



CLINICAL REPORT

Lactose Intolerance in Infants, Children, and Adolescents

Melvin B. Heyman, MD, MPH, for the Committee on Nutrition

Guidance for the Clinician in Rendering
Pediatric Care

ABSTRACT

The American Academy of Pediatrics Committee on Nutrition presents an updated review of lactose intolerance in infants, children, and adolescents. Differences between primary, secondary, congenital, and developmental lactase deficiency that may result in lactose intolerance are discussed. Children with suspected lactose intolerance can be assessed clinically by dietary lactose elimination or by tests including noninvasive hydrogen breath testing or invasive intestinal biopsy determination of lactase (and other disaccharidase) concentrations. Treatment consists of use of lactase-treated dairy products or oral lactase supplementation, limitation of lactose-containing foods, or dairy elimination. The American Academy of Pediatrics supports use of dairy foods as an important source of calcium for bone mineral health and of other nutrients that facilitate growth in children and adolescents. If dairy products are eliminated, other dietary sources of calcium or calcium supplements need to be provided.

INTRODUCTION

SIGNIFICANT CHANGES in our knowledge and approach toward lactose intolerance have occurred over the past quarter century, since the first statement on lactose intolerance was published by the American Academy of Pediatrics Committee on Nutrition.¹ Lactose ingestion in certain susceptible individuals can cause abdominal symptoms that are variable and can be treated with dietary restriction or enzyme replacement, depending on the amount of lactose consumed and the degree of lactase deficiency. Pediatricians and other pediatric care providers should maintain awareness of the benefits and controversies related to the consumption of dietary milk products and milk-based infant formula. The lactose content of milk often influences, correctly or not, the ultimate decision about the use or continuation of milk in the diet. Milk and dairy-product avoidance has a negative effect on calcium and vitamin D intake in infants, children, and adolescents. Other nutrients such as protein make dairy products an important source of nutrition for growing children. This revised statement will update the initial statement of 1978 while incorporating changes from the 1990 supplement² and current state-of-the-art relating to lactose intolerance. Recommendations regarding dietary calcium have been updated recently.³

Lactose, a disaccharide that comprises the monosaccharides glucose and galactose, is the primary carbohydrate found exclusively in mammalian milk. Absorption of lactose requires lactase activity in the small intestinal brush border to split the bond linking the 2 monosaccharides. A β -galactosidase termed "lactase-phlorizin hydrolase" (lactase) accounts for most of the lactase activity in the intestinal

www.pediatrics.org/cgi/doi/10.1542/peds.2006-1721

doi:10.1542/peds.2006-1721

All clinical reports from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

Key Words

abdominal pain, breath tests, calcium, dietary, dairy products, diarrhea, flatulence, lactase, malabsorption, pediatric

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2006 by the American Academy of Pediatrics

mucosa.⁴ Lactase is found in the small intestine and localized to the tips of the villi, a factor of clinical importance when considering the effect of diarrheal illness on the ability to tolerate milk.

Milk intolerance may be attributed to either the lactose or the protein content. Lactose intolerance can occur among infants and young children with acute diarrheal disease, although the clinical significance of this is limited except in more severely affected children. Symptoms of lactose intolerance are relatively common among older children and adolescents; however, associated intestinal injury is infrequently seen. Lactose intolerance is a distinct entity from cow milk–protein sensitivity, which involves the immune system and causes varying degrees of injury to the intestinal mucosal surface. Cow milk–protein intolerance is reported in 2% to 5% of infants within the first 1 to 3 months of life, typically resolves by 1 year of age, and is not the subject of this statement.^{5,6}

DEFINITIONS

Following are definitions of terms used in the remainder of this statement:

- Lactose intolerance is a clinical syndrome of 1 or more of the following: abdominal pain, diarrhea, nausea, flatulence, and/or bloating after the ingestion of lactose or lactose-containing food substances. The amount of lactose that will cause symptoms varies from individual to individual, depending on the amount of lactose consumed, the degree of lactase deficiency, and the form of food substance in which the lactose is ingested.
- Lactose malabsorption is the physiologic problem that manifests as lactose intolerance and is attributable to an imbalance between the amount of ingested lactose and the capacity for lactase to hydrolyze the disaccharide.
- Primary lactase deficiency is attributable to relative or absolute absence of lactase that develops in childhood at various ages in different racial groups and is the most common cause of lactose malabsorption and lactose intolerance. Primary lactase deficiency is also referred to as adult-type hypolactasia, lactase nonpersistence, or hereditary lactase deficiency.
- Secondary lactase deficiency is lactase deficiency that results from small bowel injury, such as acute gastroenteritis, persistent diarrhea, small bowel overgrowth, cancer chemotherapy, or other causes of injury to the small intestinal mucosa, and can present at any age but is more common in infancy.
- Congenital lactase deficiency is extremely rare; teleologically, infants with congenital lactase deficiency would not be expected to survive before the 20th century, when no readily accessible and nutritionally

adequate lactose-free human milk substitute was available.

- Developmental lactase deficiency is now defined as the relative lactase deficiency observed among preterm infants of less than 34 weeks' gestation.

