were not related to lactose intolerance. The authors conclude that long-term premenopausal calcium deficiency differentially affects bones, with weight bearing non-ankle bones being at the greatest risk of suffering reduced strength.

The Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, National Institutes of Health, National Heart, Lung and Blood Institute (NHLBI), recommends an adequate intake of calcium, potassium, and magnesium along with other lifestyle modifications for the prevention and treatment of hypertension. Milk and milk products are an important source of all three of these minerals, contributing 73% of the calcium, 19% of the potassium, and 16% of the magnesium to the U.S. food supply. These recommendations came after a
clinical trial investigating Dietary Approaches to Stop Hypertension (DASH), funded by the NHLBI, found that a diet including 3 servings of lowfat dairy products and 8 to 10 servings of fruits and vegetables lowered blood pressure in people with or without existing hypertension. The eating plan for the DASH diet, which is low in fat, and high in dietary fiber, potassium, calcium, and magnesium, is included in the appendix of the JNC-VI report. For more detailed information on this topic, see Dairy Foods and Hypertension, Chapter 3.

Epidemiological studies, animal studies, and in vitro studies using human cancer cells, indicate that several nutrients/components in milk and milk products may be protective against cancer. The potentially anticarcinogenic agents include calcium, vitamin D, protein, vitamin A, beta-carotene, lactic acid bacteria, and components of milkfat, such as sphingolipids, conjugated linoleic acid (CLA), butyric acid, and ether lipids. For further information, see Chapter 4 on Dairy Foods and Colon Cancer.

VII. STRATEGIES FOR DIETARY MANAGEMENT OF PRIMARY LACTOSE MALDIGESTION

Several strategies are available for managing primary lactose maldigestion without compromising nutritional status or health. Total elimination of dairy foods is unnecessary and not recommended. Milk and other dairy foods contribute high quality protein to the diet and contribute 73% of the calcium, 33% of the phosphorus, 31% of the riboflavin, 21% of the vitamin B, 19% of both the potassium and zinc, and 16% of the magnesium available for consumption in the U.S. Therefore, it is important to help those who maldigest lactose understand how they can include dairy foods in their diet.

Several factors influence an individual’s tolerance to dairy foods including: the amount of lactose, type of dairy food, whether the lactose-containing food is eaten with a meal, whether the food has been fermented or hydrolyzed with an enzyme preparation, and colonic adaptation. Employing strategies, which have been developed with these factors in mind, will allow most people with primary lactose intolerance to comfortably include dairy foods in their diet.

A. Amount of Lactose

As discussed earlier, most of those with limited lactose digestion can tolerate the amount of lactose contained in an 8-ounce (240 ml) serving of milk. Few individuals may need to consume smaller amounts (i.e., 4 ounces or 120 ml) at a time. Milk is also better tolerated when it is consumed with a meal, whether the food has been fermented or hydrolyzed with an enzyme preparation, and colonic adaptation. This finding led to further studies that demonstrated similar alterations in breath hydrogen kinetics when lactose was consumed with a meal. When lactose-containing foods are consumed with other solid foods, gastric emptying is delayed, both reducing and delaying peak hydrogen production. Martini and Savaiano found that only 3 out of 12 subjects experienced symptoms following a
19 g lactose load (equivalent to 1.6 glasses or 384 ml of milk) consumed with a breakfast meal.\(^{44}\) This amounted to a three-fold reduction in both severity and incidence of symptoms when compared to aqueous lactose. Delayed gastric emptying allows more time for any endogenous lactase enzyme present to digest dietary lactose. It also reduces the amount of undigested lactose that reaches the colon at any one time.

**B. Type of Dairy Food**

People with limited lactose digestion tolerate some types of dairy foods better than others. Some studies have shown that whole milk is better tolerated than lower fat milks,\(^{92,93}\) however not all studies have confirmed this.\(^{94}\) The fat content of milk influences milk tolerance, presumably by slowing gastric emptying. When 11 lactose-maldigesting and intolerant subjects were given 50 g of lactose as whole milk, they experienced a significantly lower rise in blood glucose and decreased severity of symptoms, than when they were given the same amount of lactose in either skim milk or an aqueous solution.\(^{92}\) Dehkordi et al. examined digestion (rather than tolerance) of various milks as measured by breath hydrogen production.\(^{95}\) They found that absolute hydrogen production of maldigesters was lower for 18 g of lactose in whole milk than for skim milk, but the differences were not significant and neither milk completely alleviated lactose malabsorption (breath hydrogen <20 ppm). Only consumption of whole milk (18 g of lactose) with cornflakes significantly improved lactose digestion when compared to whole, fat free, chocolate, or commercial milk containing *L. acidophilus* and *Bifidobacterium*. Limitations of this study include the small number of subjects (5) and the relatively short collection time for breath hydrogen (5 vs. 8 hours). Vesa reported no differences in symptoms among free-living maldigesting subjects who consumed either fat-free or full-fat milk (8% fat). This group then conducted a more comprehensive study to determine whether raising the energy content of milk slows gastric emptying and improves tolerance.\(^{96}\) Gastric emptying in 11 lactose maldigesting adults was significantly longer after ingestion of the high-energy milk (18 g of lactose) than after the half-skimmed milk, symptoms were not significantly improved, though there was a trend toward improved lactose digestion. The authors conclude that the positive effect was not strong enough to recommend high-energy milk to lactose maldigesters as a way to improve tolerance. The same group also found that increasing the viscosity of high-energy milk formulas with rice starch did not affect the rate of gastric emptying or improve milk tolerance.\(^{97}\)

