

Lactose Intolerance

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Key words: lactose intolerance, gastrointestinal symptoms, review

Lactose maldigestion has been under intensive research since its discovery in the 1960's. We know the prevalence of lactose maldigestion in a great number of countries and ethnic groups. However, there is often no provision made for the secondary type of maldigestion, and the study populations have sometimes been selected rather than picked at random. New methods for the measurement of lactose digestion have been developed, and its genetic mechanisms have received a great deal of attention during the last few years. However, in many studies the measurement and/or reporting of symptoms has quite often been overlooked. In this review, various topics related to lactose intolerance are discussed with a special emphasis on its symptoms.

Key teaching points:

- Many lactose maldigesters tolerate small to moderate amounts of lactose without remarkable discomfort. However, when consumption of liquid dairy products reach a couple of servings per day or more, some individuals will benefit of the use of products with reduced lactose content (hydrolyzed lactose, fermented dairy products).
- Yoghurt is well tolerated by lactose maldigesters, even pasteurized yoghurt.
- Symptoms of lactose intolerance resemble those of some other gastrointestinal dysfunctions such as functional bowel disorders and other maldigestions.
- The severity and perhaps also the nature of symptoms may change with age and with variable physiological conditions. It is therefore advisable to test one's own tolerance every once in a while.

INTRODUCTION

Among the physiological factors that affect the amount of lactose digested and its tolerance are gastrointestinal transit, intestinal lactase activity, visceral sensitivity and the presence of functional bowel disorders, and possibly the composition of the colonic microflora. In addition, factors related to the sensory and central nervous systems modify symptom perception. Taking into account these complex factors and their interactions, it is not surprising that marked inter- and intraindividual differences exist in the symptoms of lactose intolerance.

Some topics with which recent studies have dealt are tolerance of fermented dairy products, tolerance of different amounts of lactose, adaptation to lactose consumption and influence of gastric emptying on tolerance. The results of many of these studies are controversial. The explanation may be the above mentioned interactions and complexity of factors that affect gastrointestinal symptoms.

DESCRIPTION OF SUBJECT

Lactose and Lactase

It is not quite clear why there has to be a special carbohydrate in milk. Mustapha *et al.* [1] hypothesize that lactose solubility may be matched best with milk synthesis and expression, and it may provide appropriate energy while minimizing osmotic load. As far as is known, lactose has no special nutritional importance for adults. It is the most important source of energy during the first year of a human's life, providing almost half the total energy requirement of infants.

Lactose has several applications in the food industry. It is used, for instance, in sweets, confectionery, bread and sausages because of its physiological properties: lactose provides good texture and binds water and color. Lactose is only about one third as sweet as saccharose and less than half as sweet as glucose.

To be absorbed, lactose needs to be hydrolyzed in the intestine by a β -galactosidase, lactase-phlorizin hydrolase (EC 3.2.1.23/26), generally called lactase. Lactase is found most

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abundantly in the jejunum (at the beginning of the small intestine), and it specifically only hydrolyses lactose. It is found at the tip of the intestinal villi and is therefore more vulnerable to intestinal diseases that cause cell damage than other disaccharidases, which are located deeper.

Pharmaceutical preparations of fungal or yeast-derived β -galactosidase have been developed for the treatment of lactose maldigestion. There is evidence that these preparations increase lactose digestion and alleviate symptoms [2, 3], but different preparations seem to vary in their effectiveness [4], and they do not help all subjects [2]. Compared to lactose in yoghurt or in pre-hydrolyzed milk, these products seem less efficient [5, 6]. One case report on allergy to supplemental lactase enzyme has been published [7].

Hypolactasia, Lactose Maldigestion and Lactose Intolerance

Hypolactasia may be primary (i.e. genetic) or secondary. The genetically determined reduction of lactase activity occurs soon after weaning in almost all animals and in many human groups [8]. The activity drops to about one tenth or less of the suckling level, and this situation is referred to as hypolactasia, (adult-type) lactase deficiency or lactase non-persistence. Congenital lactase deficiency (CLD) is extremely rare [9]. There have been only a few dozen documented cases in the world, most of them in Finland.