Primary Lactase Deficiency

Approximately 70% of the world's population has primary lactase deficiency.^{7,8} The percentage varies according to ethnicity and is related to the use of dairy products in the diet, resulting in genetic selection of individuals with the ability to digest lactose (Table 1). In populations with a predominance of dairy foods in the diet, particularly northern European people, as few as 2% of the population has primary lactase deficiency. In contrast, the prevalence of primary lactase deficiency is 50% to 80% in Hispanic people, 60% to 80% in black and Ashkenazi Jewish people, and almost 100% in Asian and American Indian people.^{9–11} The age of onset and its prevalence differ among various populations. Approximately 20% of Hispanic, Asian, and black children younger than 5 years of age have evidence of lactase deficiency and lactose malabsorption,¹² whereas white children typically do not develop symptoms of lactose intolerance until after 4 or 5 years of age. Recent molecular studies of lactase-phlorizin hydrolase (lactase) have correlated the genetic polymorphism of messenger RNA expression with persistence of lactase activity, demonstrating early loss (at 1–2 years of age) of messenger RNA expression and enzyme activity in Thai children and late (10–20 years of age) loss of activity in Finnish children.^{11,13} The clinical relevance of these observations is that children with clinical signs of lactose intolerance at an earlier age than is typical for a specific ethnic group may warrant an evaluation for an underlying cause, because primary lactase deficiency would otherwise be unusual at such a young age. Although primary lactase deficiency may present with a relatively acute onset of milk intolerance, its onset typically is subtle and progressive over many years. Most lactase-

TABLE 1 Prevalence of Acquired Primary Lactase Deficiency⁶⁹

Examples of groups among whom lactase deficiency predominates (60%–100% lactase deficient)
Near East and Mediterranean: Arabs, Ashkenazi Jews, Greek Cypriots, Southern Italians
Asia: Thais, Indonesians, Chinese, Koreans
Africa: South Nigerians, Hausa, Bantu
North and South America: black Americans, Latinas, Eskimos, Canadian and American Indians, Chami Indians
Examples of groups among whom lactase persistence predominates (2%–30% lactase deficient)
Northern Europeans
Africa: Hima, Tussi, Nomadic Fulani
India: individuals from Punjab and New Delhi

deficient individuals experience onset of symptoms in late adolescence and adulthood.

Reports that focus on clinical symptoms of lactase deficiency are prone to subjectivity, confounding clinical diagnosis. For instance, when lactase-deficient adults were given 2 glasses of milk or 2 glasses of lactose-hydrolyzed milk per day in a double-blind, crossover study, no statistical differences in symptoms of lactose intolerance were found regardless of whether the individual described himself or herself as lactose intolerant.¹⁴ Even lactose-intolerant adults may find that 1 glass of milk or a scoop of ice cream is tolerated, whereas an additional glass of milk or other milk product may produce symptoms. Because of the variation of dairy intake in each individual's diet and in the amount of lactose contained in different products, symptoms may vary and be modified by diet and by milk-containing foods (see "Management"). For these reasons, dietary history is an unreliable means to confirm or exclude the diagnosis of lactose intolerance.

Secondary Lactase Deficiency

Secondary lactase deficiency implies that an underlying pathophysiologic condition is responsible for the lactase deficiency and subsequent lactose malabsorption. Etiologies include acute infection (eg, rotavirus) causing small intestinal injury with loss of the lactase-containing epithelial cells from the tips of the villi. The immature epithelial cells that replace these are often lactase deficient, leading to secondary lactose deficiency and lactose malabsorption, although several reports indicate that lactose malabsorption in most children with acute gastroenteritis is not clinically important.¹⁵ Several recent studies and a meta-analysis found that children with rotaviral (and other infectious) diarrheal illnesses who have no or only mild dehydration can safely continue human milk or standard (lactose-containing) formula without any significant effect on outcome, including hydration status, nutritional status, duration of illness, or success of therapy.^{16–18} However, in the at-risk infant (eg, younger than 3 months or malnourished) who develops infectious diarrhea, lactose intolerance may be a significant factor that will influence the evolution of the illness. Giardiasis, cryptosporidiosis, and other parasites that infect the proximal small intestine often lead to lactose malabsorption from direct injury to the epithelial cells by the parasite. Secondary lactase deficiency with clinical signs of lactose intolerance can be seen in celiac disease, Crohn disease, and immune-related and other enteropathies and should be considered in these children. Diagnostic evaluation should be directed toward these entities when secondary lactase deficiency is suspected and an infectious etiology is not found.

Young infants with severe malnutrition develop small intestinal atrophy that also leads to secondary lactase deficiency.¹⁹ Although uncommon in the United States,

malnutrition is associated with lactose malabsorption and carbohydrate intolerance in developing countries.²⁰ Lactose malabsorption has also been associated with poor growth in these countries.²¹ Most infants and children with malabsorption attributable to malnutrition are able to continue to tolerate dietary carbohydrates, including lactose.²² However, the World Health Organization recommends avoidance of lactose-containing milks in children with persistent postinfectious diarrhea (diarrhea lasting more than 14 days) when they fail a dietary trial of milk or yogurt.²³

Treatment of secondary lactase deficiency and lactose malabsorption attributable to an underlying condition generally does not require elimination of lactose from the diet but, rather, treatment of the underlying condition. Once the primary problem is resolved, lactose-containing products can often be consumed normally, and these excellent sources of calcium and other nutrients need not be unnecessarily excluded from the diet.