Chocolate milk appears to be better tolerated than unflavored milk by lactose maldigesters,\(^{98}\) which can be explained by reduced breath hydrogen production when compared to fat free milk.\(^{95}\) The addition of cocoa to 250 ml of milk formula significantly reduced the breath hydrogen response and symptoms of bloating and cramping in 37 lactose maldigesters.\(^{98}\) While the mechanism for cocoa’s affect on lactose tolerance is unclear, the authors propose three possible mechanisms (1) cocoa might stimulate lactase activity; (2) cocoa might reduce the number of gas-producing bacteria in the colon; or (3) cocoa might slow gastric emptying. These possible mechanisms need further study.
Some dairy foods, such as hard cheeses, cottage cheese, ice cream and yogurt, contain a lower amount of lactose per serving relative to milk, and therefore cause fewer symptoms. For example, Cheddar cheese contains a small amount of lactose. During the cheese-making process, the whey is removed from the curds. Since 94\% of the lactose remains primarily with the whey portion, the finished cheese has a relatively low lactose content.

C. Fermented Milk Products

Yogurt with active microbial cultures improves the digestion of lactose. Yogurt with up to 20 g of lactose is well tolerated by a majority of lactase deficient individuals. Improved lactose digestion with yogurt appears to be partly the result of its reduced lactose content, but is primarily due to autodigestion within the intestine by the microbial beta-galactosidase enzyme. Three related factors appear to be important to the survival and expression of microbial enzyme activity from yogurt (1) the buffering of stomach acid by yogurt; (2) protection by the intact microbial cell to degradation by stomach acid or enzymes; and (3) action of digestive enzymes and bile acids on the microbial cell which releases beta-galactosidase activity.

In yogurt-making, the starter cultures \textit{Lactobacillus bulgaricus} and \textit{Streptococcus thermophilus} are incubated with fresh milk to which milk solids have been added. Both of these organisms synthesize the beta-galactosidase enzyme. The action of the beta-galactosidase present in these two organisms reduces the level of lactose in the concentrated milk. During the fermentation process the pH falls to about 4.6. (Beta-galactosidase is rapidly destroyed at pH 3.0.). Further lactase activity is inhibited by the combination of low pH and low temperature during storage. When yogurt is eaten, the casein, lactase, and calcium phosphate in the yogurt act as buffers to the stomach acid, allowing the microbes (and the enzyme activity) to reach the duodenum intact.

The buffering capacity of yogurt was found to be almost three times that of whole milk, presumably due to the proteins in the added milk solids. Kolars et al. demonstrated that lactase activity in the duodenum after yogurt ingestion is enough to digest 50 to 100\% of a 20 g lactose load. Factors influencing the extent to which the beta-galactosidase enzyme of the yogurt-borne bacteria facilitates lactose digestion in the human body are not completely understood. A number of variables may influence the delivery of beta-galactosidase to the duodenum, including gastric acid secretion, rate of gastric emptying, quantity of yogurt ingested, pancreatic and intestinal digestive enzyme activity, and lipid emulsification by bile acids. There is some evidence that after the intact bacteria reach the intestinal tract they are disrupted by bile acids, releasing the enzyme to digest lactose. Pochart et al. confirmed the earlier finding of Kolars et al. that beta-galactosidase activity in yogurt survives passage through the stomach (Figure 8.6). In addition they found that minimal lactose hydrolysis occurred in the duodenum after yogurt ingestion, indicating that digestion probably occurs further along the intestinal tract as bacterial (yogurt) lactase activity is stimulated by the progressively increasing pH.

Kolars et al. used the breath hydrogen technique to determine whether lactose in yogurt is better absorbed by lactose maldigesters than is lactose in milk. The
total area under the breath hydrogen curve was significantly lower for 440 g of yogurt (18 g of lactose) than for milk or a lactose solution containing a similar amount of lactose. Hydrogen production after ingestion of yogurt was only about one third that of milk. A smaller amount of yogurt (270 g) containing 11 g of lactose, an amount closer to that typically consumed, produced only a negligible amount of hydrogen. Symptoms of diarrhea or flatulence were experienced by 80% of the subjects when they consumed 18 g of lactose in milk, but all subjects were symptom-free after consuming the same amount of lactose in yogurt.

