

Lactose Intolerance

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Define key terms and concepts !

Lactase non-persistence:

In a majority of humans, the enzyme lactase at the jejunal brush border is reduced in activity after weaning. In some individuals, this reduced activity can cause symptoms after lactose ingestion.

Lactase persistence:

Lactase persistence: Persistence of a high activity of the enzyme lactase into adulthood. This phenotype facilitates digestion of larger amounts of lactose.

Lactose malabsorption

Inefficient digestion of lactose due to lactase non-persistence or other intestinal pathologies.

Lactose malassimilation:

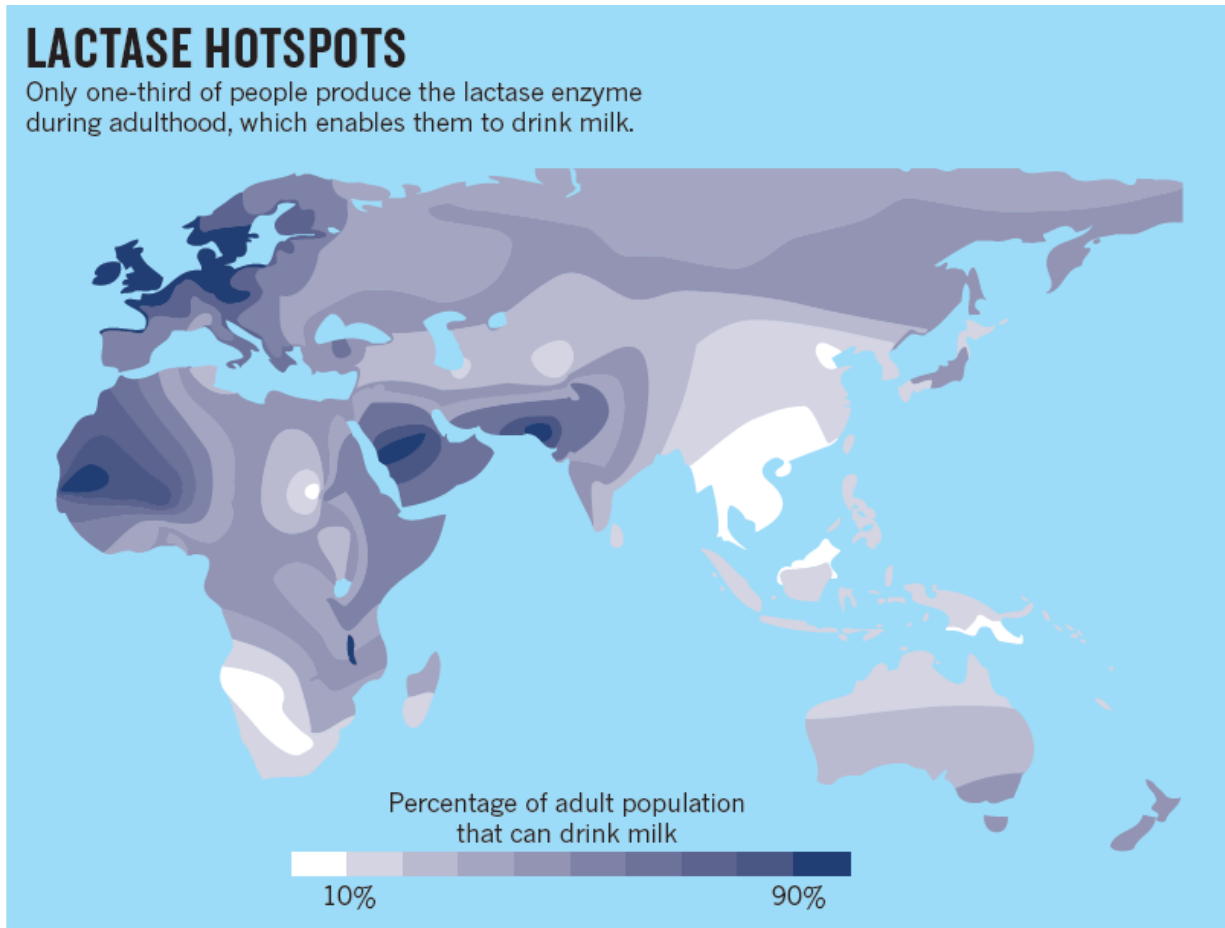
Inefficient absorption of lactose due to lactose malabsorption.

Lactase intolerance:

Gastrointestinal symptoms in an individual with lactose malabsorption.

What is the prevalence of lactose persistence?