Developmental (Neonatal) Lactase Deficiency

In the immature gastrointestinal tract, lactase and other disaccharidases are deficient until at least 34 weeks' gestation.²⁴ One study in preterm infants reported benefit from use of lactase-supplemented feedings or lactose-reduced formulas,²⁵ and the use of lactose-containing formulas and human milk does not seem to have any short- or long-term deleterious effects in preterm infants.²⁶ Up to 20% of the dietary lactose may reach the colon in neonates and young infants. Bacterial metabolism of colonic lactose lowers the fecal pH (5.0–5.5 is normal), which has a beneficial effect, favoring certain organisms (eg, *Bifidobacterium* and *Lactobacillus* species) in lieu of potential pathogens (*Proteus* species, *Escherichia coli*, and *Klebsiella* species) in young infants. Antimicrobial agents may also affect this colonization.

Congenital Lactase Deficiency

Congenital lactase deficiency is a rare disorder that has been reported in only a few infants.^{27,28} Affected newborn infants present with intractable diarrhea as soon as human milk or lactose-containing formula is introduced. Small intestinal biopsies reveal normal histologic characteristics but low or completely absent lactase concentrations.^{29,30} Unless this is recognized and treated quickly, the condition is life-threatening because of dehydration and electrolyte losses. Treatment is simply removal and substitution of lactose from the diet with a commercial lactose-free formula.

DIAGNOSIS

Symptoms of lactose intolerance, including abdominal distention, flatulence, abdominal cramping, and (ultimately) diarrhea, are independent of the cause of lactose malabsorption and are directly related to the quantity of ingested lactose. These symptoms are not necessarily

correlated with the degree of intestinal lactase deficiency. Malabsorbed lactose generates an osmotic load that draws fluid and electrolytes into the intestinal lumen, leading to loose stool. The onset of diarrhea and other symptoms is related to the amount of lactose that is not absorbed. As little as 12 g of lactose (the amount of lactose in an 8-oz glass of milk) may be sufficient to cause symptoms in children with chronic abdominal pain.³¹ In addition, unabsorbed lactose is a substrate for intestinal bacteria, especially in the colon. Bacteria metabolize lactose, producing volatile fatty acids and gases (methane, carbon dioxide, and hydrogen), leading to flatulence. The fatty acids lower the fecal pH, making the fecal pH test a nonspecific but sometimes helpful marker for lactose (or other carbohydrate) malabsorption. When sufficient intestinal gas is produced by the bacterial metabolic processes to cause stimulation of the intestinal nervous system by intestinal distention, visceral (abdominal) cramping results.

Initial studies using lactose hydrogen breath tests documented lactose malabsorption in up to 40% of children and adolescents presenting with abdominal pain.³² However, recent studies suggest that the prevalence of abdominal symptoms related to lactose intolerance documented by hydrogen breath tests is variable and ranges from 2% in Finnish children to 24% in southern US children.^{33,34}

A good clinical history often reveals a relationship between lactose ingestion and symptoms. When lactose intolerance is suspected, a lactose-free diet can be tried (Tables 2 and 3).³⁵ During a diagnostic lactose-free diet, it is important that all sources of lactose be eliminated, requiring the reading of food labels to identify "hidden" sources of lactose. Generally, a 2-week trial of a strict lactose-free diet with resolution of symptoms and subsequent reintroduction of dairy foods with recurrence of symptoms can be diagnostic. In more-subtle cases, the hydrogen breath test is the least invasive and most helpful test to diagnose lactose malabsorption. The test has been shown to be more reliable than history, because some patients think they are lactose intolerant when they prove not to be, and others prove to be lactose intolerant (lactose malabsorbers) when they think they are not.^{36,37} The test is performed by administration of a standardized amount of lactose (2 g/kg, up to a maxi-

TABLE 3 Hidden Sources of Lactose⁷²

Bread and other baked goods
Processed breakfast cereals
Mixes for pancakes, biscuits, and cookies
Instant potatoes, soups, and breakfast drinks
Margarine
Nonkosher lunchmeats
Salad dressings
Candies and other snacks

mum of 25 g, equivalent to the amount of lactose in 2 8-oz glasses of milk) after fasting overnight and then measuring the amount of hydrogen in expired air over a 2- to 3-hour period. An increase (>20 ppm) in the hydrogen expired after approximately 60 minutes is consistent with lactose malabsorption. Factors that may produce false-negative or false-positive results include conditions affecting the intestinal flora (eg, recent use of antimicrobial agents), lack of hydrogen-producing bacteria (10%–15% of the population), ingestion of high-fiber diets before the test, small intestinal bacterial overgrowth, or intestinal motility disorders. A pediatric gastroenterologist should be consulted to interpret the results of this test.