Recent studies in adults and children suggest that the semi-solid nature of yogurt, which slows its gastric emptying, may be an important factor in its improved tolerance. Researchers at Johns Hopkins School of Medicine in Boston tested whether yogurt was better tolerated than milk in 14 lactose-malabsorbing children (mean age 9.5 years). The children experienced significantly fewer symptoms after consumption of 8 ounces of yogurt containing active cultures than after consuming milk. Since the children experienced improved tolerance to both yogurt with live active cultures and pasteurized yogurt (which decreased bacterial activity) the authors suggest that yogurt’s osmolality, energy density, and delayed transit time played a greater role in improving tolerance than did its ability to “autodigest” lactose. Researchers in France reached a similar conclusion when three yogurts containing different bacterial cultures and lactase activity were equally digested and tolerated by fifteen lactase deficient adults.
Although consuming yogurt (when compared with milk) reduces the occurrence and severity of symptoms associated with lactose maldigestion, lactase activity varies considerably between brands of active-culture yogurt. In addition, if yogurt is pasteurized after the addition of active cultures (which is sometimes done to extend shelf-life of the product), it loses much of its ability to hydrolyze lactose in the gut. Furthermore, eating yogurt may not assist the digestion of lactose from other dairy foods eaten with it as part of a meal. Ingestion of yogurt over eight days provided no additional benefit.

Some people find flavored yogurts more acceptable than plain. When lactose digestion was compared between milk, flavored and plain yogurt in 16 lactase deficient subjects, flavored yogurt produced a breath hydrogen level slightly higher than that of plain yogurt, but lower than milk. Although only the hydrogen production from the plain yogurt was statistically significantly lower than that of milk, none of the subjects experienced any symptoms after eating either variety of yogurt, while three reported symptoms after drinking milk. It is unclear how the addition of fruit, sweeteners, and flavorings might reduce the beta-galactosidase activity in flavored yogurts. Frozen yogurt that has been pasteurized prior to freezing (typical commercial practice) lacks beta-galactosidase activity. Lactose maldigestion and tolerance have been found to be similar between frozen yogurt, ice milk, and ice cream. However lactase deficient persons may tolerate significant amounts of these products, presumably due to their slower gastric transit time owing to its high solids and/or fat content.

D. Unfermented Milk with Bacterial Cultures

Whether non-fermented dairy products containing bacterial starter cultures, such as sweet acidophilus milk or yogurt milk, have the potential to improve lactose tolerance is controversial. Acidophilus milk is a nonfermented beverage made by adding viable \textit{L. acidophilus} strains to cold milk, then refrigerating to prevent further growth of the organism. It has an advantage over yogurt in that it doesn’t have a tart taste. Yogurt milk is prepared in a manner similar to acidophilus milk, except that \textit{Streptococcus thermophilus} and \textit{Lactobacillus bulgaricus} are added to the fresh milk.

Several studies conducted in the 1980s found that acidophilus milk or capsules containing high concentrations of mixed lactic acid bacteria or \textit{Bifidobacteria bifidum} did not improve lactose digestion or alleviate symptoms in lactose maldigesting subjects. It has since been learned that certain factors, such as insufficient concentration of the culture, extended storage, use of frozen concentration starter culture, level of lactic acid, and use of inappropriate substrates for culture growth, contribute to the ineffectiveness of these unfermented products. The strain of \textit{L. acidophilus} used in studies of lactose maldigestion is of critical importance, since beta-galactosidase activity, bile sensitivity, and acid tolerance vary considerably among strains.

For example, acidophilus milk (prepared with three different strains of \textit{L. acidophilus} in two different concentrations) and yogurt milk (prepared with two concentrations of \textit{S. thermophilus} and \textit{L. bulgaricus}) were evaluated on the basis of
beta-galactosidase activity, bile tolerance, and ability to digest lactose in 10 lactose-maldigesting adults.\textsuperscript{115} Only yogurt milk and acidophilus milk prepared with the highest concentration (10\textsuperscript{8} cfu/ml) of starter cultures were effective in significantly decreasing breath hydrogen concentrations in the subjects. Only the most bile-sensitive strain of \textit{L. acidophilus} was effective in this regard. This characteristic appears to be important for the release of beta-galactosidase within the intestinal tract. Furthermore, subjects who normally experienced symptoms after ingestion of 20 g of lactose, reported fewer symptoms following consumption of 400 ml of yogurt milk containing 10\textsuperscript{8} cfu/ml than with 400 ml of acidophilus milk containing the same cell concentration. The researchers conclude that consumption of non-fermented yogurt milk containing high concentrations of yogurt cultures was able to reduce breath hydrogen concentrations 3-fold. This is similar to the effect of fermented yogurt, which reduces gas production by 3 to 4-fold, when compared to milk.\textsuperscript{115} Montes et al. tested digestibility and tolerance of unfermented milks among 20 children with limited lactose digestion.\textsuperscript{116} They found that consumption of 250 ml of lowfat milk inoculated with 10\textsuperscript{10} cells of \textit{Lactobacillus acidophilus} improved tolerance, while consumption of the same amount of milk inoculated with a commercial yogurt starter culture containing 10\textsuperscript{8} cells of \textit{Lactobacillus lactis} and 10\textsuperscript{10} cells of \textit{Streptococcus thermophilus}, improved both digestion and tolerance, compared to regular milk.

