DEFICIENCIES OF DUODENAL DISACCHARIDASES

Major Dietary Disaccharides

Disaccharide	Structure	Natural occurrence
Maltose	Glcα(1 **à** 4)Glcα	Plants (starch) and animal (glycogen)
Sucrose	Glcα(1 **à** 2)Fruβ	Many fruits, seeds, roots, honey
Lactose	Galβ (1 **à** 4)Glc	Milk, some plant sources
Trehalose	Glcα (1 **à** 1)Glcα	Mushrooms, yeast, insects, shrimp
Cellobiose	Glcβ(1 **à** 1)Glc	Plants (cellulose)

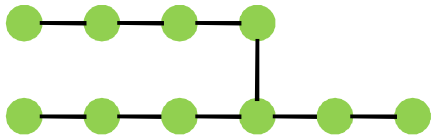
A Typical Western diet contains 400g of carbohydrate

60% starch (plant and animal (glycogen))

20% amylose

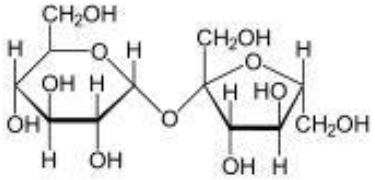
long chains of glucose joined by α-1-4 linkages

80% amylopectin

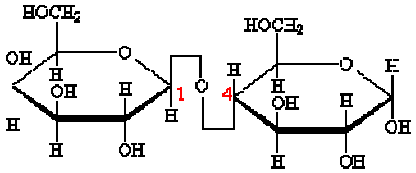


branched by α-1-6 linkages
~ every 25 glucose

30% sucrose



10% lactose



Digestion of starch begins in the saliva

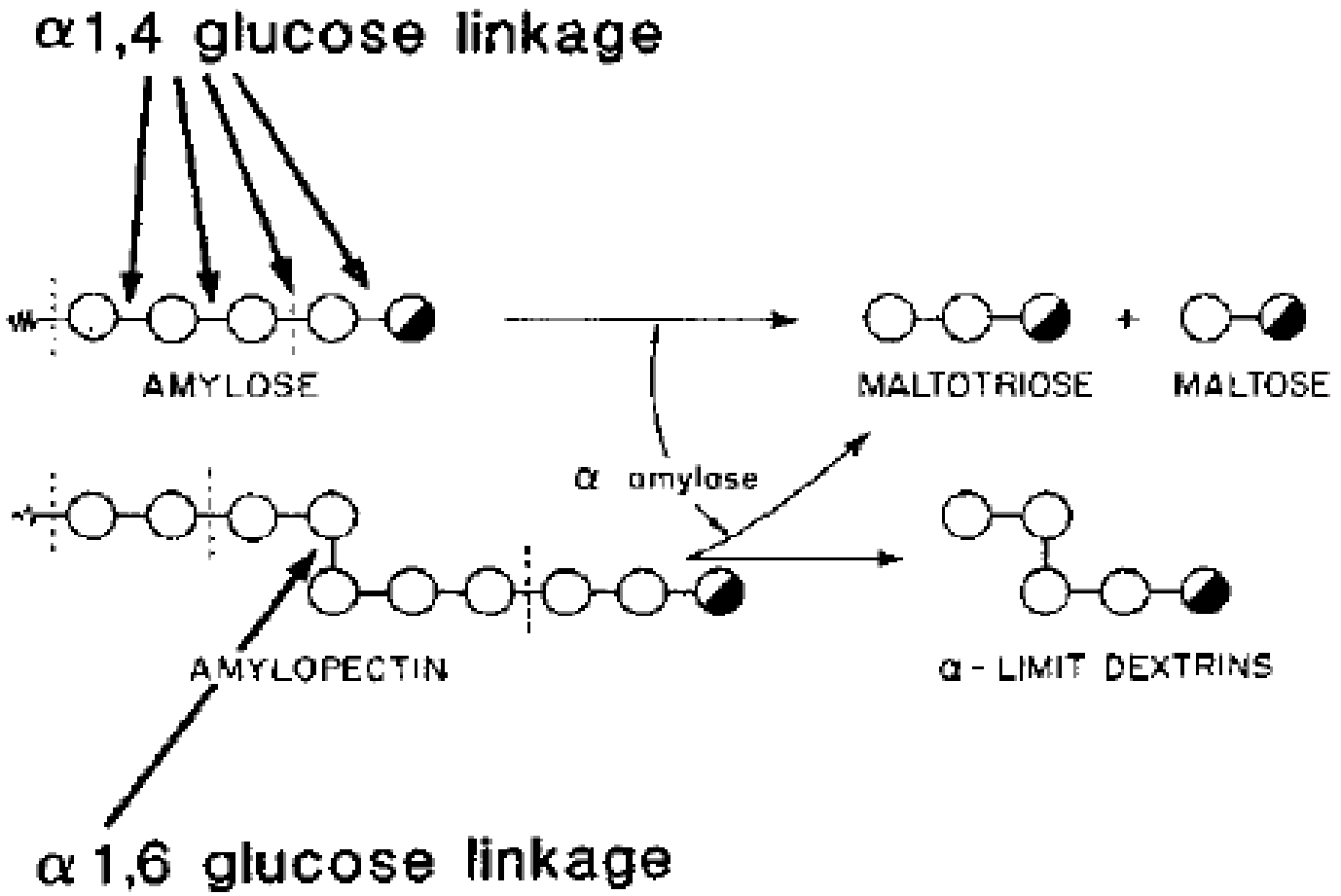
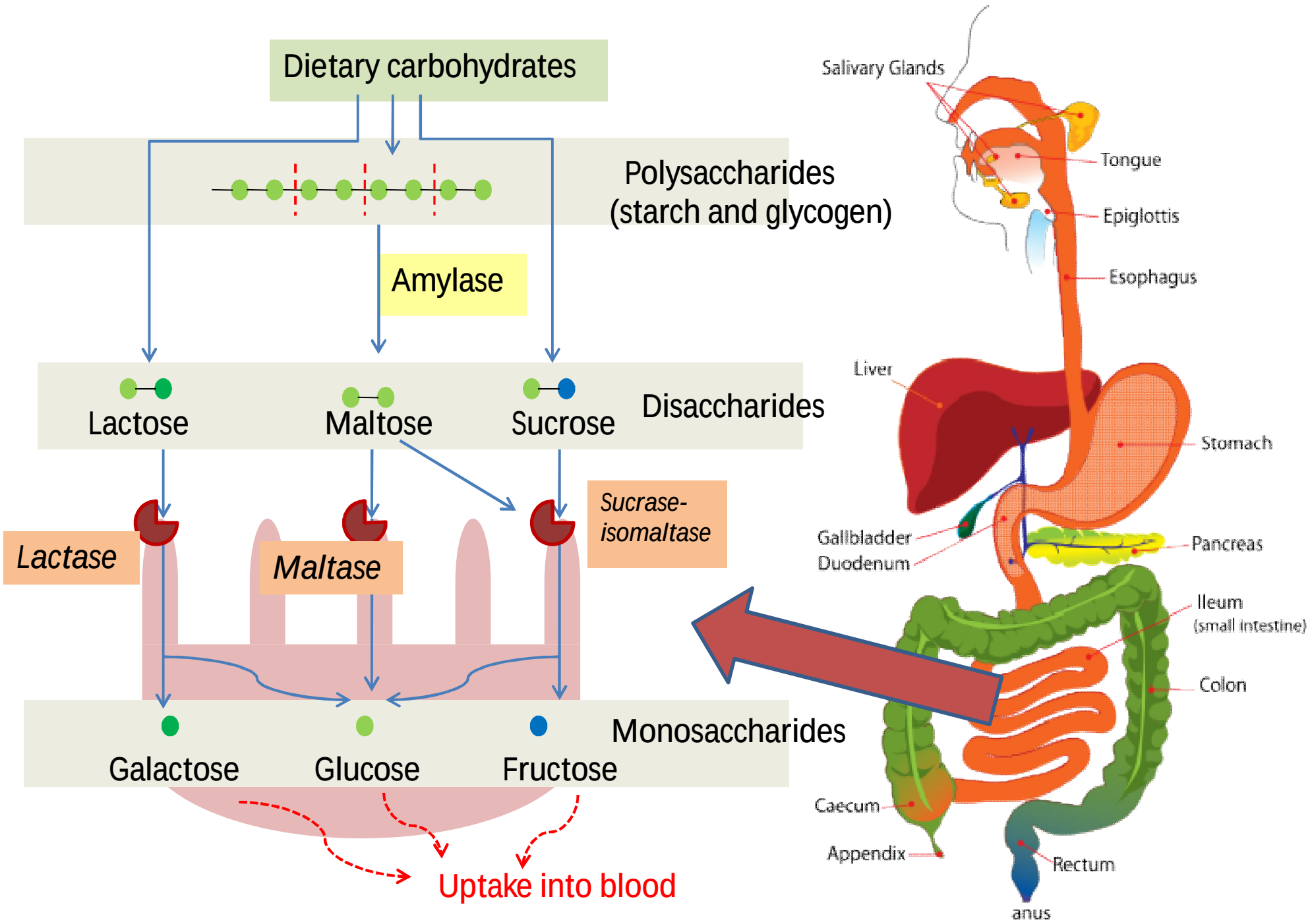


