Evolution of Lactase Persistence

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Outline

- History of dairying
- Lactose and lactase
- Dairying without lactase
- Evidence for natural selection
- When did lactase persistence evolve in Europe?

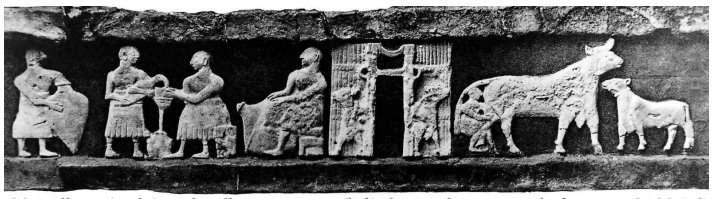
Domesticated Cattle

- Earliest fossils: $\sim$ 8000 BP (Near East)
- Maybe 9000 BP (Sahara)
- Uses
  - Draft animal
  - Meat
  - Blood (like the Masai)
  - Sour milk

Prehistory of dairying

- 7500 BP: Milk residues in pottery around Sea of Marmara, Turkey.
- 6800 BP: up Danube River
- 6000 BP: Britain, Scandinavia, central Europe
- 5300 BP: East into steppes, but not past Ural Mountains.

Temple Frieze from Iraq 2500 BCE



39 *Milking (right) and milk-processing (left) depicted on a temple frieze, c. 2500 BC, from Tell al-'Ubaid, Iraq.*

Delacroix, Ovid among the Scythians

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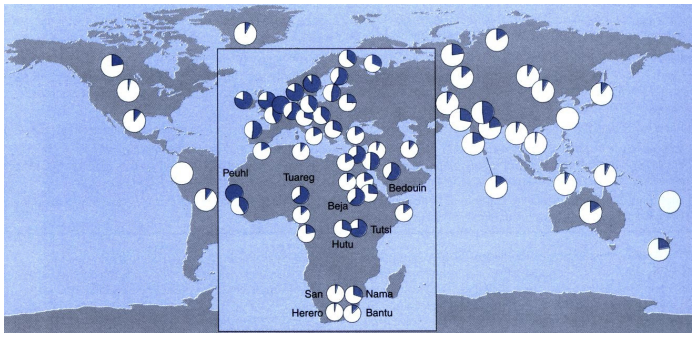
The trouble with fresh milk

- Contains the sugar *lactose*
- Digesting lactose requires the enzyme *lactase*
- Most humans don't produce it after age 5.
- Fresh milk gives them gas and diarrhea.
- 8000 years ago, all humans had this problem.

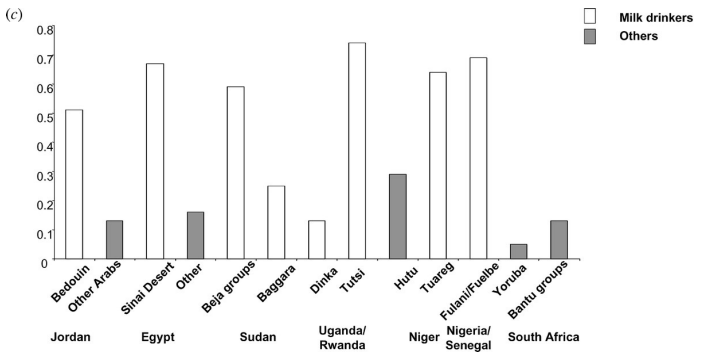
Lactase persistence

- Some modern humans produce lactase throughout life.
- Digest fresh milk as adults.
- Caused by mutation near lactase gene.
- When and where?

Distribution of lactase persistence (dark blue)



Within countries, lactase persistence more common in populations that drink milk



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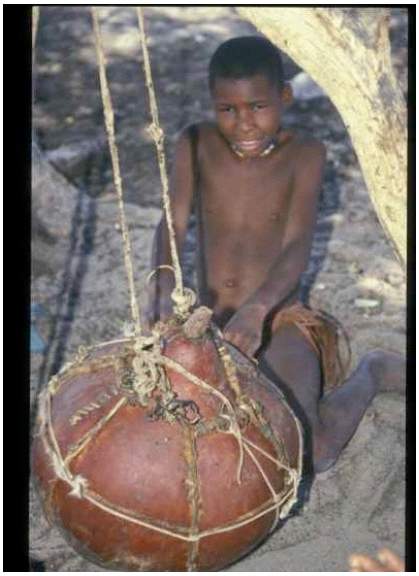
Herero live off of cattle and goat products, which they may sell. They also plant small gardens and hunt and gather.