Most recently, researchers at Purdue University tested four strains of \textit{L. acidophilus} with varying degrees of lactose transport, beta-galactosidase activity, and bile acid sensitivity on lactose digestion and tolerance in a group of lactose maldigesting adults.\textsuperscript{114} Acidophilus milk prepared with the bacterial strain with the greatest bile and acid tolerance was the most effective in improving lactose digestion and tolerance. Further studies are needed, however, to determine the extent of the importance of these factors.

Bifidobacteria may have potential for use in products designed to improve lactose digestion because they contain a relatively high level of beta-galactosidase activity and are stable under normal storage conditions. A study conducted among 15 lactose-maldigesting adults showed that unfermented milk containing \textit{Bifidobacteria longum} that was grown in a lactose-containing medium, had the greatest beta-galactosidase activity and significantly improved lactose digestion (per breath hydrogen) and symptoms of flatulence compared to other bifido strains or regular lowfat milk.\textsuperscript{117}

\textbf{E. Enzyme Preparations}

Lactose-hydrolyzed milk or commercial oral enzyme replacement therapy has proven beneficial in adults and children and is recommended as a strategy for improving lactose tolerance.\textsuperscript{2,7,87,118,119} Oral enzyme replacement in tablet form offers the advantage of allowing a more liberal use of lactose-containing dairy foods. This may prove a useful therapy even for young children, making specialized nutritional management unnecessary.\textsuperscript{120} Beta-galactosidases extracted from yeast, \textit{Kluyveromyces lactis}; or fungi, \textit{Aspergillus niger} or \textit{Aspergillus oryzae}, have been found effective.\textsuperscript{72,121,122} These enzymes as well as the final products of their addition to food have been classified as Generally Recognized as Safe (GRAS) by the Food and Drug
Administration under the broad classification of carbohydrates. Lactose reduced milk is prepared at a processing plant by adding the liquid enzyme to previously pasteurized milk and holding for 24 hours. When the appropriate level of reduction has been reached, usually 70%, the milk is pasteurized again to stop lactose hydrolysis. Milk that has 99.9% of its lactose hydrolyzed, labeled “lactose free,” is now available on the market. A milk labeled “lactose reduced” must contain at least 70% less lactose than regular milk. In addition to lactose-reduced milk, other lactose-reduced dairy products are now on the market.

Lactose hydrolyzed milk and an oral enzyme tablet taken with milk were evaluated along with milk, acidophilus milk, and yogurt, for their effectiveness in facilitating lactose digestion and for their acceptability. Acidophilus milk induced the greatest rise in breath hydrogen production, followed by whole milk, whole milk plus a lactase tablet, hydrolyzed lactose milk, and yogurt, respectively. Even though yogurt was the most effective at reducing breath hydrogen production compared to exogenous lactase products, the study subjects did not like it as well as milk. Acceptability of hydrolyzed-lactose milk did not differ significantly from yogurt. While some found yogurt unacceptable because of its tart taste, others gave hydrolyzed lactose milk a lower rating due to its sweetness. When lactose is hydrolyzed into glucose and galactose, the free glucose makes the product taste slightly sweeter. Children have found lactose hydrolyzed milk quite acceptable for this reason. At least a 50% reduction of lactose content in milk is adequate to relieve symptoms of lactose intolerance in a majority of lactose maldigesters. Those more sensitive to lactose (e.g., those with secondary lactose intolerance) may need lactose free milk or additional lactase tablets to relieve symptoms.

Below is a summary of management strategies aimed at improving lactose tolerance while keeping dairy foods and the nutrients they provide in the diet:

**Management Strategies for Those with Lactose Intolerance**

1. Drink milk in servings of one cup or less.
2. Drink milk with a meal or with other food.
3. Try whole or chocolate milk.
4. Try cheese. Much of the lactose is removed during processing.
5. Try yogurt with active cultures.
6. Use milk and other dairy foods that are lactose-reduced or lactose-free.
8. Use an oral lactase supplement before consuming dairy foods.

**F. Colonic Adaptation**

Although continued exposure to lactose does not induce the intestinal synthesis of the lactase enzyme, there is evidence that adaptation to lactose occurs in the colon. This phenomenon was first noted in the 1950s when supplemental milk feeding programs for preschool and school-aged children were initiated as part of global relief.
efforts. When milk was first introduced, it was sometimes associated with complaints of diarrhea and gastrointestinal discomfort. However, these complaints soon stopped as the program continued. This phenomenon was initially explained as a child’s psychological reaction to an unfamiliar food. An early clinical trial, however, demonstrated that continued lactose intake increases the amount of lactose tolerated without symptoms, and without change in intestinal lactase activity.  

