

# Lactose Intolerance

Milk sugar

Lactase – responsible for the whole mess

Types of lactose deficiency

Diagnostics

Consumption of dairy products in Poland

Not only milk – sources of lactose in the diet

Low-lactose products

Enzyme supplementation

## Milk sugar

Lactose, or milk sugar, is an organic chemical compound belonging to carbohydrates. It is a disaccharide composed of two simpler molecules: D-galactose and D-glucose linked by a specific chemical bond, the so-called  $\beta$ -1,4-glycosidic bond. Lactose is the main sugar found in the milk of mammals; its content in cow's milk is about 5% and in human milk about 7%. Yet it cannot be absorbed by the body directly from the digestive system but must be broken down into simple sugars under the influence of the lactase enzyme.

## Lactase – responsible for the whole mess

**Lactase** (E.C. 3.2.1.108) is an enzyme produced by the cells located in the brush border epithelium of the small intestine. It has  $\beta$ -galactosidase activity which means, to put it simply, that it is able to cut through the chemical bond present in the lactose molecule. In most mammals, including humans, the activity of lactase decreases with age. It is at its highest in the small intestine during infancy, when breast milk is the child's main source of food, but milk remains the only source of mammalian food for a relatively short time. When it becomes gradually replaced by other foods, lactase is no longer needed in the body therefore its activity decreases with age to about 1/10 of the initial value (sometimes the drop is even higher). However, with the development of animal husbandry and dairying, animal milk has become a permanent part of the human diet. In fact, the adaptation to the new diet has resulted in the appearance of specific mutations in some populations, which allow for the production of lactase in the body throughout the person's life [1,4].

The congenial or acquired lack of lactase synthesis in the human body results in a number of unpleasant digestive complaints during the exposure to this sugar, which manifests itself as the so-called intolerance. When the undigested part of lactose passes through the small intestine into the large intestine, there may be various biochemical and physiological processes involving the gut bacteria, which ferment lactose to acids and gases. The products of bacterial fermentation of lactose are primarily hydrogen, carbon dioxide, methane (responsible for bloating, rumbling and colic) and short-

chain organic acids (lactic, acetic, propionic, butyric, etc.) that irritate the intestinal mucosa. In physiological processes, the accumulated lactose causes an increase in the osmotic pressure and the passage of water from tissues to the intestine, which leads to diarrhea. Chronic diarrhea combined with intestinal irritation and accelerated peristalsis may lead to malnutrition and dehydration of the body. [1,2,3,4,5]

## Types of lactase deficiency

There are three types of lactase deficiency:

- a) alactasia – congenital lactase deficiency,
- b) adult hypolactasia – primary deficiency of lactase, which is a natural state in a large part of the human population,
- c) secondary lactase deficiency – acquired.

The total lack of lactase in the body, called alactasia, is very rare. It is a congenital metabolic error that causes various clinical symptoms, e.g. diarrhea occurring from birth in newborn (soon after eating even a small amount of breast milk). In this case, a lactose-free diet is required throughout a person's life.

In Poland, the primary deficiency of lactase (adult hypolactasia) may affect up to 37% of the population. [4] This type of deficiency results from the previously described natural process of lactase activity decreasing with age.

Lactose intolerance may be also the effect of the secondary or acquired lactase deficiency. It is the result of diseases or various other factors that lead to the damage to the intestinal epithelium and lactase-producing intestinal villi, e.g.

- Leśniowski-Crohn's disease (especially in the acute phase and in the period of remission);
- necrotizing,
- Whipple's disease
- short bowel syndrome;
- gastrointestinal infections, e.g. acute or chronic diarrhea caused by bacteria (most commonly *Escherichia coli* and *Salmonella*) or viruses

- (usually rotaviruses and adenoviruses);
- parasitic infections of the digestive tract: lambliasis, giardiasis, taeniasis
- Coeliac disease;
- Duhring's disease (dermal manifestation of gluten intolerance);
- food allergy, e.g. allergy to cow's milk or soy protein;
- cystic fibrosis;
- taking medicines such as antibiotics or acetylsalicylic acid.

## Lactose intolerance

Regardless of what the underlying causes of lactase deficiency are, the symptoms of lactose intolerance are the result of the same mechanism. Lactose intolerance manifests itself in the occurrence of clinical symptoms after lactose intake, due to the inability to digest and absorb it. The disturbed lactose absorption occurs as a result of abnormal digestion, limited absorption surface, reduced transport of enterocytes through the cell membrane (these are the small intestine cells, building the epithelium of the mucosa) and the impact of pathological bacterial flora of the intestine. Lactose intolerance should be distinguished from milk allergy.

