

Lactase activity

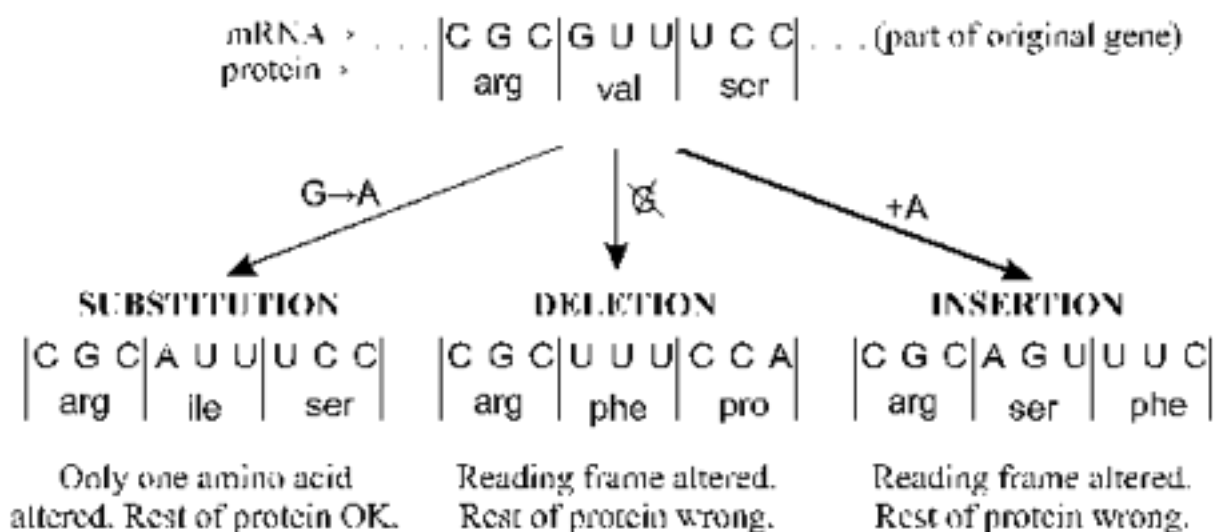
- Only 50% of lactase activity needed
- Lactase only present when necessary
- Persistence due to a mutation in the lactase gene
- Non-persistence = wild type
- **Wild type** = it is the allele that encodes the phenotype most common in a particular natural population. It is the normal allele as opposed to the mutant gene or allele. In genetic shorthand it is "+".

Genetics of lactase expression

Polymorphisms

- Two genetic single nucleotide polymorphisms (SNP) have been identified in northern Europeans which could be responsible for lactase persistence
- The lactase gene is on chromosome 2
- **Genetic polymorphism:** is a DNA sequence variation that is common in the population. No single allele is considered as the standard sequence. There are two or more equally acceptable alternatives
- To be classed as a polymorphism the LEAST common allele must have a frequency of 1% or more in the population
- 90% of northern Europeans are lactose tolerant as a result
- The polymorphism in the lactase gene are C/T and G/A substitutions at 14 and 22 kb upstream at the end 5' end of the lactase gene in a DNA region
- This DNA region acts as a **cis element** which are regions of non-coding DNA which regulate the transcription of nearby genes
- Cis element influences lactase gene promoter
- C/T is the dominant polymorphism
- C allele tends to decrease in Lacase mRNA expression

Below is a diagram showing what a mutation and what a polymorphism is on a random gene



Diagnosis

Early studies

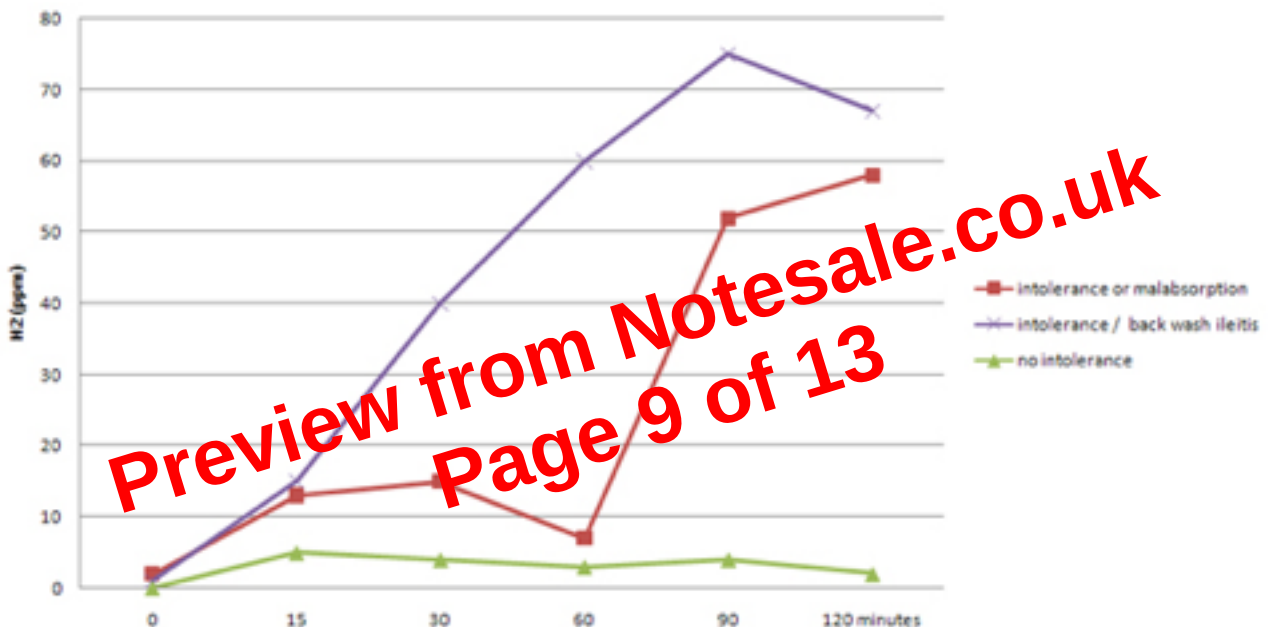
- Glucose levels measured following 50g intake of lactose
- Increase in levels ==> high lactase activity (after 30 mins)

Recent methods

- Jejunal biopsies used: small pieces of tissue removed from lining of jejunum. To do this an endoscope is used.
- This method is not very effective

Hydrogen breath test

- 50g of lactose taken orally (equal to the amount in 1 litre of milk)
- Measures hydrogen levels the following 3-6 hours
- If the levels are more than 20ppm then it indicates lactose intolerance
- Better to measure it after 6 hours



False-negatives

- False negatives can occur where there is no excretion of hydrogen. This occurs in 20% of people with lactose intolerance
- The reason for this false negative can be:
 1. Methane producing bacteria use hydrogen to reduce carbon dioxide to methane
 2. There is interference and competition from other bacteria ==> significant hydrogen excretion and moderate methane production

Some people get positive results from the test without actually having any previous symptoms of intolerance. This indicates towards lactose malabsorption but there were no previous symptoms due to other dietary restrictions.