The older lactose-tolerance test was previously relied on as the primary test of lactose malabsorption before the breath hydrogen test became available. Lactose intolerance was diagnosed by onset of symptoms and/or positive test results after ingestion of a standard lactose dose (2 g/kg of body weight or 50 g/m² of body surface area; maximum 50 g in a 20% water solution). If the maximum increase in blood glucose concentration was less than 26 mg/dL after a lactose-tolerance test dose, lactose malabsorption was diagnosed. The lactose-tolerance test is not sensitive enough to determine if a subject is malabsorbing some lactose. It is also often falsely positive because of lack of an increase of blood glucose concentration attributable to normal insulin response to the carbohydrate load. Given the high rate of false-negative and false-positive results, this test should not be used and has been replaced by the hydrogen breath test.

Other tests are available in consultation with a pediatric gastroenterologist to diagnose lactose intolerance. If an underlying cause for secondary lactose intolerance is suspected, testing for intestinal etiologies includes stool examination, particularly for parasites affecting the upper gastrointestinal tract such as *Giardia lamblia* and *Cryptosporidia* species, and blood tests for celiac disease (ie, total immunoglobulin A concentration and anti-tissue transglutaminase antibody^{38,39}) or immunodeficiency (quantitative immunoglobulins). Intestinal biopsy may be needed to uncover an underlying gastrointestinal mucosal problem that is causing the lactose malabsorption. Biopsies can yield direct measurement of disaccharidase concentrations to document lactase deficiency directly and assess the status of the other

TABLE 2 Lactose and Calcium Content of Common Foods^{70,71}

Dairy Products	Calcium Content, mg	Lactose Content, g
Yogurt, plain, low fat, 1 cup	448	8.4
Milk, whole (3.25% fat), 1 cup	276	12.8
Milk, reduced fat, 1 cup	285	12.2
Ice cream, vanilla, 1/2 cup	92	4.9
Cheddar cheese, 1 oz	204	0.07
Swiss cheese, 1 oz	224	0.02
Cottage cheese, creamed (small curd), 1 cup	135	1.4

brush-border disaccharidases (sucrase, maltase, isomaltase), which may also be deficient under various circumstances. However, intestinal lactase concentrations do not seem to correlate well with symptoms of lactose intolerance.⁴⁰

Newer tests may eventually yield additional detailed information pertaining to the prevalence and significance of lactose intolerance.⁴¹ For example, the [¹³C]lactose breath test is being considered as a test to augment the accuracy of the breath hydrogen test but is still primarily an investigational tool.^{42,43}

In infants with diarrhea in whom lactose (or other carbohydrate) intolerance is suspected, stool can be screened for malabsorbed carbohydrate by testing fecal pH, which decreases with carbohydrate malabsorption as a result of the formation of volatile fatty acids. It should be remembered that fecal pH will normally be lower (5.0–5.5) in infants compared with older children and adolescents because of the physiologic overload of lactose in their diets, which in turn helps to favor growth of *Lactobacillus* species in the colon. Fecal reducing substances can also be measured and become positive by excretion of a reducing sugar in the stools. Reducing sugars include lactose, glucose, fructose, and galactose but not sucrose. Because some patients may only malabsorb enough carbohydrates, such as lactose, to lower the fecal pH but not increase excretion of carbohydrate in the stool, the pH test is a more sensitive test for carbohydrate malabsorption.

MANAGEMENT

When children are diagnosed with lactose intolerance, avoidance of milk and other dairy products will relieve symptoms. However, those with primary lactose intolerance have varying degrees of lactase deficiency and, correspondingly, often tolerate varying amounts of dietary lactose. Lactose-intolerant children (and their parents) should realize that ingestion of dairy products resulting in symptoms generally leads to transient symptoms without causing harm to the gastrointestinal tract (as compared with celiac disease or allergic reactions, including milk-protein intolerance, that can lead to ongoing inflammation and mucosal damage). Although lactose malabsorption does not predispose to calcium malabsorption,⁴⁴ avoidance of milk products to control symptoms may be problematic for optimal bone mineralization. Children who avoid milk have been documented to ingest less-than-recommended amounts of calcium needed for normal bone calcium accretion and bone mineralization.^{45,46}

Lactose-free and lactose-reduced milks (and lactose-free whole milk for children younger than 2 years) are widely available in supermarkets and can be obtained with WIC (Special Supplemental Nutrition Program for Women, Infants, and Children) vouchers. Although lactose-free milk is more expensive than regular milk, some

major chain stores sell less-expensive lactose-free milk under their own brand names.