Food allergy is a medical condition in which the discomfort is conditioned by immunological mechanisms. When an allergen gets into the digestive tract, the body produces antibodies, trying to neutralize it and remove it from the body. A group of antibodies called immunoglobulin E (IgE) takes part in this type of response. [2,5].

This is not the case in lactose intolerance. An allergic reaction, however, can be triggered, for example, by the proteins found in milk.

Symptoms of lactose intolerance are non-specific and resemble the symptoms of many diseases of the gastrointestinal tract (especially the irritable bowel syndrome), such as:

- diarrhea (stools have a distinctive sour smell)
- bloating
- stomach pain
- rumbling in the abdomen

- giving away excessive amounts of gas
- colic in infants
- nausea and vomiting (in some people). [1,2,3,4,5]

The severity of these symptoms depends mainly on the amount of lactose consumed (the higher the dose, the more severe the symptoms), as well as the degree of lactase deficiency and the form of the lactose-containing food. Notably, the symptoms of lactose intolerance usually occur several hours after the consumption of this sugar, which is why patients often find it hard to see the relationship between their problems and drinking milk or eating dairy products.

## Diagnostics

The diagnostics of lactose intolerance is mainly based on the analysis of the patient's medical history and diet as well as the clinical picture, and direct or indirect diagnostic tests. The most popular test to check how lactose is digested measures the hydrogen concentration in the exhaled air. The second test checks the patient's blood for lactose tolerance (indirect methods). Stool pH testing may also be included. Primary and congenital intolerance can be confirmed by performing a small intestine biopsy or genetic testing (direct methods).

The hydrogen concentration test is based on an assumption that in a healthy person hydrogen is almost absent from the exhaled air but in lactose intolerant people, the undigested disaccharide is fermented by bacteria in the large intestine.

The fermentation process generates gases, including hydrogen which diffuses into the blood vessels and then, along with the blood, it gets to the lungs and is exhaled. Patients who take this test have to drink a lactose solution and then the presence of hydrogen in the exhaled air is measured at regular intervals. Lactose intolerance can be found at a hydrogen concentration of over 20 ppm (number of parts per million). Unfortunately, in 15-20% of patients the result is false negative (that is in these cases the test result incorrectly indicates that the patient is healthy, despite the fact that he or she actually suffers from lactose intolerance), while the positive result

does not give 100% certainty as to the causes of the condition [15]. This is because the results might be affected by many factors, including taking antibiotics or smoking cigarettes.

The blood test for lactose tolerance is complementary to the hydrogen concentration test. It is based on measuring the patient's blood glucose after eating lactose. In a healthy human, lactose is digested into glucose and galactose, which are absorbed into the bloodstream. The liver then converts galactose to glucose, which additionally increases its level in the blood. In people with lactose intolerance, lactose consumption causes only a slight increase in blood glucose, which provides the basis for the diagnosis. The hydrogen concentration test and the blood test together provide the basis for lactose intolerance diagnosis at the level of 95%. Additionally, the irregular digestion and absorption of carbohydrates may be revealed by the lowered pH of the stool.

The small intestine biopsy is performed for the measurement of the activity of three digestive enzymes: lactase (L), sucrose (S) and maltase, as well as the lactase to sucrose (L/S) ratio activity in the samples taken directly from the patient's digestive tract. A reduced lactase activity may indicate lactose intolerance. The measurement of the L/S ratio makes it possible to distinguish between the primary and secondary lactose intolerance. In the case of secondary intolerance, which is the result of damage to the mucous membrane, the activity of all enzymes produced in the small intestine decreases. In the case of primary intolerance, the decrease in the activity affects only lactase [15]. This is one of the most reliable diagnostic methods, but its invasiveness is a disadvantage.

Genetic tests can be also used in the diagnosis of lactose intolerance. In the human population, there are groups of people with slight differences in the DNA sequences that code for lactase or control its activity. The differences are called polymorphisms and they can be linked to lactose intolerance.

Just like the small intestine biopsy, the studying of these sequences allows for distinguishing between the primary and secondary lactase deficiency. In addition, it provides for distinguishing between lactose intolerance and milk allergy. Genetic tests also help avoid the exposure of the patient's body

to lactose, which happens in case of indirect tests. The predictive value of genetic testing is 97%. Genetic testing is not very invasive (it is enough to take an oral swab from the patient) but relatively expensive.