Secondary hypolactasia or maldigestion can result from small intestinal resections, and from gastrectomy [10] and from diseases that damage the intestinal epithelium, e.g. untreated coeliac disease or intestinal inflammation [11, 12]. When the epithelium heals, the activity of lactase returns. However, secondary maldigestion does not automatically lead to severe symptoms of intolerance [13, 14].

In populations where the prevalence of primary hypolactasia is high, the decline of lactase activity begins at the ages of two to three years. In Finns, on the other hand, the onset most commonly occurs in adolescence [15]. Hypolactasia leads to lactose maldigestion, which in turn can—and in the great majority of cases does—lead to symptoms of lactose intolerance when lactose is ingested in amounts of dozens of grams at a time, e.g. the 50 grams used in the lactose tolerance test. As to the intake of smaller amounts of lactose, the onset of symptoms is highly individual. Symptom responses after ingestion of different amounts of lactose will be discussed below.

Genetics of Lactose Maldigestion

Selective adult-type hypolactasia is inherited through a single autosomal recessive gene [16]. Both pretranscriptional and posttranscriptional mechanisms seem to be involved in the expression of the low enzyme activity [17]. A Finnish group has recently reported assignment of the CLD gene [18]. Their analyses indicate that one major mutation in a novel gene causes CLD in the Finnish population.

A culture-historical hypothesis has been proposed for lactase persistence [19]: After the beginning of dairy farming, when there were periods of dietary stress, there would have been an advantage for those individuals who had high levels of intestinal lactase. As a result of increased survival, high intestinal lactase activity would have become typical of such a group. Lactase persistence is, indeed, more common in the areas with long traditions of dairy farming. However, production of the enzyme does not seem to be induced by lactose consumption.

Prevalence of Lactose Maldigestion

Scrimshaw and Murray [20] and Sahi [21] have reviewed the prevalences of lactose maldigestion globally. The prevalence is above 50% in South America, Africa, and Asia, reaching almost 100% in some Asian countries. In the United States, the prevalence is 15% among whites, 53% among Mexican-Americans and 80% in the Black population. In Europe it varies from around 2% in Scandinavia to about 70% in Sicily (Fig. 1). Australia and New Zealand have prevalences of 6% and 9% respectively. In general, it can be stated that about two thirds of the world adult population is lactase non-persistent.

Age

In Blacks and Asians, hypolactasia usually manifests itself in early childhood, whereas in whites, it seems to occur later in childhood or in adolescence [20]. Lactose intolerance is not common in young white children. However, rotavirus infections may be an important cause of secondary lactose maldigestion in children, and, as the infection is cured, lactose maldigestion disappears as well.

There is some evidence that intestinal lactase activity does not continue to decline with age, because there were no differences in the prevalence of hypolactasia between older and younger adults [22]. However, the prevalence of hypolactasia is more common in adults than in children [23, 24].

Results of the experience of symptoms according to age are contradictory. Jussila *et al.* [22] found that the mean age of symptomatic lactose maldigesters was higher (46 years) than that of non-symptomatic lactose maldigesters (31 years), whereas Suarez and Savaiano [25] reported no difference in the symptoms between the age groups of over 65 years and 20 to 40 years. It is possible that the subjects in the latter study had been specially selected, since they had been recruited by announcements in certain neighborhoods. However, the number of subjects to date is probably too small to draw definitive conclusions as to the effect of age on the experience of symptoms.

There might be differences in hydrogen production after ingestion of lactose according to age, but the findings are not entirely consistent. The amount of breath hydrogen was shown to increase with age up to the age of 64 to 70 years [23, 26] and after lactulose challenge in a group of elderly subjects whose

Origin of Symptoms of Lactose Intolerance

Symptoms of lactose intolerance include loose stools, abdominal bloating and pain, flatulence, nausea and borborygmi. The mechanism of loose stools induced by unabsorbed carbohydrate is well documented. The osmotic load of the carbohydrate causes secretion of fluid and electrolytes until osmotic equilibrium is reached [34, 35]. Dilatation of the intestine, caused by the osmosis, induces an acceleration of small intestinal transit, which increases with the degree of maldigestion [36]. The accelerated transit further reduces the hydrolysis of lactose, because the contact time between lactose and the residual enzyme is decreased.