Weaning Technology

Milk energetics

1 liter of cow's milk has

lactose	250 Cal	35%
fat	300 Cal	42%
protein	170 Cal	24%
	720 Cal	

Without lactase, you loose 35% of the energy.

Milk to cheese

1 liter milk yields 100 g cheese.

- 400 Cal vs. 720 Cal in original milk
- 45% energy loss

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We know that lactase persistence is

- under genetic control, and
- more common in populations that drink milk.
- But which is cause and which is effect?
  - Do they drink milk because they can?
  - Or did lactase persistence evolve because they drink milk?

The drift hypothesis

- Differences in lactase persistence arose by random changes in allele frequency (genetic drift).
- A slow process
- Many recombinants near persistence allele.
- Short block of LD.

The selection hypothesis

- Selection favors persistence allele where people drink milk.
- Allele increased rapidly within past 10,000 years.
- Little time for recombination.
- Large block of LD

What really happened?

- In Europeans, persistence allele surrounded by a million bases of LD.
- Indicates strong selection.
- Statistical tests reject the drift hypothesis (Bersaglieri et al 2004)
- Increasing for ∼10,000 years (Coelho et al 2005).

DNA sequences from region of human lactase gene

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   cgcttcaggcattcctatctaaacagaccaacgtaAgggtacaatgcctaacccagacgtttcaactct
20 ....................................................................
21 ....................................................................
22 ....................................................................
23 ....................................................................
24 ....................................................................
25 ....................................................................
26 ....................................................................
27 ................t...................................................
28 ................t...................................................
29 ..............................................c.....................
37 ..................................G..a.gt.....t.........gac.c.tgtct.
38 ...ccgga....gat..at..gg..c.....tc.gGaaa.g..cctttt...tg......c...t.t...
39 ...ccgga....gat..at..gg..c.....tc.gGaaa.g..cctttt...tg......c...t.t...
40 ..tcc...agtag.t.cat..g.....t..ttccgG..a.gt.....t.........gac.c.tgtct.
41 ..tcc...agtag.t.cat..g.....t.gttccgG..a.gt.....t.........gac.c.tgtct.
42 ..tcc...agtag.t.cat..g.....t.gttccgG..a.gt.....t.........gac.c.tgtct.
43 ..tcc...agtag.t.cat..g.....t.g.tc.gG..a.gt.....t.........gac.c.tgtct.
44 ..tcc...agtag.t.cat..g.....t..ttc.gG..acgt.....t.........gac.c.tgtct.
45 ..tcc...agtag.t.cat..g.....t.gttc.gG..a.gt.....t.........gac.c.tgtct.
46 ...ccgga....gat..at..gg..c.....tc.gGaaa.g..cctttt...tg......cg.gt.t..c
47 ..tcc...agtag.t.cat..g.....t.gttccgG..a.gt.....t.........gac.c.tgtct.
48 ..tcc...agtag.t.cat..g.....t.gttccgG..a.gt.....t.........gac.c.tgtct.
49 ..tcc...agtag.t.cat..g.....t.gttccgG..a.gt.....t.........gac.c.tgtct.
50 tatccgga....g.tc.atcgg.tc.g.tg.tc.gG..a.g.g....tg....ggt...cg.gt.t..c
51 ta.ccgga....g.t..atcgg.tc.g.tg.tc.gG..a.g.g....tg....ggt...cg.gt.t..c
52 ta.ccgga....g.t..atc.g.tc.g.tg.tc.gG..a.g.g....tg....ggt...cg.gt.t..c
53 ta.ccgga....g.t..atcgg.tc.g.tg.tc.gG..a.g.g....tg....ggt...cg.gt.t..c
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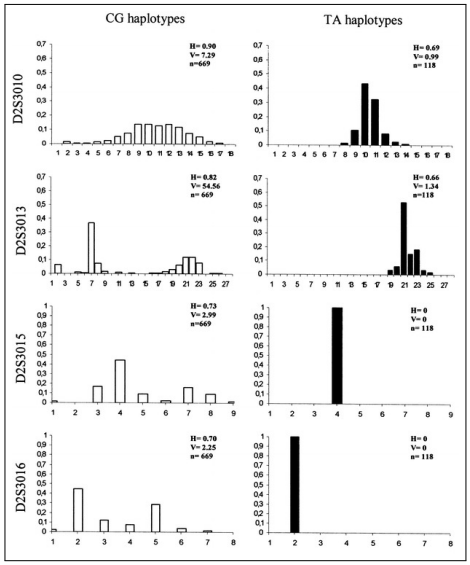
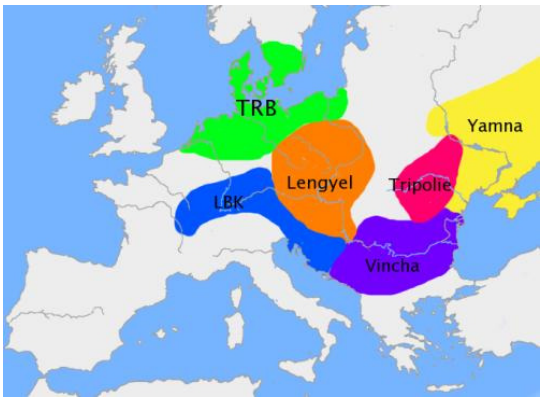


