



LACTOSE INTOLERANCE

What is lactose intolerance?

Patients suffering from lactose intolerance are not able to cleave the alimentary disaccharide lactose. In contrast to milk protein allergy lactose intolerance is not an atopic reaction of the immune system, but a loss of activity of the enzyme lactase.

Lactose tolerant patients can cleave lactose into its components glucose and galactose with the enzyme lactase, which is localized in the mucous membrane of the small intestine. This biochemical process leads to a measurable increase of blood glucose concentration.

Lactose intolerant patients are suffering from reduced or missing lactase activity and therefore, lactose can not be metabolized. Thus lactose is microbially fermented in the lower parts of the intestine. The non-fermented lactose leads to an increase of the osmotic activity in the intestine. Typical symptoms are meteorism (drum belly), flatulences and diarrhea [1].

Prevalence

The prevalence of lactose intolerance varies significantly between the worldwide different ethnic groups. With a prevalence of less than 30% lactose intolerance occurs rather infrequently amongst Europeans [2]. 20-25 % of Austrians are reported to suffer from primary adult lactose intolerance [1]. Concerning the worldwide situation a prevalence of 50% of lactose intolerance is assumed, whereas a strong North-South and West-East gradient has been described. Scandinavians are up to 95% milk tolerant, whereas Tais show a prevalence of lactose intolerance of nearly 100%. Reasons for this difference can be attributed to the tradition of northern Europeans to consume dairy products where lactose tolerance mediates an evolutionary advantage.

Reasons of lactose intolerance

Genetic (primary lactose intolerance) or gastrointestinal diseases (secondary lactose intolerance) can cause lactose intolerance. The most severe form of primary lactose intolerance is alactasia (congenital lactase deficiency). Alactasia is a rare inherent enzyme defect (autosomal recessive), characterized by a total loss of lactase. Disorders like diarrhea, dehydration, and malnutrition can be seen in newborn infants and may lead to severe cerebral damages.

The physiological form of lactose tolerance is induced by an activating mutation near the MCM6 gene (**m**inichromosome **m**aintenance gene) on chromosome 2, near the lactase gene (lactase phlorizin hydrolase gene, LPH gene).

Activating mutation means that mutation carriers have a biological advantage compared to non-mutation carriers. In heterozygous carriers the lactose intolerance may be partially compensated [1, 3]. Wild type carriers may develop a lactase deficiency after breastfeeding.



LACTOSE INTOLERANCE

This deficiency usually deteriorates with age leading to lactose intolerance. Thus lactose is not effectively cleaved into the monosaccharides glucose and galactose that cause the above mentioned symptoms.

The secondary form of lactose intolerance is not a hereditary genetic disorder, but rather a consequence of intestinal diseases (e.g. celiac disease, Crohn's disease) and injuries which are characterized by an impaired mucosa integrity. Lactase is localized at the top of the microvilli in the intestine and as a consequence of the impaired mucosa integrity a decreasing enzyme activity occurs [5]. This form of lactose intolerance is mostly transient.

Diagnosis and therapy

At the following indications the possibility of lactose intolerance should be analysed:

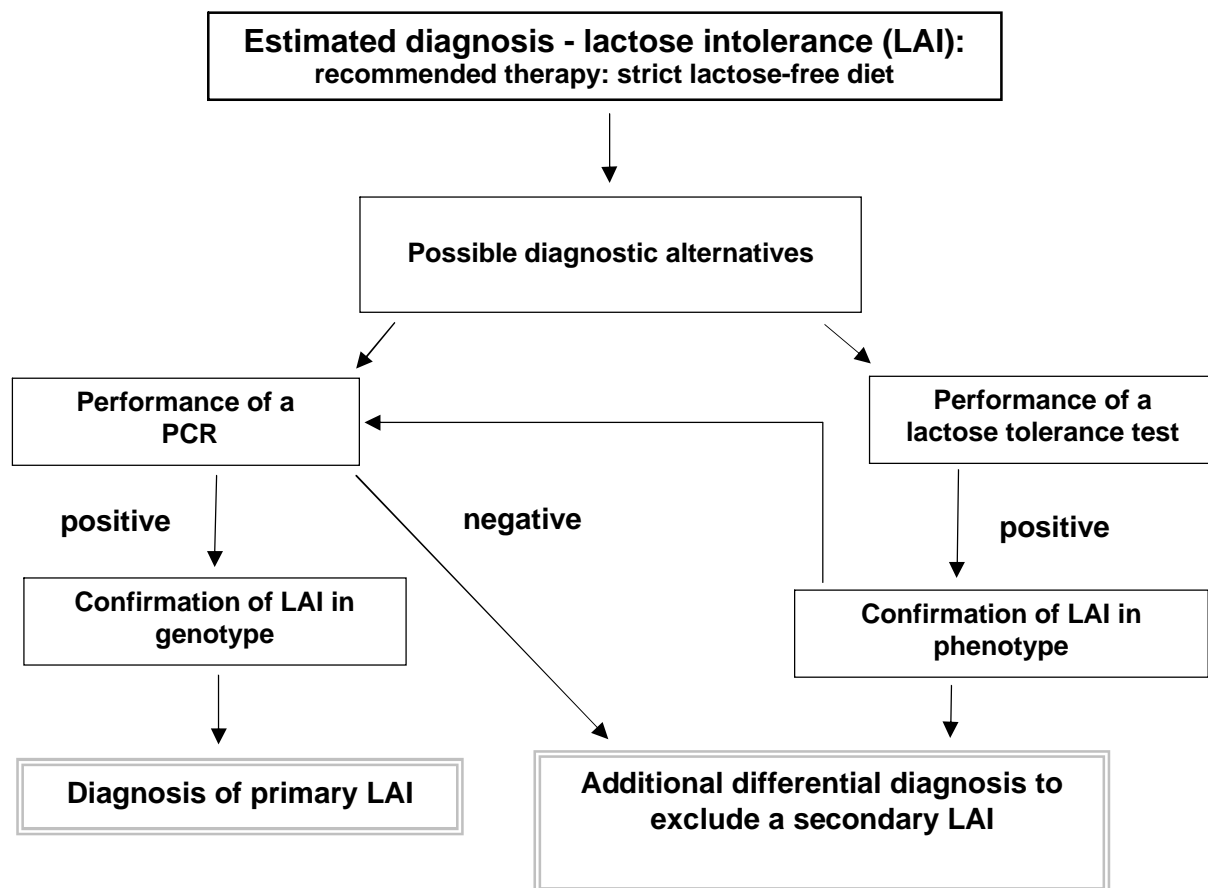
Typical symptoms of a lactase maldigestion like meteorism (drum belly), flatulences, and diarrhea after consumption of milk or adiry products.

The lactase tolerance test with determination of the blood glucose or galactose concentration and the H₂-breath test are established methods to detect lactose intolerance, however, allow no statement whether the patient is suffering from **a primary or secondary lactose intolerance**. Only mutation analysis gives a clear answer to the question about a possible hereditary ethiopathogenesis.

Genetic analysis

DNA is isolated from whole blood and subjected to genetic analysis. Highly specific primers allow a reliable detection of the genotype of the patient. As described before the polymerase chain reaction (PCR) analyses an activating mutation within the promoter region of the lactase gene. If the genetic analysis shows a negative result a secondary lactose intolerance should be taken into account.

Diagnostic scheme



Literature:

1. Obermayer-Pietsch B: Knochendichte und Laktoseintoleranz – Übersicht über aktuelle Entwicklungen. J Mineralstoffwechsel, 2004, 11 (3): 20-23.
2. Sahi T: Genetics and epidemiology of adult-type hypolactasia. Scand J Gastroenterol, 1994, 29 Suppl 202: 7-20.
3. Sibley E.: Genetic variation and lactose intolerance. Am J Pharmacogenomics 2004, 4 (4): 239-245.
4. Srinivasan R et al.: When to suspect lactose intolerance. Postgraduate Medicine, 1998, 104 (3): 109-23.
5. Tuula H.V. et al.: Lactose intolerance. J Am College of Nutr, 2000, 19 (2), 165-175.



LACTOSE INTOLERANCE

GA Generic Assays' product group for the differential diagnosis of lactose intolerance

Primary lactose intolerance	
1045	attomol®Laktoseintoleranz -13910C>T
Secondary lactose intolerance	
Celiac Disease	
3700	Anti-Gliadin IgA
3800	Anti-Gliadin IgG
4002	CeliAK IgG Dot (IgG to Gliadines and transglutaminase)
4008	CeliAK Dot (IgA to Gliadines and transglutaminase)
4033	Anti-huTransG (IgA to transglutaminase)
4044	Anti-hu tTG IgG (IgG to transglutaminase)
4035	CeliAK EmA human (IgA to endomysial antigens)
4045	CeliAK EmA human IgG (IgG to endomysial antigens)
Crohn's Disease	
4006	ASCA IgA (IgA gegen Saccharomyces cerevisiae)
4007	ASCA IgG (IgG gegen Saccharomyces cerevisiae)
4032	ASCAcombi (IgA und IgG gegen Saccharomyces cerevisiae)
Food intolerance	
4071	MiliAK Dot (IgG gegen β- Lactoglobulin und Soya)

Please contact for further information your local dealer!

- GA Generic Assays -

Your reliable partner in laboratory diagnostics!