Beyond infancy, substitutes for cow milk based on rice, soy, or other proteins are readily available and are generally free of lactose, although the nutrient content of most of these milks is not equivalent to cow milk. Other mammalian milks, including goat milk, are not free of lactose. Tolerance to milk products may be partial, so that dietary maneuvers alone may help avoid symptoms in some individuals. Small amounts of lactose in portions of 4 to 8 oz spaced throughout the day and consumed with other foods may be tolerated with no symptoms.^{47–51} Some children are able to drink 1 to 2 glasses of milk each day without difficulty but cannot tolerate more without developing symptoms.¹⁴ Many lactose-intolerant individuals who are intolerant of milk can tolerate milk chocolate⁵² and/or yogurt (plain better than flavored), because the bacteria in the yogurt partially digest the lactose into glucose and galactose before consumption.^{53,54} In addition, yogurt's semisolid state slows gastric emptying and gastrointestinal transit, resulting in fewer symptoms of lactose intolerance.⁵⁵ Furthermore, ingestion of other solid foods delays gastric emptying, providing additional time for endogenous lactase to digest dietary lactose. Aged cheeses tend to have lower lactose content than other cheeses and, thus, may also be better tolerated. Finally, oral lactase-replacement capsules or predigested milk or dairy products with lactase are readily available and will often permit a lactose-intolerant individual to be able to take some or all milk products freely.⁵⁶ Because the vitamin D content in milk-substitute products varies, labels must be checked to verify the vitamin D content of individual brands.

Even among population groups with significant lactose intolerance, the importance of dietary dairy products has been stressed. For example, the National Medical Association recently recommended that black people consume 3 to 4 servings per day of low-fat milk, cheese, and/or yogurt and that lactose-free milk be used as an alternative for those who are intolerant of these other products to help reduce the risk of nutrient-related chronic diseases such as hypertension and diabetes.⁵⁷

Milk and dairy products are often well tolerated by many children with underlying inflammatory conditions of the intestines, including Crohn disease and ulcerative colitis, in whom the prevalence of lactose intolerance does not seem to be any greater than in the general population.^{58–61}

Lactose-Free Formulas

In developed countries, even in the case of acute gastroenteritis, enough lactose digestion and absorption are preserved so that low-lactose and lactose-free formulas have no clinical advantages compared with standard lactose-containing formulas except in severely undernourished children, in whom lactose-containing formu-

las may worsen the diarrhea and lactose-free formulas may be advantageous.⁶² Breastfed infants should be continued on human milk in all cases.⁵⁷ This has also been reviewed recently in the American Academy of Pediatrics' practice guideline for acute gastroenteritis.⁶³ The use of lactase in formulas for preterm infants has been noted above. Although lactose-free cow milk-protein-based formulas are readily available and popular, no studies have documented that these formulas have any clinical impact on infant outcome measures including colic, growth, or development.⁶⁴

Lactose, Calcium Absorption, and Bone Mineral Content

Recent evidence indicates that dietary lactose enhances calcium absorption and, conversely, that lactose-free diets result in lower calcium absorption.⁶⁵ Thus, lactose intolerance (and lactose-free diets) theoretically may predispose to inadequate bone mineralization, a problem now recognized in many other disorders affecting pediatric patients.^{45,46} The effects of lactose-free diets in childhood on long-term bone mineral content and risk of fractures and osteoporosis with aging remains to be clarified. Calcium homeostasis is also affected by protein intake, vitamin D status, salt intake, and genetic and other factors, making long-term studies essential to determine the risks of each or all of these to bone health. Recent studies suggest that in the future, genetic testing may be useful for identifying individuals at increased risk of lactase deficiency and consequent diminished bone mineral density,⁶⁶ potentially allowing early intervention with dietary manipulation or nutrient supplementation. Recent research has even suggested that gene-replacement therapies might someday be available for susceptible individuals.⁶⁷

SUMMARY

Lactose intolerance has been recognized for many years as a common problem in many children and most adults throughout the world. Although rarely life-threatening, the symptoms of lactose intolerance can lead to significant discomfort, disrupted quality of life, and loss of school attendance, leisure and sports activities, and work time, all at a cost to individuals, families, and society. Treatment is relatively simple and aimed at reducing or eliminating the inciting substance, lactose, by eliminating it from the diet or by "predigesting" it with supplemental lactase-enzyme replacement. Calcium must be provided by alternate nondairy dietary sources or as a dietary supplement to individuals who avoid milk intake.

CONCLUSIONS

1. Lactose intolerance is a common cause of abdominal pain in older children and teenagers.

2. Lactose intolerance attributable to primary lactase deficiency is uncommon before 2 to 3 years of age in all populations; when lactose malabsorption becomes apparent before 2 to 3 years of age, other etiologies must be sought.
3. Evaluation for lactose intolerance can be achieved relatively easily by dietary elimination and challenge. More-formal testing is usually noninvasive, typically with fecal pH in the presence of watery diarrhea and hydrogen breath testing.
4. If lactose-free diets are used for treatment of lactose intolerance, the diets should include a good source of calcium and/or calcium supplementation to meet daily recommended intake levels.
5. Treatment of lactose intolerance by elimination of milk and other dairy products is not usually necessary given newer approaches to lactose intolerance, including the use of partially digested products (such as yogurts, cheeses, products containing *Lactobacillus acidophilus*, and pretreated milks^{56,68}). Evidence that avoidance of dairy products may lead to inadequate calcium intake and consequent suboptimal bone mineralization makes these important as alternatives to milk. Dairy products remain principle sources of protein and other nutrients that are essential for growth in children.