«Only one third of adults produce the enzyme lactase, which enables them to drink milk»

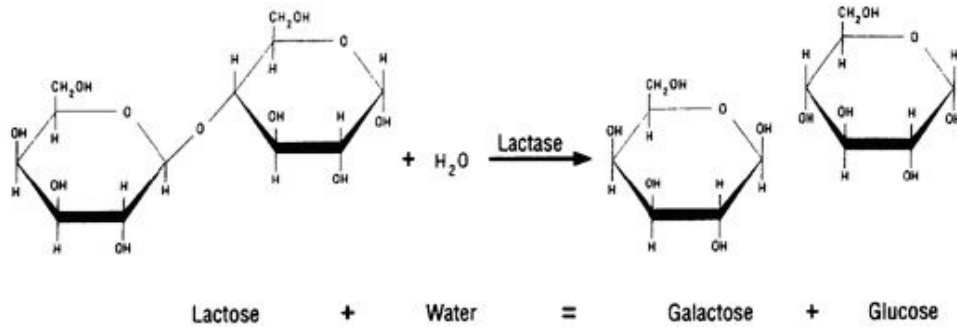


What causes lactase deficiency?

- Lactase non-persistence
- Congenital lactase deficiency
- Secondary lactase deficiency (small bowel bacterial overgrowth, coeliac disease, inflammatory bowel disease, radiation enteritis, infectious enteritis (giardiasis))

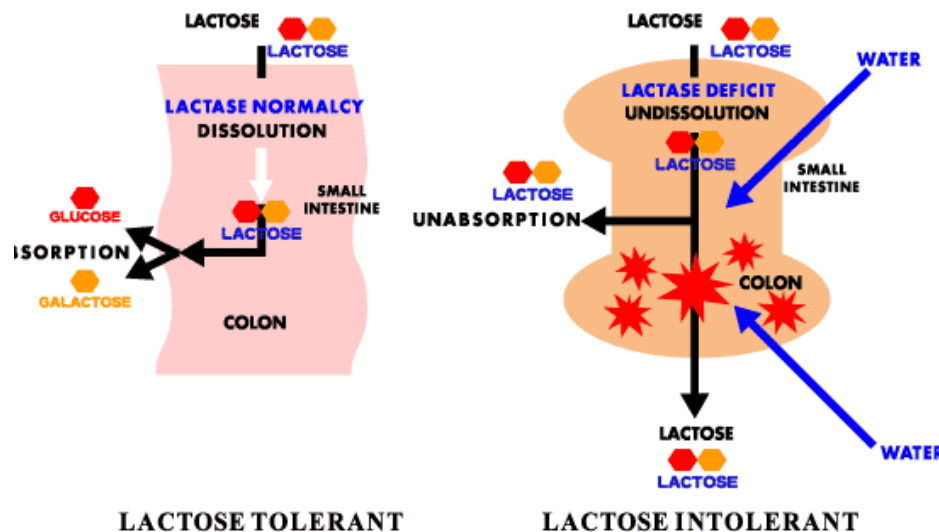
How is lactose digested?