Recent clinical trials have demonstrated that the colonic flora of persons with limited lactose digestion adapts to continued milk intakes. Twenty-five African American adolescents and young adults, who were confirmed lactose maldigesters and intolerant to the amount of lactose in one glass of milk (12 g), were given gradually increasing amounts of lactose in milk (beginning at 5 g) over a period of time until their maximum level of tolerance was determined. Of the 22 subjects who completed the study, 77% tolerated 12 g of lactose (the amount in 8 ounces or 240 ml of milk) without disturbing symptoms. All individuals were able to adapt to 7 g of lactose, the amount in 150 ml of milk. Objective testing of breath hydrogen production revealed that a majority of the subjects continued to maldigest the lactose dose they tolerated.

Hertzler and Savaiano conducted a two-part blinded, controlled crossover trial to determine the effect of continued lactose feeding on (1) the ability of fecal bacteria to metabolize lactose, and (2) the symptomatic response to lactose. Results from the first part of the study indicated that lactose feeding altered the ability of fecal bacteria to metabolize lactose. Fecal beta-galactosidase began to rise within 48 hours of beginning lactose feeding, and by 10 days had peaked at 3 times the control value. In part two of the study, subjects were given 0.6 g/kg body weight per day of lactose in water divided between breakfast, lunch, and dinner. This amount was increased by 0.2 g/kg increments every other day, up to a maximum of 1.0 g/kg per day. Subjects increased their intake of lactose over a 10-day period from an average of 42 g to 70 g per day (equivalent to the amount of lactose in 800 to 1500 ml of milk). Symptoms in the lactose group were not significantly different from the control group (fed dextrose), and did not increase from the beginning to the end of the lactose feeding period, even though the lactose dose was nearly doubled. In fact, a breath-hydrogen test, administered at the end of the study, indicated that the subjects had no increase in breath hydrogen. The authors conclude that adaptation of the colonic flora offers a simpler and less expensive solution for subjects who wish to consume large amounts of lactose containing foods on a regular basis.

A double-blind study conducted by researchers in France among severely intolerant (all experienced diarrhea) Asian subjects, also demonstrated metabolic adaptation and reduction of symptoms (except diarrhea) to lactose in water feeding (17 g twice daily) over 13 days. The control group (fed sucrose), also reported fewer symptoms, though they did not demonstrate biochemical adaptation (e.g., increased fecal beta-galactosidase activity, lower pH, and decreased breath hydrogen), as did the group fed lactose. The authors suggest that improved clinical tolerance may sometimes be the result of becoming familiar with the test procedures. They recommend that those with severe symptoms avoid consuming lactose in the fasting state. Instead, they should consume lactose in the form of yogurt or together with other foods.
The mechanism by which adaptation occurs is not completely understood, however, the following mechanisms have been proposed (1) The presence of unhydrolized lactose in the colon stimulates organic acid production which lowers the pH inhibiting further fermentation and hydrogen production; (2) undigested lactose may alter the composition of colonic bacteria by reducing the number of gas-forming bacteria in favor of non-gas-producing organisms; or (3) lactose in the colon stimulates colonic bacterial fermentation and the removal of end products.\textsuperscript{130}

Theoretically, a reduction in breath hydrogen after continued lactose feeding could be either the result of decreased absolute hydrogen production or increased hydrogen consumption by colonic bacteria. Using a technique that distinguishes production from consumption, Hertzler et al. established that lactose feeding decreased absolute hydrogen production, possibly by stimulating the proliferation of bacterial species such as bifidobacteria, which ferment lactose without producing hydrogen.\textsuperscript{133} Jiang and Savaiano, simulating lactose adaptation \textit{in vitro}, found that supplementation of the culture medium with \textit{Lactobacillus acidophilus} enhanced lactose utilization during the first day.\textsuperscript{117} They conclude that \textit{L. acidophilus} may enhance lactose fermentation in the colon during the early period of lactose feeding before adaptation is established.

\section*{VIII. TREATMENT OF MALNUTRITION/DIARRHEAL DISEASE IN CHILDREN}

Infants and children with infectious gastroenteritis and accompanying diarrhea, experience lactase deficiency and intolerance secondary to damage of the intestinal mucosa. Diarrhea caused by most common organisms is self-limiting, and rarely persists for more than 4 to 5 days. Even during acute infectious enteritis, the gut retains a significant capacity to assimilate nutrients.\textsuperscript{134} During this phase, the goal of nutritional management is to maintain hydration status and prevent starvation in the malnourished infant; the number and character of stools should not guide management.\textsuperscript{134} Current recommendations support continued breast-feeding of infants during diarrhea with concurrent use of a glucose-electrolyte solution to maintain hydration. For bottle-fed infants and those receiving solid foods, usual feedings can be reintroduced after the rehydration phase, but should not be delayed longer than 24 hours.\textsuperscript{135}

Whether lactose containing formulas should be used for young children with acute diarrhea has been a matter of frequent debate. No firm recommendations have been developed. This issue has policy implications for feeding programs in developing countries where diarrheal disease in children is a common health problem, and where lactose-reduced products are expensive and unavailable.