Less is known about the origin of abdominal distension and cramps. It has been suggested that these symptoms originate from the small intestine and are not caused by colonic fermentation [35]. On the other hand, a recent study showed that symptoms seemed to originate from the colon, since lactose both ingested orally and introduced directly to the colon caused similar symptoms [37]. In only 38% of the cases, however, did the symptoms coincide with colonic motor events. In subjects with chronic abdominal discomfort (functional bowel disorders), the complaints may have resulted from disordered intestinal motility and abnormal pain response to gut distension rather than from increased gas volumes, since the volume or the accumulation rate of gas infused in the intestinal tract did not differ between the subjects with symptoms and the control subjects [38]. In the study of Hammer *et al.* [39], gas seemed to serve as a trigger for symptoms, as suggested by the significant correlation between the time of the occurrence of peak symptoms and the time of peak breath hydrogen concentration.

The production of hydrogen depends on colonic acidity. Reduced hydrogen excretion was seen after continuous ingestion of the non-digestible sugar, lactulose, which resulted in increased colonic acidity [40–42]. Reduced hydrogen excretion and symptoms have been reported after continuous lactose consumption [43, 44]. This topic is further discussed below, under the heading **Adaptation to Lactose Consumption**.

It is possible that the symptoms originate from both the small intestine and the colon, and modifications of the small intestinal and colonic conditions, such as transit time and the composition of the flora, may also affect the induction and the severity of the symptoms.

Lactose Intolerance in Relation to Amounts of Lactose

Ingestion of 50 grams of lactose in a clinical tolerance test caused symptoms in 80% to 100% of lactose maldigesters [22, 45–47], and one third to half of the lactose maldigesters experience symptoms after consumption of 200–250 mL of milk [48]. In many studies ingestion of hydrolysed lactose milk has reduced symptoms more readily than regular milk [49].

An interesting question arises that has not yet been answered: what is the smallest amount of lactose that can possibly

cause symptoms to any individual? We studied the symptoms of lactose maldigesters after ingestion of lactose amounts of up to seven grams in fat-free milk [50]. The completely lactose-free control milk induced symptoms in as many subjects as the milk containing seven grams of lactose, nor was there any difference in the severity of symptoms. Hertzler *et al.* [51] reported a higher mean increase in breath hydrogen excretion after ingestion of six grams lactose than after two grams, indicating at least partial lactose maldigestion with the higher dose. However, the fairly high baseline values of breath hydrogen, approximately 20 ppm, complicate the interpretation of their results. The subjects reported no more symptoms after six grams lactose than after none or two grams. Suarez *et al.* [52, 53] found no difference in the symptom response after daily ingestion of one or two glasses of regular and lactose-free milk with a meal.

Even after ingestion of large amounts of lactose, a small percentage of maldigesters remained symptom-free [20]. The reason for this is unknown, but the presence of symptom-free subjects is a common observation in connection with other carbohydrate maldigestions as well: only about half of the fructose maldigesters experienced abdominal symptoms after ingesting 50 grams of fructose [54] and after 25 grams of fructose and five grams of sorbitol [55].

Most studies have shown low-lactose or lactose-free milk to be better tolerated than lactose-containing milk, but the controversial results of the most recent, well-controlled works, which revealed no difference in the tolerance between these milks [50, 52, 53] nor demonstrated the possibility of a placebo effect [43], necessitate the reconsidering and reinvestigation of this topic.

Fermented and Non-Fermented Dairy Products

Lactose maldigesters digest and tolerate lactose in yoghurt better than an equivalent quantity of lactose in milk [56–59], but the importance of lactase activity present in yoghurt is not clear. Several authors emphasize the importance of the living bacteria of yoghurt or other fermented milks in connection with lactose digestion [60–62]. However, in two of these studies, the tolerance of heat-treated yoghurt was not significantly inferior to that of fresh yoghurt with viable bacteria [58, 61]. Similarly, digestion and tolerance of lactose were equal after ingestion of three fermented dairy products which had a four-fold difference in their β -galactosidase activity [63]. In addition, several works have shown that lactose digestion was improved when bacterial cells were destroyed by sonication or by the presence of bile, compared to intact cells [58, 60, 64, 65]. However, contradictory results have also been published [66]. This may have been due to differences in the tolerance to acid and bile between the bacterial species and strains present in the fermented products.