A



B

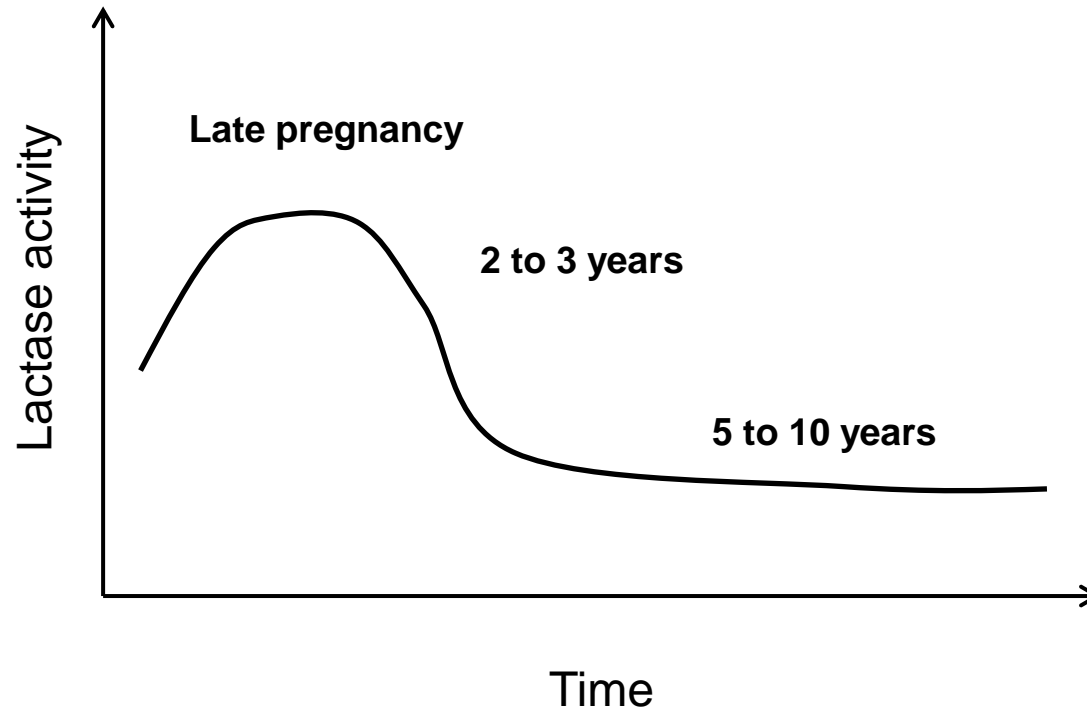
Mechanism of lactose digestion



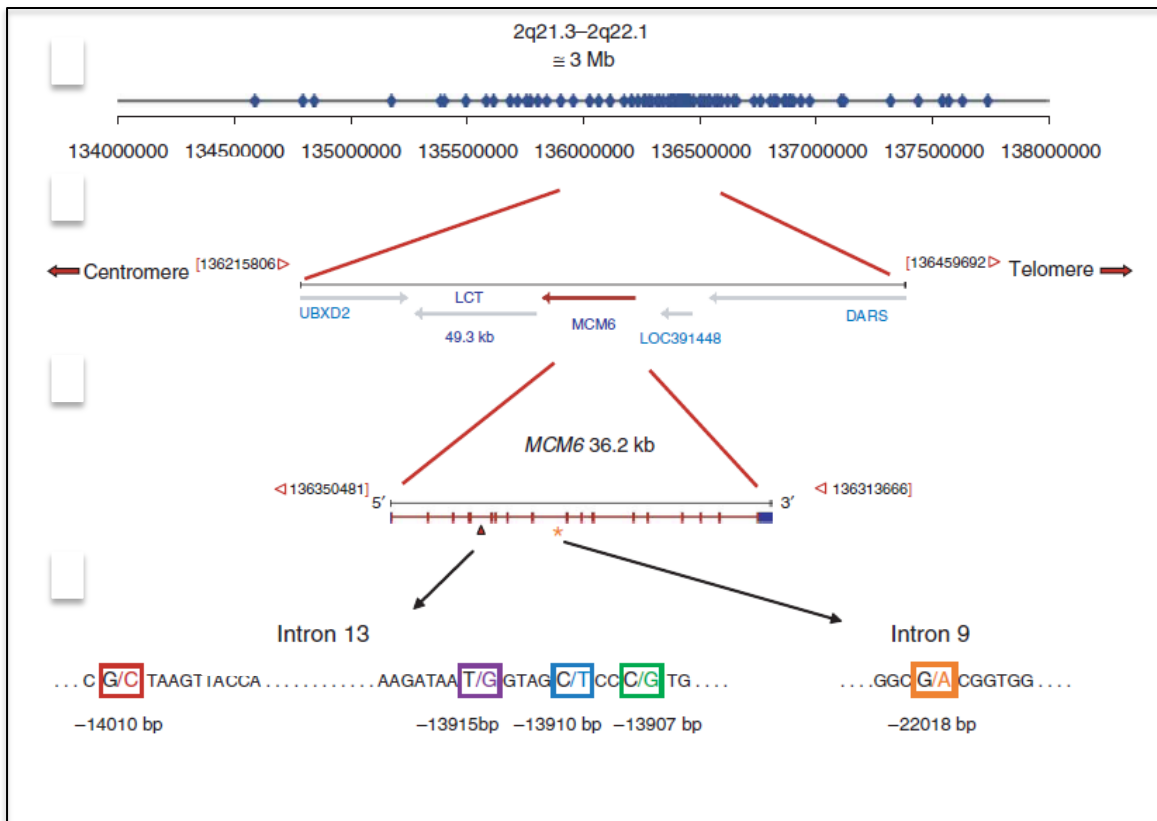
Lactase non-persistence does not necessarily lead to lactose intolerance

Distinguish between lactose malabsorption and intolerance

How does lactase activity change over development?



What is the genetics of lactase non-persistence?



- In Caucasian individuals the -13910 C/T variant is most common (1390 bp upstream of the LCT gene, T persistence C non-persistence)
- Other variants are responsible of lactase persistence in African tribes
- Developed around 10000 years ago in different regions independently

Why has lactase persistence developed?