FIGURE 10. The action of pancreatic α-amylase on linear (amylose) and branched (amylopectin) starch. Circles indicate glucose residues and the reducing glucose unit.
SOURCE: Gray GM. Mechanisms of digestion and absorption of food. In: Sleisenger MH, Fordtran JS (eds.), Gastrointestinal disease: pathophysiology, diagnosis, management. 3d ed. Philadelphia: WB Saunders, 1983:851.


Dietary carbohydrates
Polysaccharides
(starch and glycogen)
Amylase
Lactose
Maltose
Sucrose
Disaccharides
Lactase
Maltase
Sucrase-
isomaltase
Galactose
Glucose
Fructose
Monosaccharides
Uptake into blood
Salivary Glands
Tongue
Epiglottis
Esophagus
Liver
Stomach
Gallbladder
Duodenum
Pancreas
Ileum
(small intestine)
Colon
Caecum
Appendix
Rectum
anus

The Four Disaccharidase Complexes

Enzyme or complex	Substrates include
Maltase-Glucoamylase complex	Maltose (1,4-α-bonds)
Sucrase-isomaltase complex	Sucrose, isomaltose, maltose, maltotriose (1,4-α-bonds) Splits 1,6-α-bonds from a-limit-dextrans
b -Glycosidase complex (Lactase-phlorizin hydrolase)	Lactose, cellobiose, cellotriose
Trehalase	Trehelose

Symptoms of Disaccharidase Deficiency

Diarrhoea
Flatulence
Bloated stomach
Stomach pains / cramps
Borborygmi (stomach rumbling)
Nausea

Severity depends on the amount and type of sugars ingested, the rate of gastric emptying, metabolic activity of colonic bacteria and absorptive capacity of the colon.

Symptoms are due to excess disaccharidases in the colon

1. Disaccharides osmotically attract water into the bowel
2. Bacteria in the colon metabolize the disaccharides, generating hydrogen, carbon dioxide, methane, lactic acid and short chain fatty acids (acetic, propionic, butyric)