Recently a meta-analysis of 29 randomized clinical trials was conducted evaluating the use of non-human milks or formulas in the dietary management of acute diarrhea in children.\textsuperscript{136} The studies compared the effectiveness of lactose containing vs. non-lactose containing diets and the effect of using undiluted vs. diluted milk or delayed milk feeding. In general, treatment failure, defined as greater stool frequency, increased duration of symptoms, recurrent dehydration, and weight loss, was increased in those receiving lactose containing diets, but only in patients who initially presented with
severe dehydration. The authors conclude, however, that “nondehydrated children can be managed as successfully with lactose containing diets as with lactose-free regimens.” They emphasize the importance of rapidly correcting dehydration with an oral electrolyte solution, as recommended in the standardized treatment protocol of the World Health Organization (WHO). Feeding with undiluted milk was a less effective treatment than diluted milk in children with the most severe illness. This small advantage of feeding with diluted milk was offset by poorer weight gains. Thus, there is a trade-off between risking relapsing diarrhea and suboptimal nutritional status. Therefore, when the diarrhea is relatively mild, it is preferable to feed with undiluted milk. The clinical trials taken as a whole indicate that children who continue to receive lactose containing milk diets have a treatment failure rate of about 10%. The authors conclude, “the vast majority of young children with acute diarrhea can safely continue to receive undiluted, nonhuman milk.”

Some practitioners recommend that infants younger than 6 months who have persistent diarrhea should be treated with a lactose-free soy-based formula or a low lactose protein hydrolysate formula for the first few days or weeks after acute gastroenteritis. Cow’s milk formula may be reintroduced after the diarrhea and intestinal damage which promote lactase deficiency have resolved, usually in about four weeks. Others, however, contend that infants under 6 months with diarrhea should be given full-strength formula as soon as dehydration is corrected. The generally accepted method of treatment for children older than 9 months is full-strength milk or formula immediately following 24 hours of treatment with a glucose-electrolyte solution. Infants or children with secondary lactose intolerance due to gastrointestinal diseases leading to villus atrophy such as Crohn’s disease or protein-sensitive enteropathy must be managed by temporarily restricting lactose in the diet, and may benefit from a protein-hydrolyzed formula.

In the case of older children who are eating a variety of solid foods, practitioners should assess the severity of the lactose maldigestion and individualize the diet accordingly. Lower lactose dairy products such as yogurt, aged cheeses, and lactose hydrolyzed milk should be encouraged. Many children will be able to tolerate 4 to 6 ounces of milk with meals. Various types of milks and infant formulas can be treated with a lactase enzyme preparation that is added to milk in the form of drops, then allowed to incubate for 24 hours. As much as 100% of the lactose can be hydrolyzed in this manner for severe cases of lactose intolerance. In severe cases of intolerance it will also be necessary to read labels on non-dairy foods and avoid purchasing products that have ingredients that contain lactose: these include whey powder, casein, casein hydrolysate, sodium caseinate, and lactalbumin.

Children with severe protein energy malnutrition (PEM) commonly have reduced activity of intestinal lactase due to nutritional injury and infection. Milk has been used extensively along with other protein sources in refeeding programs aimed at reversing PEM. A study involving 20 Guatemalan preschool children with PEM demonstrated that lactose-hydrolyzed milk offered no advantages over lactose containing milk in recovery from PEM. The group receiving intact lactose experienced more diarrhea, but recovery was satisfactory in both groups during the 45-day refeeding period, with no differences in rates of growth, body protein repletion, restoration of energy reserves, or intestinal function. A study of malnourished Senegalese children

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age 6 to 36 months demonstrated that fermented milk may also be useful in the treatment of malnourished children with acute diarrhea and sugar intolerance.⁴⁰

IX. RECOMMENDATIONS FOR FEEDING PROGRAMS

The American Academy of Pediatrics stated the following position in 1978, which was reaffirmed in 1990, “On the basis of present evidence it would be inappropriate to discourage supplemental milk feeding programs targeted at children on the basis of primary lactose intolerance.”⁸⁸

A. International

Milk can provide an inexpensive source of carbohydrate, protein, and calcium to children in countries where protein-calorie malnutrition is prevalent. In Gambia West Africa, for example, growth failure and undernutrition is common, as is lactose maldigestion after the second year of life. In a study involving Gambian children, lactose maldigestion was not associated with growth failure. Consumption of cow’s milk was common among the children and was rarely associated with any adverse affects.¹⁴¹ The authors recommend that cow’s milk be given to Gambian children after weaning as a means of supplementing their diet.

As discussed in the section on adaptation, children who receive milk as part of a supplemental feeding program usually tolerate it quite well. Powdered fermented milk might also be a viable option for providing supplemental milk to children in countries where there is a high prevalence of lactase deficiency.¹⁴² When 25 Gabonese lactase deficient children consumed 150 ml of powdered fermented milk formula containing 10.5 g lactose, breath hydrogen production was reduced to normal levels and symptoms of intolerance were reduced by one-third, when compared to a regular milk formula. Since this product may be purchased in dry powdered form, it has advantages for use in developing countries where refrigeration may not be available.