In direct *in vivo* measurements, maldigestion of 18 grams of

lactose was 9.6% after ingestion of yoghurt, 12.5% after pasteurized yoghurt and 39% after milk [58]. The gastric β -galactosidase:lactose ratio fell rapidly within two hours of ingestion of yoghurt [66], but part of the β -galactosidase obviously survived the passage through the stomach. Yoghurt ingestion caused significantly fewer symptoms in lactose maldigesters than did milk [67]. When the tolerance of unmodified, low-fat and lactose-hydrolyzed yoghurt was compared, the modification of lactose or fat content did not have any effect on the tolerance of yoghurt, but symptoms were significantly and equally reduced with all the yoghurts compared with milk [59].

Non-fermented milk containing bacteria grown on lactose also reduced breath hydrogen excretion [68]: hydrogen excretion was significantly lower in lactose maldigesters after ingestion of one dose of milk containing *Bifidobacterium longum* B6 grown on lactose, as compared with milk containing *Bifidobacterium longum* B6 grown on lactose and glucose or *Bifidobacterium longum* ATCC 15708 grown on lactose. The former milk contained the highest β -galactosidase activity, which probably accounted for the good digestion. *Bifidobacterium longum* B6 was also the most bile tolerant strain.

Non-fermented milk containing *Lactobacillus bulgaricus* 449 reduced breath hydrogen and symptoms whereas *L. acidophilus* B only slightly reduced breath hydrogen without an effect on the symptoms [69]. Bile sensitivity and β -galactosidase activity of these strains were similar, but the cell wall structures of this and other *L. acidophilus* strains tested were tougher than those of *L. bulgaricus* strains. Another strain of *L. acidophilus* also failed to alleviate lactose intolerance when ingested twice a day for seven days [70].

Prolonged consumption of non-pasteurized yoghurt appeared to improve the digestion of lactose, because the excretion of breath hydrogen decreased after 6- and 12-day periods of yoghurt consumption [71]. Diarrhoeal symptoms decreased after 12 days of consumption. However, there was no change in the fecal β -galactosidase activity. In the same study, administration of pasteurized yoghurt did not alter breath hydrogen excretion or diarrhea, but the activity of fecal β -galactosidase increased after both six and 12 days of consumption.

Although food ingested simultaneously with milk has been

shown to improve lactose digestion [72, 73], this did not apply to yoghurt [74], presumably because lactose digestion from yoghurt is already very efficient [56, 58].

The Effect of Milk Fat and Gastrointestinal Transit

It has been suggested that full-fat milk causes fewer symptoms in lactose maldigesters than lactose-free milk [75, 76]. Leichter [77] showed that, in adults, full-fat milk reduced lactose maldigestion and intolerance compared with fat-free milk. Solomons *et al.* [78] obtained similar results when they compared full-fat milk with aqueous lactose solution. Other researchers have not been able to confirm these results [79–81]. Dehkordi *et al.* [73] reported a slight decrease in the maldigestion of lactose in full-fat milk compared to fat-free milk, whereas there was no improvement in symptoms. Martini *et al.* [66] did not observe any significant difference in the severity of symptoms or the degree of lactose maldigestion in lactose maldigesters who had consumed ice-cream and low-fat ice-cream with a substantial difference in the fat content between the products, 10% and 3% fat respectively. However, the composition of ice-cream and low-fat ice-cream differs from that of milk, and the results may not be applicable to milk. Table 1 presents studies on the effect of milk fat on lactose intolerance.