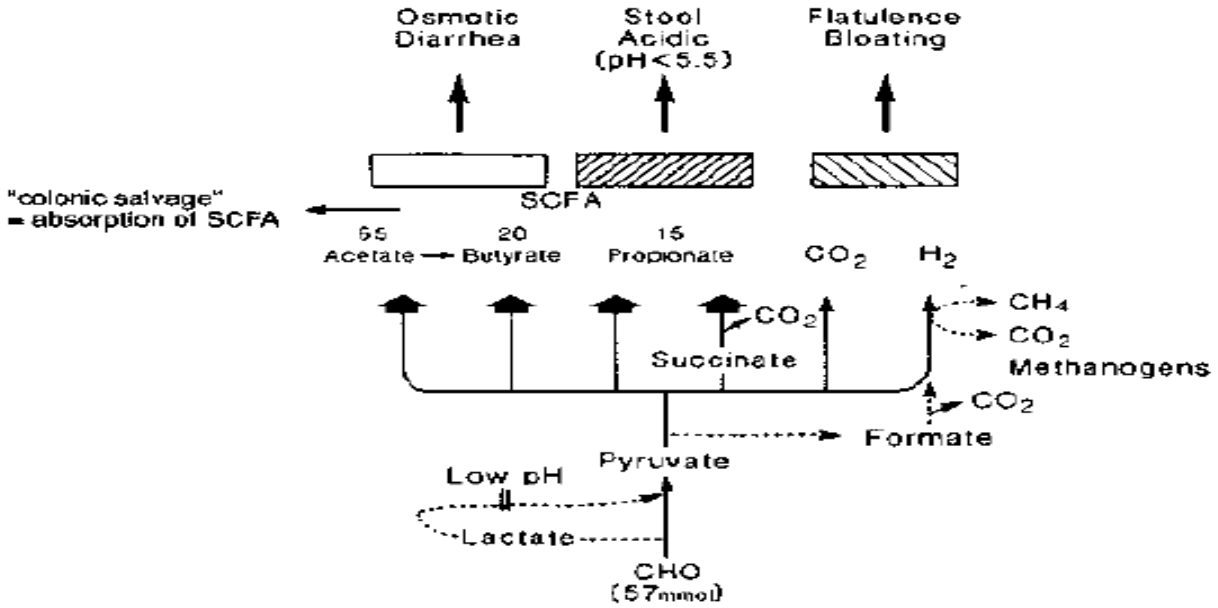


FIGURE 13. Intermediate and end products of anaerobic bacterial fermentation of carbohydrates. Minor pathways are depicted by dashed lines.
SOURCE: Soergel KH. The role of the colon in case of inhibition of carbohydrate absorption. In: Creutzfeldt W, Fölsch UR (eds.), Delaying absorption as a therapeutic principle in metabolic diseases. Stuttgart and New York: Thieme Verlag, 1983:854.

Causes of disaccharidase deficiencies

Primary	Secondary
Hereditary	Acquired
Very rare*	Relatively common
Usually only affects 1 disaccharidase	All disaccharidases affected
Presents at birth*	Presents at any age
Not associated with intestinal disease	Associated with disorder of small intestinal mucosa
Irreversible Managed by dietary control	May be reversed if disorder heals

*except adult onset lactase deficiency

Primary causes of disaccharidase deficiencies

Congenital maltose glucoamylase deficiency

Since sucrase-isomaltase digests most of the maltose a deficiency is usually masked .

Congenital trehalase deficiency

Present in 8% of Greenland. Trehalose is not a major part of the diet so is not a problem.