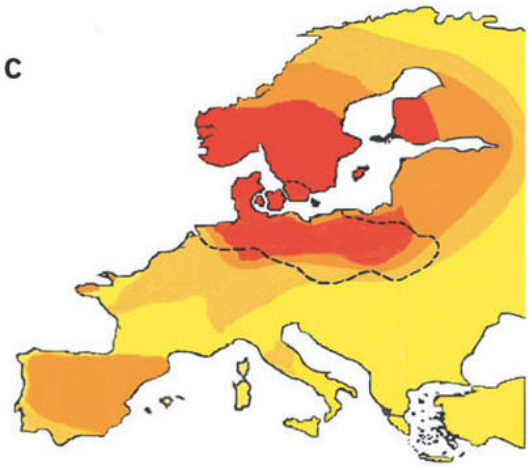
- Rows are different STRs
- Lactase persistence allele: haplotype TA.
- Has reduced SNP variation,
- Indicates recent origin.
- Age: 7,450 or 12,300 years (depending on assumptions)

Green: Funnelbeaker Culture



- 6300–4800 BP
- Heavy clay soils hard to farm w/o steel plows
- Cattle
- Weaned calves early ⇒ dairying

Lactase persistence in Europe

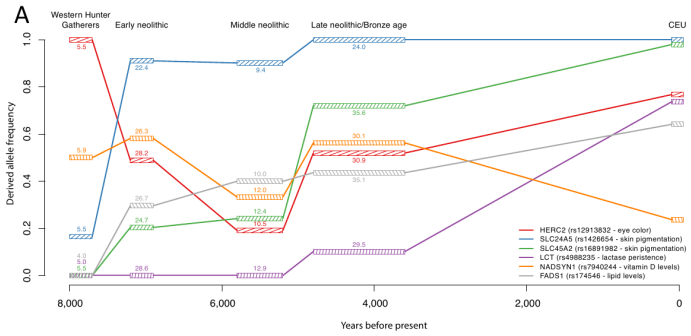


- Modern Europeans
- Dashes: Funnelbeaker culture

Study of Mathieson et al 2015

- DNA from 83 ancient Europeans.
- Track changes in allele frequencies over time.

History of evolution in Europe



Lactase persistence appears ∼4.3 kya in Germany, in Bell Beaker Culture.

Summary

- Cattle domesticated by ∼8 kya.
- Dairying throughout Europe by 6 kya
- Lactase persistence by 4.3 kya
- Saves 35–45% of energy in milk.
- Strong selective sweep.
- Lactase persistence most common in dairying populations.