B. United States

Supplemental feeding programs in the United States, such as the National School Lunch Program (NSLP), the National School Breakfast Program (NSBP) and the Women, Infants and Children Supplemental Food Program (WIC), serve clients with a variety of ethnic backgrounds. While many schools serve populations where lactose maldigestion is common, milk is not contraindicated, and dairy products are included as part of the standard meal plan. Nearly all children with low lactase activity can tolerate the 8 ounces of milk required in the school meal pattern, especially since it is served with a meal.

However, studies of milk drinking among African American children at school report that some students may reject milk at school or drink only part of the 240 ml provided.¹⁴³ There is evidence that children’s milk drinking habits may be more influenced by cultural attitudes towards milk as they get older than by lactose tolerance.
status. This is illustrated by the fact that, regardless of lactose tolerance status, the parents of Black children consume less milk than those of White children.

After the age of eight, milk intake decreases in some student populations, increasing the chance of clinical consequences. Therefore it may be beneficial for schools serving such populations to make available a selection of dairy foods, such as aged cheese, yogurt, whole and chocolate milk. Yogurt is approved for use in school meals as a meat alternate.

High school students have the option of declining milk if they so choose under the offer versus serve guidelines. If a younger child has severe milk intolerance, however, the school is allowed (or required in some states) to make an appropriate substitution. The child must bring a letter from a physician, dietitian, or nurse describing the need for a food substitution and a recommendation of substitute foods.

Fifty-eight percent of those enrolled in the WIC program belong to ethnic groups with a high prevalence of lactose maldigestion, including Black (25.4%), Hispanic (26.1%), Asian (2.6%), and Native American (1.7%). Lactose intolerance is not a major issue for WIC-eligible children, since the prevalence of lactose maldigestion for children under age 5 is low. A review of WIC food packages, conducted by researchers at Pennsylvania State University in cooperation with the Food Nutrition Service, concluded that although many adults in the ethnic minority populations served by WIC are potentially affected by lactose maldigestion, dairy products can be and are consumed by these individuals. They add that dairy foods of some type may be acceptable to most WIC participants, and a number of management strategies are available for improving tolerance to dairy foods. Educational materials that outline these strategies are supplied to WIC participants who need them. In addition to milk and cheese, it has been a long-standing policy of the WIC program to allow lactose-reduced milk to participants with lactose intolerance.

Cultural food values, rather than lactose intolerance, is the main factor affecting acceptance of dairy products among WIC participants. Nevertheless, the panel who reviewed WIC food packages feels there are valid scientific reasons for accommodating food preferences, whether they have a biological or cultural basis. Therefore, several non-dairy foods that would provide alternative sources of calcium and protein are under consideration for inclusion in WIC food packages. Though USDA solicited public comment on this issue in 1994, they have not yet published a final ruling.

X. FUTURE RESEARCH NEEDS

Further work is needed in the areas of genetics, management, and education. Animal studies are continuing to investigate the molecular mechanisms involved in developmental changes in the lactase enzyme. Studies are underway investigating the regulation of lactase gene expression in the human intestine. A further understanding of how the colon adapts to continued milk intakes is important; this will allow development of protocols for encouraging milk intake in those with lactase nonpersistence. More research is needed on the strains of organisms used as bacterial cultures in fermented and nonfermented dairy foods that will aid the hydrolysis of lactose in vivo most effectively. This knowledge will lead to the development of new, more effective
products. More can be done to educate practitioners and the public about appropriate diagnosis and treatment strategies available for those with lactose intolerance.

XI. CONCLUSION

Lactose intolerance, whether real or perceived, causes individuals to reduce or eliminate milk and milk products from their diet. Tolerance to dairy foods can be improved by following the simple strategies outlined in this chapter. Research has shown that current calcium recommendations can be met through the strategic use of dairy foods by most people who have low lactase levels. While most with limited lactose digestion can tolerate milk in moderate amounts, the loss of intestinal lactase in early childhood does have clinical and nutritional significance. A low intake of milk and milk products has been shown to increase the risk of osteoporosis, hypertension, and some forms of cancer. Future research will further our knowledge in the areas of genetics and the development of new dairy products that will be well tolerated by those with low lactase activity. Nearly all children and most adults should be encouraged to benefit from the nutritional value of milk, even if lactose intolerance limits the quantities they can consume at one time, or the forms in which they may enjoy dairy products.

XII. GLOSSARY OF TERMS

Lactase Beta-galactosidase, an enzyme of the hydrolase class that catalyzes the hydrolysis (digestion) of lactose, a disaccharide, into its monosaccharide components of glucose and galactose. Lactase is present on the brush border of the intestinal mucosa where such digestion takes place.

Lactase nonpersistence Refers to the decrease in lactase activity that occurs after weaning. This characteristic is transmitted as an autosomal-recessive trait.

Lactase persistence Refers to the retention of significant intestinal lactase into adulthood. This characteristic is transmitted as an autosomal-dominant trait.