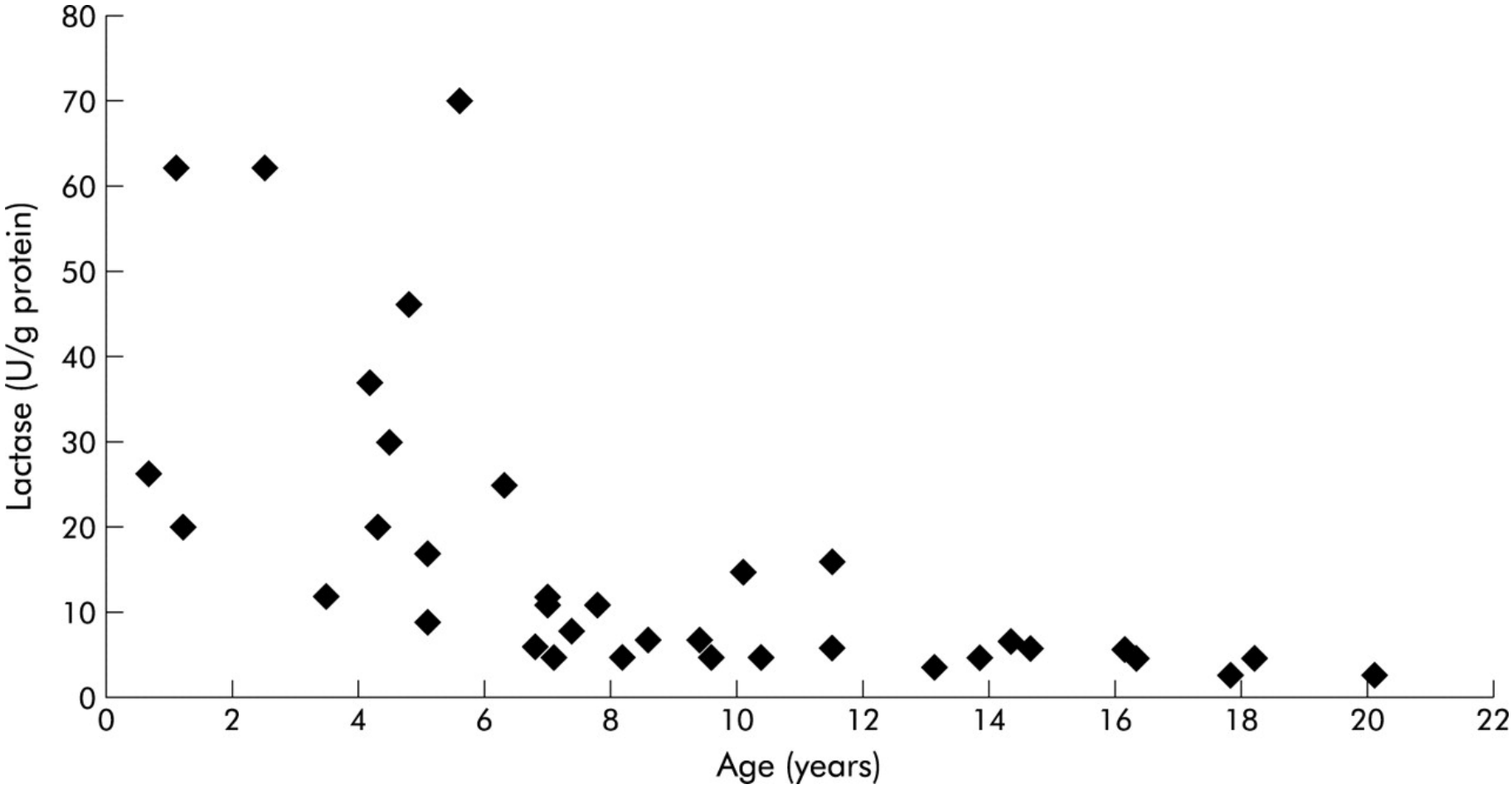
Congenital sucrase-isomaltase deficiency

Babies breast fed or on lactose-only feeds do not show problems until weaned or on solids. There is a tendency towards spontaneous improvement. Affected adults may have increased bowel frequency and minor abdominal distension.