COMMITTEE ON NUTRITION, 2005–2006

Frank R. Greer, MD, Chairperson
Jatinder J. S. Bhatia, MD
Stephen R. Daniels, MD, PhD
Melvin B. Heyman, MD
Marcie B. Schneider, MD
Dan W. Thomas, MD
Robert D. Baker, Jr, MD, PhD

LIAISONS

Sue Ann Anderson, PhD, RD
Food and Drug Administration
Donna Blum-Kemelor, MS, RD
US Department of Agriculture
Margaret P. Boland, MD
Canadian Paediatric Society
Laurence Grummer-Strawn, PhD
Centers for Disease Control and Prevention
Capt Van S. Hubbard, MD, PhD
National Institutes of Health
Benson M. Silverman, MD
Food and Drug Administration

STAFF

Raymond J. Koteras, MHA

REFERENCES

1. American Academy of Pediatrics, Committee on Nutrition. The practical significance of lactose intolerance in children. *Pediatrics*. 1978;62:240–245

2. American Academy of Pediatrics, Committee on Nutrition. Practical significance of lactose intolerance in children: supplement. *Pediatrics*. 1990;86:643–644
3. American Academy of Pediatrics, Committee on Nutrition. Optimizing bone health and calcium intake of infants, children, and adolescents. *Pediatrics*. 2006;117:578–585
4. Semenza G. Anchoring and biosynthesis of stalked brush border membrane proteins: glycosidases and peptidases of enterocytes and renal tubuli. *Annu Rev Cell Biol*. 1986;2:255–313
5. American Academy of Pediatrics, Committee on Nutrition. Hypoallergenic infant formulas. *Pediatrics*. 2000;106:346–349
6. Host A, Jacobsen HP, Halken S, Holmenlund D. The natural history of cow's milk protein allergy/intolerance. *Eur J Clin Nutr*. 1995;49(suppl 1):S13–S18
7. Kretchmer N. Lactose and lactase: a historical perspective. *Gastroenterology*. 1971;61:805–813
8. Kretchmer N. On the homology between human development and pediatrics. *Pediatr Res*. 1968;2:283–286
9. Paige DM, Bayless TM, Mellitis ED, Davis L. Lactose malabsorption in preschool black children. *Am J Clin Nutr*. 1977;30:1018–1022
10. Lloyd ML, Olsen WA. Disaccharide malabsorption. In: Haubrich WS, Schaffner F, Berk JE, eds. *Bockus Gastroenterology*. 5th ed. Philadelphia, PA: Saunders; 1995:1087–1100
11. Sahi T. Genetics and epidemiology of adult-type hypolactasia. *Scand J Gastroenterol Suppl*. 1994;202:7–20
12. Woteki CE, Weser E, Young EA. Lactose malabsorption in Mexican-American children. *Am J Clin Nutr*. 1976;29:19–24
13. Wang Y, Harvey CB, Hollox EJ, et al. The genetically programmed down-regulation of lactase in children. *Gastroenterology*. 1998;114:1230–1236
14. Suarez FL, Savaiano D, Arbisi P, Levitt MD. Tolerance to the daily ingestion of two cups of milk by individuals claiming lactose intolerance. *Am J Clin Nutr*. 1997;65:1502–1506
15. Sandhu BK, Isolauri E, Walker-Smith JA, et al. A multicentre study on behalf of the European Society of Paediatric Gastroenterology and Nutrition Working Group on Acute Diarrhoea. Early feeding in childhood gastroenteritis. *J Pediatr Gastroenterol Nutr*. 1997;24:522–527
16. Bhatnagar S, Bhan MK, Singh KD, Saxena SK, Shariff M. Efficacy of milk-based diets in persistent diarrhea: a randomized, controlled trial. *Pediatrics*. 1996;98:1122–1126
17. Sperotto G, Barison EM, Baldacci ER, Okay Y. Use of undiluted whole cow's milk is effective for the routine treatment of children with acute diarrhea and severe dehydration. *Arq Gastroenterol*. 1998;35:132–137
18. Brown KH, Pearson JM, Fontaine O. Use of nonhuman milks in the dietary management of young children with acute diarrhea: a meta-analysis of clinical trials. *Pediatrics*. 1994;93:17–27
19. Nichols BL, Dudley MA, Nichols VN, et al. Effects of malnutrition on expression and activity of lactase in children. *Gastroenterology*. 1997;112:742–751
20. Northrop-Clewes CA, Lunn PG, Downes RM. Lactose maldigestion in breast-feeding Gambian infants. *J Pediatr Gastroenterol Nutr*. 1997;24:257–263
21. Wharton B, Howells G, Phillips I. Diarrhoea in kwashiorkor. *Br Med J*. 1968;4:608–611