Low lactase activity or hypolactasia Low levels of the intestinal enzyme, lactase, in the brush border membrane. Low lactase activity (lactase deficiency) can be measured directly by small bowel biopsy, or indirectly using the lactose tolerance test or the breath-hydrogen test.

Lactose A disaccharide which yields upon hydrolysis the monosaccharides, glucose and galactose. Since milk is the sole natural source of lactose, it is commonly referred to as milk sugar.

Lactose intolerance The clinical signs and symptoms which include bloating, flatulence, abdominal pain, and diarrhea following consumption of a dose of lactose greater than the body’s ability to digest and absorb. “Tolerance” and “intolerance” are not synonymous with “digestion” and “maldigestion” and should be used only in reference to a defined dose of lactose delivered in a specific vehicle (i.e., the subject was intolerant to 50 g of lactose in aqueous solution).

Congenital lactase deficiency A rare genetic abnormality in which the enzyme lactase is very low or absent at birth.

Primary lactase deficiency The normal developmental decrease in lactase activity beyond the age of weaning.
Secondary lactase deficiency  Temporary low levels of the lactase enzyme due to an underlying disease or medical condition affecting the gastrointestinal tract, such as gastroenteritis, tropical sprue, recovery from gastrointestinal surgery, radiation therapy, or certain drugs.

Lactose maldigestion  Reduced digestion of lactose due to low lactase activity.

Milk intolerance due to lactose One or more clinical signs of abdominal pain, bloating, flatulence, or diarrhea experienced a few hours after ingestion of a known quantity of milk or milk-containing products in a person with proven lactose maldigestion.

**XIII. LACTOSE CONTENT OF DAIRY PRODUCTS**

<table>
<thead>
<tr>
<th>Product</th>
<th>Lactose (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Milk</strong> (1 cup)</td>
<td></td>
</tr>
<tr>
<td>Whole</td>
<td>9 – 12</td>
</tr>
<tr>
<td>2% reduced fat</td>
<td>9 – 13</td>
</tr>
<tr>
<td>1% low fat</td>
<td>12 – 13</td>
</tr>
<tr>
<td>Fat free</td>
<td>11 – 14</td>
</tr>
<tr>
<td>Chocolate</td>
<td>10 – 12</td>
</tr>
<tr>
<td>Buttermilk</td>
<td>9 – 12</td>
</tr>
<tr>
<td>Evaporated</td>
<td>24 – 28</td>
</tr>
<tr>
<td>Sweetened condensed</td>
<td>31 – 50</td>
</tr>
<tr>
<td>*Lactaid (lactose-reduced lowfat milk)</td>
<td>3</td>
</tr>
<tr>
<td>Goat’s milk</td>
<td>11 – 12</td>
</tr>
<tr>
<td>Acidophilus, skim</td>
<td>11</td>
</tr>
<tr>
<td><strong>Yogurt</strong>, lowfat (1 cup)</td>
<td>4 - 17</td>
</tr>
<tr>
<td><strong>Cheese</strong> (1 oz.)</td>
<td></td>
</tr>
<tr>
<td>Cottage (1/2 cup)</td>
<td>0.7 – 4</td>
</tr>
<tr>
<td>Cheddar, sharp</td>
<td>0.4 – 0.6</td>
</tr>
<tr>
<td>Swiss</td>
<td>0.5 – 1</td>
</tr>
<tr>
<td>Mozzarella, part skim, low moisture</td>
<td>.08 – .9</td>
</tr>
<tr>
<td>American, pasteurized, processed</td>
<td>0.5 – 4</td>
</tr>
<tr>
<td>Ricotta (1/2 cup)</td>
<td>0.3 – 6</td>
</tr>
<tr>
<td>Cream</td>
<td>0.1 – .8</td>
</tr>
<tr>
<td><strong>Butter</strong> (1 pat)</td>
<td>0.04 – 0.05</td>
</tr>
<tr>
<td><strong>Cream</strong> (1 tbsp.)</td>
<td></td>
</tr>
<tr>
<td>Light</td>
<td>0.6</td>
</tr>
<tr>
<td>Whipping</td>
<td>0.4 – 0.5</td>
</tr>
<tr>
<td>Sour</td>
<td>0.4 – 0.5</td>
</tr>
<tr>
<td><strong>Ice Cream</strong> (1/2 cup)</td>
<td>2 – 6</td>
</tr>
<tr>
<td><strong>Ice Milk</strong> (1/2 cup)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Sherbet</strong> (1/2 cup)</td>
<td>0.6 – 2</td>
</tr>
</tbody>
</table>


* Bowes & Church’s *Food Values of Portions Commonly Used*, Jean A. Pennington, 1989.

Studies have shown that yogurt with live active cultures is significantly better tolerated than milk because of its high lactase activity.100
REFERENCES


89. Savaiano, D. A. and Kotz, C., Recent advances in the management of lactose intolerance, *Contemporary Nutr.*, 13(9,10), 1988.

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