Delayed gastric emptying has been proposed as one explanation for improved lactose tolerance after ingestion of full-fat milk compared with skimmed milk or ingestion of milk with a meal instead of milk on its own [72, 78]. The gastric emptying rate and the intestinal transit time alter the time that lactose is exposed to intestinal lactase. After a meal, the stomach contents are progressively emptied into the duodenum over a period of several hours, depending on the energy content and the composition of the meal [82]. The temperature of a meal or a drink also influences gastric emptying. Ingestion of a cold drink of 4°C slowed down the initial phase of gastric emptying for approximately 10 minutes after ingestion, compared with a control drink of 37°C [83]. There was a tendency towards delayed emptying of a drink of 50°C, but the difference was not significant as compared to the control drink.

Table 1. Comparison of Lactose Digestion and Tolerance in Lactose Maldigesters after Ingestion of Milks with Different Fat Content

Reference	n	Test meal and amount/d	Result
77	11	Milk, full-fat and fat-free 1050 ml	More symptoms after fat-free milk
80	17	Milk, full-fat and fat-free 500 ml	No difference in symptoms
79	40	Milk, full-fat and fat-free 125–1000 ml	No difference in symptoms
66	8	Ice cream, 400 g	No difference in symptoms
		Low-fat ice-cream, 410 g	
59	14	Yoghurt, full-fat and low-fat, 454 g	More H ₂ excreted after fat-free yoghurt
			No difference in symptoms
73	7	Milk, full-fat and fat-free, 360–385 ml	More H ₂ excreted after fat-free milk
			No difference in symptoms
81	30	High-fat milk (8%) and fat-free milk, 2 × 200 ml	No difference in symptoms

The rapidity of gastric emptying varies depending on many physiological factors. It has been suggested that delayed gastric emptying improves lactose digestion and therefore tolerance. Lactose has been better digested when consumed in milk instead of water [78], in a chocolate milk drink instead of plain milk [73, 84] or with solid food [72, 73, 85] or fibre [86]. This alleviation of symptoms is considered to be the result of delayed gastric emptying caused by an increase in the energy content and osmolality. Fat slows down the rate of gastric emptying [87] and increases the jejunal transit time [88]. We studied the influence of increased energy content of milk on gastric emptying and digestion and tolerance of lactose [89]. High-energy milk significantly delayed gastric emptying, but had only a borderline effect on lactose digestion and very little effect on the symptoms. However, pharmacological delaying of gastric emptying did improve the tolerance of lactose [90].

Ingestion of yoghurt has been shown to lengthen gastric emptying halftime and gastrointestinal transit time compared with regular milk [13, 58, 91]. The mechanism of this delay is not known, but it does not seem to be due to differences in lactose digestion, as gastrointestinal transit has been lengthened both in lactose digesters [91] and in maldigesters [58]. An indication of delayed gastric emptying after ingestion of yoghurt as compared with milk was also obtained in a study on healthy adults with no known lactose digestion status [92]. The lengthening of the gastrointestinal transit time may be due to the more solid composition or viscosity of yoghurt. However, we failed to find any difference in gastric emptying of lactose tolerance between the milks of varying viscosity [93].

Functional Gastrointestinal Disorders

Functional gastrointestinal disorders are a variable combination of chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities [94]. Among these disorders, the symptoms of functional bowel disorders and dysmotility-type dyspepsia resemble those of lactose intolerance. There are several sub-groups to the functional bowel disorders: functional abdominal bloating, functional abdominal pain, functional constipation, functional diarrhea, irritable bowel syndrome and unspecific functional bowel disorder [95]. The prevalence of functional bowel disorders is high in the Western countries. The most commonly investigated is irritable bowel syndrome, the prevalence of which has been around 17% in several studies, as determined by postal questionnaires [96, 97]. Its symptoms include abdominal pain, bloating and altered defecation habits, which resemble those experienced by lactose intolerant subjects.