22. Habte D, Hyvarinen A, Sterky G. Carbohydrate malabsorption in kwashiorkor. *Ethiop Med J*. 1973;11:33–40
23. World Health Organization, International Working Group on Persistent Diarrhoea. Evaluation of an algorithm for the treatment of persistent diarrhoea: a multicenter study. *Bull World Health Organ*. 1996;74:479–489
24. Antonowicz I, Lebenthal E. Developmental patterns of small intestinal enterokinase and disaccharidase activities in the human fetus. *Gastroenterology*. 1977;72:1299–1303
25. Erasmus HD, Ludwig-Auser HM, Paterson PG, Sun D, Sankaran K. Enhanced weight gain in preterm infants receiving lactase-treated feeds: a randomized, double-blind, controlled trial. *J Pediatr*. 2002;141:532–537
26. Shulman RJ, Feste A, Ou C. Absorption of lactose, glucose polymers, or combination in premature infants. *J Pediatr*. 1995;127:626–631
27. Lifshitz F. Congenital lactase deficiency. *J Pediatr*. 1966;69:229–237
28. Savilahti E, Launiala K, Kuitunen P. Congenital lactase deficiency: a clinical study on 16 patients. *Arch Dis Child*. 1983;58:246–252
29. Asp NG, Dahlqvist A, Kuitunen P, Launiala K, Visakorpi JK. Complete deficiency of brush-border lactase in congenital lactose malabsorption. *Lancet*. 1973;2(7824):329–330
30. Freiburghaus AU, Schmitz J, Schindler M, et al. Protein patterns of brush border fragments in congenital lactose malabsorption and in specific hypolactasia of the adult. *N Engl J Med*. 1976;294:1030–1032
31. Gremse DA, Greer AS, Vacik J, DiPalma JA. Abdominal pain associated with lactose ingestion in children with lactose intolerance. *Clin Pediatr (Phila)*. 2003;42:341–345
32. Barr RG, Levine MD, Watkins JB. Recurrent abdominal pain of childhood due to lactose intolerance. *N Engl J Med*. 1979;300:1449–1452
33. Kokkonen J, Haapalahti M, Tikkanen S, Karttunen R, Savilahti E. Gastrointestinal complaints and diagnosis in children: a population-based study. *Acta Paediatr*. 2004;93:880–886
34. Webster RB, DiPalma JA, Gremse DA. Irritable bowel syndrome and lactose maldigestion in recurrent abdominal pain in childhood. *South Med J*. 1999;92:778–781
35. Drugs.com. Lactose free diet. Available at: www.drugs.com/CG/LACTOSE-FREE-DIET.html. Accessed August 18, 2005
36. Di Palma JA, Narvaez RM. Prediction of lactose malabsorption in referral patients. *Dig Dis Sci*. 1988;33:303–307
37. Suarez FL, Savaiano DA, Levitt MD. A comparison of symptoms after the consumption of milk or lactose-hydrolyzed milk by people with self-reported severe lactose intolerance. *N Engl J Med*. 1995;333:1–4
38. Hill ID, Dirks MH, Liptak GS, et al. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2005;40:1–19
39. National Institutes of Health. NIH consensus development conference on celiac disease. Available at: <http://consensus.nih.gov/2004/2004CeliacDisease118html.htm>. Accessed August 18, 2005
40. Gupta SK, Chong SK, Fitzgerald JF. Disaccharidase activities in children: normal values and comparison based on symptoms and histologic changes. *J Pediatr Gastroenterol Nutr*. 1999;28:246–251
41. Vonk RJ, Lin Y, Koetse HA, et al. Lactose (mal)digestion evaluated by the ^{13}C -lactose digestion test. *Eur J Clin Invest*. 2000;30:140–146
42. Hiele M, Ghos Y, Rutgeerts P, Vantrappen G, Carchon H, Eggermont E. $^{13}\text{CO}_2$ breath test using naturally ^{13}C -enriched lactose for detection of lactase deficiency in patients with gastrointestinal symptoms. *J Lab Clin Med*. 1988;112:193–200
43. Koetse HA, Stellaard F, Bijleveld CM, et al. Non-invasive detection of low-intestinal lactase activity in children by use of a combined $^{13}\text{CO}_2/\text{H}_2$ breath test. *Scand J Gastroenterol*. 1999;34:35–40
44. Tremaine WJ, Newcomer AD, Riggs BL, McGill DB. Calcium absorption from milk in lactase-deficient and lactase-sufficient adults. *Dig Dis Sci*. 1986;31:376–378
45. Stallings VA, Oddleifson NW, Negrini BY, Zemel BS, Wellens R.