DAIRY DIASPORA

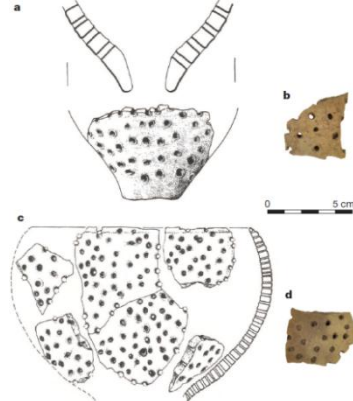
Dairying practices spread from the Middle East to Europe as part of the Neolithic transition from hunting and gathering to agriculture.



“People with mutations coding for lactase persistence would have produced up to 19% more fertile offspring than those who lacked it.”

Nature 2013 Vol 500

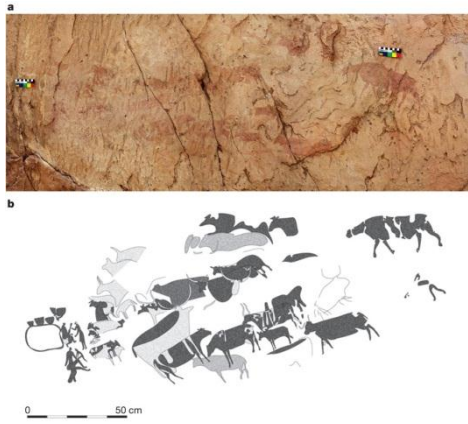
Vessels from two sites in Poland (6th millennium BC)



Reduction of lactose by separation of fat – rich milk curds from the lactose-containing whey

Nature. 2013 Jan 24;493(7433):522-5

Rock art image and tracing from Teshuinat II rock shelter, South West Libya



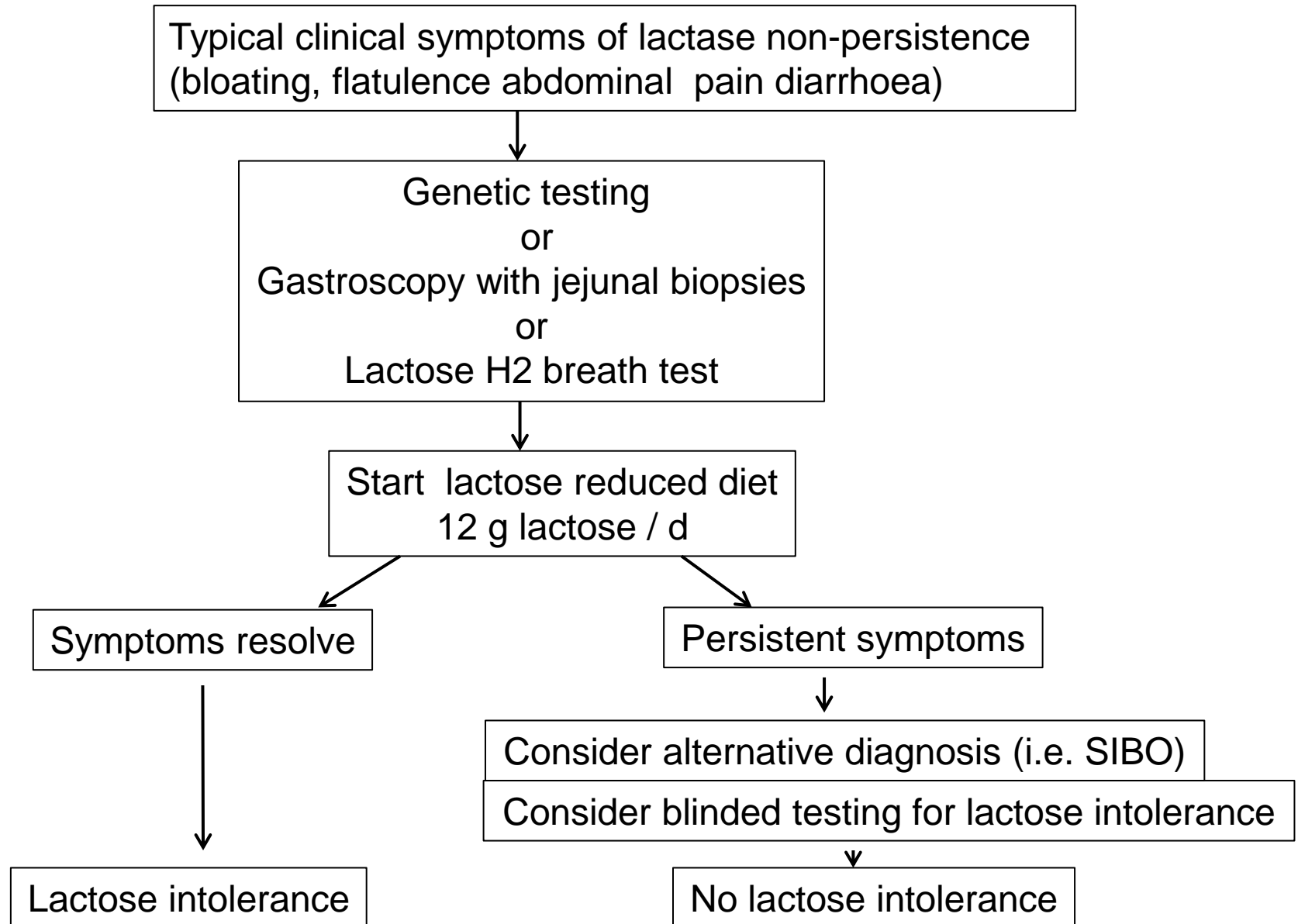
adoption of dairying practices by prehistoric Saharan African people in the fifth millennium BC.