Visceral sensitivity [98], as well as bowel motor abnormalities [99, 100] have been documented in irritable bowel syndrome. Compared with healthy people, patients with irritable bowel syndrome or functional dyspepsia, i.e. chronic or recurrent upper abdominal discomfort, have lower perception and

discomfort thresholds when the bowel or the stomach is distended gradually by gas or by an intraluminal balloon [101, 102]. In these patients, therefore, a normally non-painful distension is experienced as being painful. The visceral pain threshold and/or response magnitude is also significantly altered. The etiopathogenesis of this altered abdominal sensitivity is not known. Whitehead *et al.* [98] compared the tolerance for rectosigmoid distention in lactose maldigesters, patients with irritable bowel syndrome and healthy controls and found that the patients with irritable bowel syndrome had significantly lower tolerance to distension, but the lactose maldigesters did not differ from the controls. Patients with irritable bowel syndrome have also been shown as perceiving intestinal stimuli more diffusely than healthy controls [102].

One of the few studies to examine the role of symptom perception in lactose intolerance is that of Hammer *et al.* [39]. They suggested that the amount of maldigested lactose or the volume or rate of gas accumulation would not *per se* be the cause of the variability of symptoms, but that these were related to increased perception of gas. The same two mechanisms suggested for lowered tolerance of rectosigmoid distension may apply to the sensitivity of colonic and/or small intestinal distention. These mechanisms are 1) an altered contractile activity of the gut and 2) an altered compliance of the gut, related to wall tension or muscle tone [98]. In addition, some recent well-controlled studies have shown that both lactose digesters and maldigesters experience symptoms after ingestion of very low-lactose or lactose-free milk [44, 52, 53, 103]; this suggests that many of the symptoms experienced by lactose maldigesters are not related to lactose digestion. Also lactose digesters with subjective lactose intolerance experienced more symptoms after ingestion of indigestible carbohydrates and of lactose than did a control group of lactose digesters [104].

In a study we conducted in 427 Finnish subjects, subjective lactose intolerance was strongly related to irritable bowel syndrome, the experience of symptoms other than gastrointestinal and female gender, in addition to lactose maldigestion [105]. Age, regularity of meals and the amount of physical activity were not associated with either lactose intolerance or irritable bowel syndrome. In this study, the characteristics common to both subjective lactose intolerance and irritable bowel syndrome were female gender and the experience of abdominal pain in childhood. These relationships and the mechanisms by which the factors are associated need further investigation.

Adaptation to Lactose Consumption

Continued lactose ingestion reduces breath hydrogen excretion, which has been suggested as being due to increased colonic acidity [40, 106], and possibly to changes in the colonic flora. Ito and Kimura [107] lent support to the latter hypothesis by showing that ingestion of lactose for six days reduced the total fecal bacteria, specifically bacteroides and *Clostridium perfringens*, while increasing lactobacilli, enterococci, *Candida*

ssp, and staphylococci. Fecal short-chain fatty acids were not altered, but the concentration of formic acid and valeric acid increased, a fact which also reflects changes in the composition of the flora.

Increases in intestinal bifidobacteria have been shown in some studies in rats after lactose feeding [108] and in humans after lactulose [109] and yoghurt [110] feeding. In the study of Bartram *et al.* [110] there was no additional effect on the intestinal flora when yoghurt was supplemented with lactulose and *Bifidobacterium longum*; this suggests that yoghurt in itself has a bifidogenic effect.

So far, no study has shown an induction of intestinal lactase by lactose ingestion in humans. However, a two-week ingestion of *Saccharomyces boulardii*, a yeast that does not contain β -galactosidase activity, increased human intestinal lactase activity without morphological alteration of the mucosa [111]. The status of lactose digestion in the study group was not given, but the data indicated that the subjects were lactose digesters. This area needs further study.

Several authors have claimed that symptoms of lactose intolerance disappear in some study groups after several weeks of milk supplementation, but the data has not been presented [112, 113]. In a more recent study, fecal β -galactosidase increased and breath hydrogen excretion and symptom scores decreased after a two-week dietary supplementation with lactose [43]. Surprisingly, the symptoms of intolerance decreased as much in a control group on sucrose supplementation, suggesting that the subjects adapted, perhaps psychologically, to the study protocol. A placebo effect caused by adaptation to the test procedures may thus explain the diminished symptoms. Flatus frequency and ratings diminished in lactose maldigesters after 16 days of lactose ingestion compared with dextrose ingestion [44]. Breath hydrogen excretion also decreased and fecal β -galactosidase activity increased. These results suggest a colonic adaptation to regular lactose ingestion.