- Bone mineral content and dietary calcium intake in children prescribed a low-lactose diet. *J Pediatr Gastroenterol Nutr.* 1994;18:440–445
46. Di Stefano M, Veneto G, Malservisi S, et al. Lactose malabsorption and intolerance and peak bone mass. *Gastroenterology.* 2002;122:1793–1799
 47. McBean LD, Miller GD. Allaying fears and fallacies about lactose intolerance. *J Am Diet Assoc.* 1998;98:671–676
 48. Johnson AO, Semanya JG, Buchowski MS, Enwonwu CO, Scrimshaw NS. Adaptation of lactose maldigesters to continued milk intake. *Am J Clin Nutr.* 1993;58:879–881
 49. Hertzler SR, Savaiano DA. Colonic adaptation to the daily lactose feeding in lactose maldigesters reduces lactose intolerance. *Am J Clin Nutr.* 1996;64:232–236
 50. Pribila BA, Hertzler SR, Martin BR, Weaver CM, Savaiano DA. Improved lactose digestion and intolerance among African-American adolescent girls fed a dairy-rich diet. *J Am Diet Assoc.* 2000;100:524–528
 51. Hertzler SR, Huynh BC, Savaiano DA. How much lactose is low lactose? *J Am Diet Assoc.* 1996;96:243–246
 52. Jarvinen RM, Loukaskorpi M, Uusitupa MI. Tolerance of symptomatic lactose malabsorbers to lactose in milk chocolate. *Eur J Clin Nutr.* 2003;57:701–705
 53. Kolars JC, Levitt MD, Aouji M, Savaiano DA. Yogurt: an autodigesting source of lactose. *N Engl J Med.* 1984;310:1–3
 54. Boudraa G, Benbouabdellah M, Hachelaf W, Boisset M, Desjeux JF, Touhami M. Effect of feeding yogurt versus milk in children with acute diarrhea and carbohydrate malabsorption. *J Pediatr Gastroenterol Nutr.* 2001;33:307–313
 55. Labayen I, Forga L, Gonzalez A, Lenoir-Wijnkoop I, Nutr R, Martinez JA. Relationship between lactose digestion, gastrointestinal transit time and symptoms in lactose malabsorbers after dairy consumption. *Aliment Pharmacol Ther.* 2001;15:543–549
 56. Medow MS, Thek KD, Newman LJ, Berezin S, Glassman MS, Schwarz SM. Beta-galactosidase tablets in the treatment of lactose intolerance in pediatrics. *Am J Dis Child.* 1990;144:1261–1264
 57. Wooten WJ, Price W. The role of dairy and dairy nutrients in the diet of African Americans. *J Natl Med Assoc.* 2004;96(12 suppl):5S–31S
 58. Pfefferkorn MD, Fitzgerald JF, Croffie JM, Gupta SK, Corkins MR, Molleston JP. Lactase deficiency: not more common in pediatric patients with inflammatory bowel disease than in patients with chronic abdominal pain. *J Pediatr Gastroenterol Nutr.* 2002;35:339–343
 59. Kirschner BS, DeFavaro MV, Jensen W. Lactose malabsorption in children and adolescents with inflammatory bowel disease. *Gastroenterology.* 1981;81:829–832
 60. Mishkin S. Dairy sensitivity, lactose malabsorption, and elimination diets in inflammatory bowel disease. *Am J Clin Nutr.* 1997;65:564–567
 61. Bernstein CN, Ament M, Artinian L, Ridgeway J, Shanahan F. Milk tolerance in adults with ulcerative colitis. *Am J Gastroenterol.* 1994;89:872–877
 62. Kukuruzovic RH, Brewster DR. Milk formulas in acute gastroenteritis and malnutrition: a randomized trial. *J Paediatr Child Health.* 2002;38:571–577
 63. American Academy of Pediatrics, Provisional Committee on Quality Improvement, Subcommittee on Acute Gastroenteritis. Practice parameter: the management of acute gastroenteritis in young children. *Pediatrics.* 1996;97:424–435
 64. Heubi J, Karasov R, Reisinger K, et al. Randomized multicenter trial documenting the efficacy and safety of a lactose-free and a lactose-containing formula for term infants. *J Am Diet Assoc.* 2000;100:212–217
 65. Abrams SA, Griffin IJ, Davila PM. Calcium and zinc absorption from lactose-containing and lactose-free infant formulas. *Am J Clin Nutr.* 2002;76:442–446
 66. Obermayer-Pietsch BM, Bonelli CM, Walter DE, et al. Genetic predisposition for adult lactose intolerance and relation to diet, bone density, and bone fractures. *J Bone Miner Res.* 2004;19:42–47
 67. During MJ, Xu R, Young D, Kaplitt MG, Sherwin RS, Leone P. Peroral gene therapy of lactose intolerance using an adeno-associated virus vector. *Nat Med.* 1998;4:1131–1135
 68. Sanders ME, Klaenhammer TR. The scientific basis of *Lactobacillus acidophilus* NCFM functionality as a probiotic. *J Dairy Sci.* 2001;84:319–331
 69. Johnson JD. The regional and ethnic distribution of lactose malabsorption. In: Paige DM, Bayless TM, eds. *Lactose Digestion: Clinical and Nutritional Implications.* Baltimore, MD: Johns Hopkins University Press; 1981:11–22
 70. US Department of Agriculture. National nutrient database for standard reference. Available at: www.nal.usda.gov/fnic/foodcomp/search. Accessed August 18, 2005
 71. Matthews RH, Pehrsson PR, Farhat-Sabet M. Sugar content of selected foods: individual and total sugars. US Department of Agriculture, Human Nutrition Information Service; 1987. Available at: www.nal.usda.gov/fnic/foodcomp/Data/Other/herr48.pdf. Accessed August 18, 2005
 72. National Digestive Diseases Information Clearinghouse. Lactose intolerance. Available at: <http://digestive.niddk.nih.gov/ddiseases/pubs/lactoseintolerance>. Accessed August 18, 2005