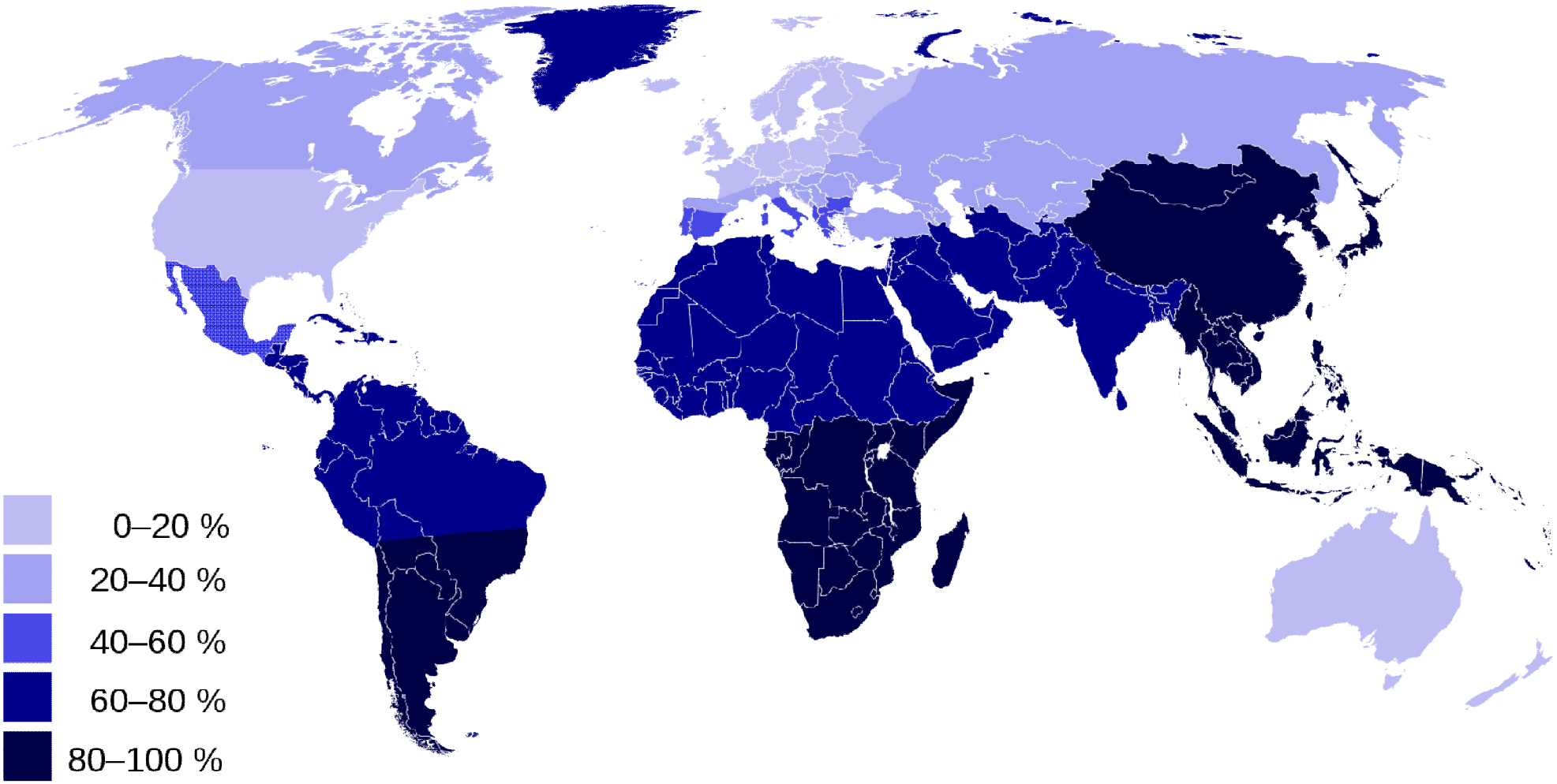
Congenital lactase deficiency

Extremely rare (~40 cases reported, most in Finland)
Severe diarrhoea in first few hours of life.
If not diagnosed early can be fatal.

Lactase activity declines with age in most children



Prevalence of primary lactase deficiency in various ethnic groups



Secondary causes of disaccharidase deficiency

Pancreatic insufficiency- reduction in amylase production so starch is not broken down

Loss/ damage of small intestinal brush border:

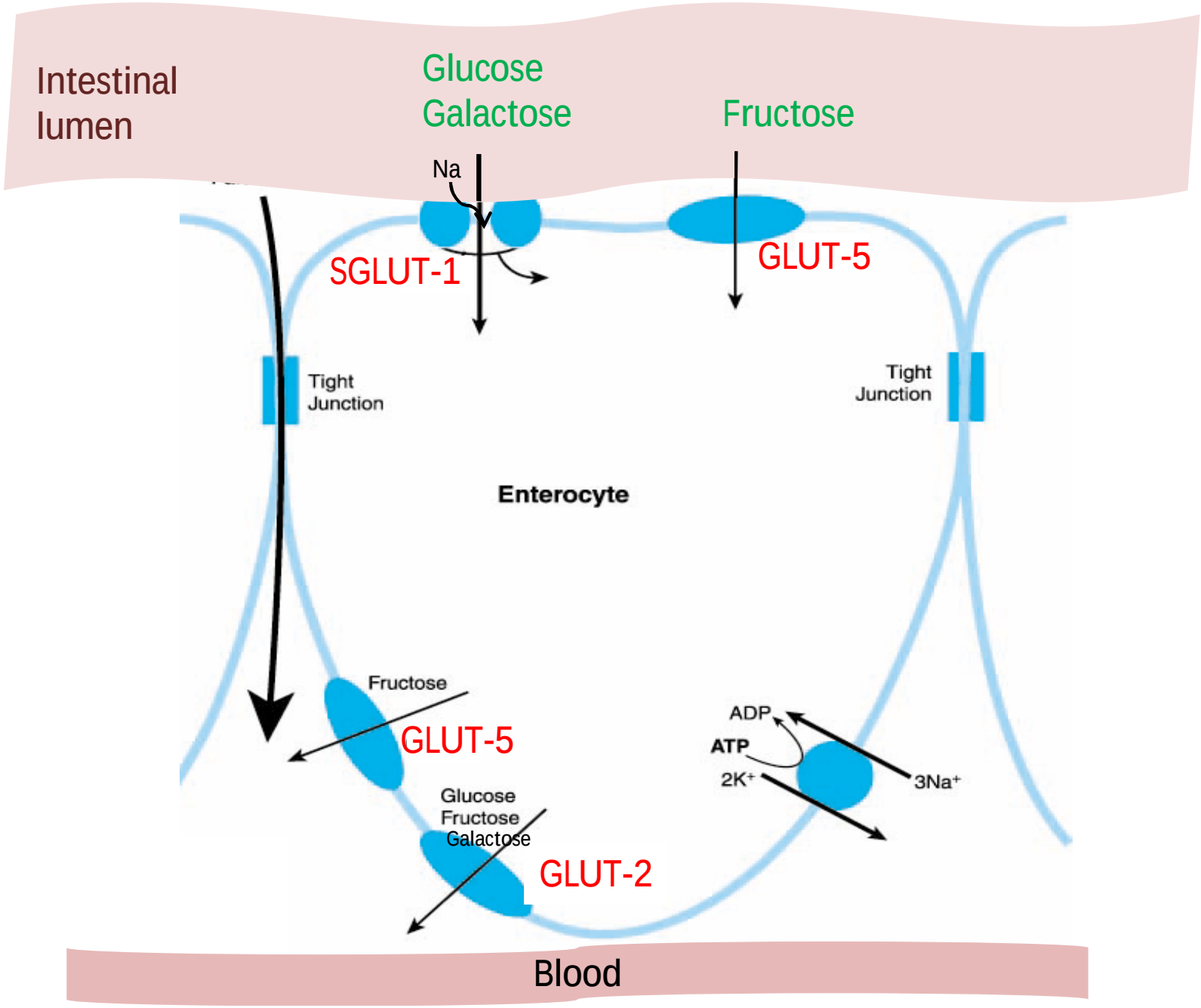
e.g.

- Coeliac disease (autoimmune reaction to gluten that lead to villous atrophy)
- Gastroenteritis
- Chron's disease
- Ulcerative colitis
- Small intestinal lymphoma
- Chemotherapy
- Long courses of antibiotics
- Alcoholism

Short gut syndrome- surgical removal of part of the intestines.

These are largely reversible

Defects in Monosaccharide Transporters



Disorders of Monosaccharide Transporters

Transporter (Gene)	Major sites of expression	Characteristics	Disorder
SGLUT-1 (*SLC5A1*)	Intestinal mucosa, kidney tubules	Cotransports 1 molecule of glucose or galactose along with 2 Na+	Glucose/ galactose malabsorption
GLUT-2 (*SLC2A2*)	Liver, pancreatic β cell, small intestine, kidney	Transports glucose, galactose and fructose. Serves as "glucose sensor" in β-cells	Fanconi-Bickel Syndrome
GLUT-5 (*SLC2A5*)	Small intestine, sperm	Transports fructose	-

Diagnosis of Disaccharide Deficiencies

1) Diet modification
2) Stool analysis
3) Hydrogen breath test
4) Lactose or sucrose tolerance test
5) Enzyme analysis