Lower fecal pH was not the explanation for lower hydrogen production in a recent study of Hertzler *et al.* [114]. These authors suggested a proliferation of non-hydrogen-producing bacterial species after continuous lactose ingestion by lactose maldigesters. They showed that it was decreased fecal hydrogen production, rather than increased hydrogen consumption, that was responsible for the decreased breath hydrogen excretion. Prolonged lactulose ingestion also induced adaptive changes in the colonic function [42]: it reduced osmotic diarrhea and fecal outputs of carbohydrates and osmotic moieties and increased orofaecal transit time, fecal concentrations of β -galactosidase, lactic acid and acidity, but did not affect other gastrointestinal symptoms of healthy adults.

In an *in vitro* study, lactose was infused to an anaerobic continuous culture inoculated with fresh samples of human feces [115]. The lactose concentration of the samples decreased rapidly within one to two days of infusion, and the β -galactosidase activity increased. When a *Lactobacillus acidophilus* strain was added to the culture, the decrease in the lactose

concentration was significantly greater, and there were increases in acetate and propionate production. These results suggest that colonic bacteria adapt quickly to lactose; this causes an efficient utilisation of lactose. The same authors evaluated the effects of *Bifidobacterium longum* supplementation on colonic fermentation of lactose in an *in vitro* continuous culture system [116]. At pH 6.7, the reduction of lactose concentration in the sample of fecal culture was greater after supplementation with the bacteria than without. At lower pH (6.2 and 5.7), the difference in the reduction of lactose concentration was not marked. Also the β -galactosidase activity was the highest at pH 6.7. The authors concluded that *B. longum* may have a potential to improve lactose fermentation. However, it must be noted that gas production increases with augmented fermentation, and this may add to gas related symptoms.

Future studies on lactose intolerance should be controlled with randomisation of the test periods and should include an accustoming of the subjects to the test procedures.

Association of Lactose Digestion with Diseases

Consumption of milk in subjects with lactase persistence has been associated with an increased risk of cataract [117, 118]. Therefore, it has been suggested that hypolactasia would protect an individual against cataract. Cataract formation has been demonstrated in animals fed large amounts of galactose [119, 120] and in humans with a congenital defect in galactose metabolism: an absence or a large decrease of the hepatic galactokinase or galactose-1-phosphate-uridyl-transferase [121]. Diabetes has been proposed as an accelerating factor in this pathophysiology [122]. However, some studies have shown a lack of relationship between lactose absorption and cataract [123–125].

Another disease which is suggested as being linked with the ability to digest lactose is ovarian cancer [126–128]. The background to this hypothesis is that galactose is suggested as an oocyte toxin [129, 130]. In addition, galactosemic women who lack galactose-1-phosphate-uridyl-transferase activity develop an early menopause [131]. However, a study showing a lack of association between galactose intake and ovarian cancer has also been published [132].

CONCLUSION

Gastrointestinal symptoms are very common, and milk is quite often put forward as the cause. Several recent well-controlled studies have clearly demonstrated that quite often gastrointestinal symptoms occur independent of lactose intake. This calls for careful diagnosis of both lactose maldigestion and symptoms of intolerance before any dietary restrictions are made. As mentioned above, several authors have called the whole concept of lactose intolerance overrated, because many lactose intolerant subjects seem to be able to consume normal

dairy products without marked symptoms. To some individuals lactose intolerance is, however, a true problem. Their symptoms can be reduced by food choices and by low-lactose products. Simple avoidance of dairy products often results in less than recommended intake of calcium and in an increased fracture risk [133].

Some areas of lactose intolerance have been well documented, but others still need investigation. For instance, there is no simple and reliable method for diagnosis of hypolactasia that would be suitable for all in the routine use. One interesting question is why does maldigested lactose not cause any symptoms to some individuals, even when ingested in important amounts? Also, the molecular genetics of adult primary hypolactasia needs to be further studied, as well as the relation of age, gender and functional bowel disorders with the symptoms of lactose intolerance.

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Received November 1999.