## Consumption of dairy products in Poland

According to the 2013 market analysis, milk production in Poland at the time amounted to approximately 12.15 billion liters (12.5 billion kg), while the consumption of dairy products and butter, expressed in raw milk equivalent, was at the level of 275 kg per capita [16]. Most Poles, regardless of their age and lactose-related digestive disorders eat dairy products. The highest consumption is among people under 25 years of age. Even people who suffer from lactose-related disorders consume dairy products because they are convinced of their high nutritional value (and also doses of lactose up to 10-12 g in one meal often do not cause serious discomfort). [7,14] The complete elimination of dairy products from the diet is associated with the risk of vitamin D, calcium and riboflavin deficiency. Therefore, the use of a low-lactose diet should be recommended only in the case of diagnosed lactose intolerance.

The presence of lactase is a necessary condition for the absorption of lactose from food. The concentration of lactose in cow's milk is 4.7 mg/100 ml, in yogurt 4.6 mg/100 ml. [2,7] The subjective observation of clinical symptoms suggests that young adults, diagnosed with lactose intolerance, can tolerate up to 200 ml of yogurt served in one meal (or one glass of milk). However, taking into consideration the breathing test results it has been established that a single dose should not exceed 100 ml. [6]

## Not only milk – sources of lactose in the diet

While milk-based products are easily associated with the presence of lactose, there are also products that contain lactose and are not produced from milk. In the process of industrial production of food, even in the products that seem to be milk-free, the addition of lactose increases the viscosity of foodstuffs, which makes the process of chewing even more pleasant. In baking, lactose produces brown coloring, so it is used as an additive in the production of bread, fries or croquettes. Lactose is also used in large quantities in sweets to prevent the crystallization of sugar solutions; in the production of drugs as a carrier for the active substance; in aromatic ingredients, sweeteners and flavor enhancers. Notably, it is added to meat products to improve their taste, smell or consistency. If we consider the huge prevalence of lactose in food products and the number of people who experience symptoms after eating lactose, this becomes an important problem to discuss and is often a subject of research or scientific debates.

## Low-lactose products

The food production market is full of milk products, often more expensive than milk itself. These include cheese (curd, processed, hard, and blue) and fermented beverages (yogurts, kefir, buttermilk), both natural and flavored. Research carried out by Dąbrowska et al. on the consumption of fermented dairy drinks by people with varied lactose tolerance show that the consumption of these beverages is high, regardless of age or the level of lactose tolerance, and the most popular of these drinks is yogurt.

This is relevant because fermented dairy products contain the same nutrients as milk, in the same or slightly different amount. However, as a result of lactic fermentation, these ingredients become more digestible, and more available to the body. As a result of the activity of lactic acid bacteria, milk proteins are partially broken down into simpler, easily digestible peptides and free amino acids.

Lactose, on the other hand, is broken down into simple sugars, lactic acid and other ingredients. As a result, it is more easily absorbed by people with partially lost or damaged secretion of the lactase enzyme. [6]

Although the consumption of fermentable products is beneficial to lactose intolerant people, according to research carried out by Baranowska et al., they prefer milk and dairy products with lactose content reduced in the production process. This is usually done by enzymatic hydrolysis of lactose, which increases the cost of milk production, making it more expensive to consumers. Although until recently, lactose-reduced milk was not easily available, nowadays it can be bought in many popular retail chains.

## Suplementacja enzymem

People who are lactose intolerant but want to try products with lactose can use oral supplementation with lactase. The enzymes used in such products are of microbiological origin. Commercially available lactase is produced by specially selected strains of bacteria, yeast or mold. *Aspergillus niger*, *Aspergillus oryzae* and yeast *Kluyveromyces lactis* are most commonly used for this purpose. All preparations containing enzymes produced by microorganisms are subjected to microbiological purity control to make sure they are safe for the consumer. However, any supplementation should be preceded by a consultation with a doctor or dietician.

## About us

**The JCI Quality Institute** belongs to the group of the Jagiellonian Innovation Center, a company found in 2004 by the Jagiellonian University in Krakow. The center manages the Life Science Park, offering a complementary range of services to entrepreneurs and scientists working within the field of life sciences, including the rental of specialist laboratory space, capital support for innovative companies, contracted research services and clinical trials.

It is the JCI Quality Institute's mission to promote high quality of food supplements, cosmetics and healthy food products among producers and consumers. Our mission is carried out through evaluation of products and awarding them with the JCI Mark of Quality, conducting our own ranking research as well as the publication of popular science articles.

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