Nature 2012 Jun 20;486(7403):390-4

How can be tested for lactose deficiency ?

	H ₂ -breath test	Lactose tolerance test	Genetic test of -13910 C/T polymorphism	Lactase activity at jejunal brush border
Test principle	Increase of H ₂ in respiratory air after lactose challenge	Increase of blood sugar after lactose challenge	Genetic Polymorphism 13910 upstream of lactase gene	Enzymatic activity of lactase enzyme in biopsy sample
Cut off	>20 ppm within 3 hours	<1.1 mmol/l within 3 hours	13910C/C indicates lactase non-persistence	<17-20 IU/g
Availability	Good	Excellent	Variable	Rare
False positives (malabsorption incorrectly diagnosed)	Rapid GI-transit, small-intestinal bacterial overgrowth	Rapid GI-transit, impaired glucose tolerance	Rare (<5%) in Caucasians	Probably rare
False negatives (malabsorption wrongly excluded)	Non-H ₂ -producers. Full colonic adaptation.	Fluctuations in blood sugar	All causes of secondary lactose malabsorption	Patchy enzyme expression
Secondary causes	Cannot be excluded, kinetic of H ₂ -increase can be suggestive	Cannot be excluded	Cannot be excluded	Can be excluded (histopathology obtained at same procedure)
Assessment of symptoms/lactose tolerance	Possible	Possible	Not possible	Not possible
Comment	Method of choice for assessment of lactose malabsorption and intolerance	Rarely performed due to inferior sensitivity and specificity	Definitive test for lactase non-persistence in Caucasians. Less suitable in other populations. Not suitable in patients with intestinal disease at risk of secondary lactase deficiency.	Reference standard for detection of lactase deficiency (primary or secondary)
Cost	Low	Lowest	High	Highest

What are the typical symptoms of lactose intolerance? How is lactose intolerance treated?



What are the problems of lactose free diet?

Lactose non-persistence is a risk factor for osteoporosis / bone fractures in aged people

Women

Aged 19-50 y 1000 mg / day

Aged > 50 y 1200 mg /day

Men

Aged 19-70 y 1000 mg / day

Aged > 71 y 1200 mg / day

	Serving size	Lactose	Calcium
Milk, regular	1cup, 250 ml	12 g	285 mg
Milk, reduced fat	1cup, 250 ml	13 g	340 mg
Yoghurt, regular	200 g	9 g	340 mg
Yoghurt, reduced fat	200 g	12 g	420 mg
Cheese, cheddar	30 g	0.02 g	260 mg
Cheese, creamed cottage	30 g	0.1 g	22 mg
Butter	1 teaspoon	0.03 g	1 mg
Ice cream	2 scoops, 50 g	3 g	55 mg

United European Gastroenterol J. 2013 Jun;1(3):151-9

But why is then the prevalence of osteoporosis lower in Asian countries as compared to Europe?

Thank you

What are the clinical symptoms of lactose intolerance?

- Bloating
- Diarrhea
- Flatulence
- Abdominal pain
- **Systemic complains?**
 - Fatigue
 - Skin disease
 - Rheumatologic symptoms

- Distinguish between lactose malabsorption and intolerance
- Lactase persistence per se does not explain clinical symptoms
- NIH guidelines require a placebo controlled testing for lactose intolerance – clinical practicability?