2. Stool analysis

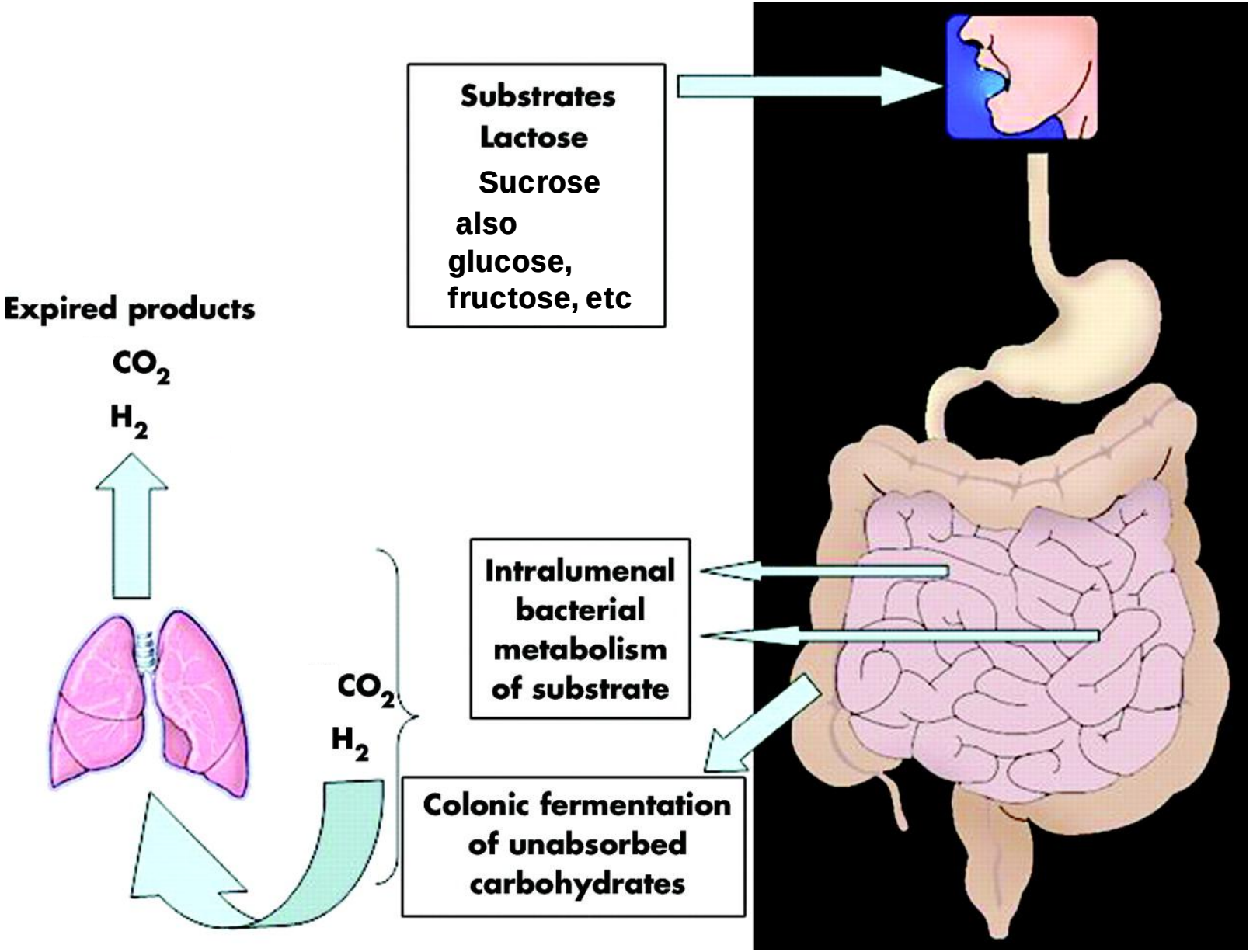
Reducing sugars in faeces will reduce blue Cu^{2+} (Clinitest or Benedict's reagent) to Cu^{+}. This is precipitated as red-orange copper (I) oxide.

Does not differentiate between the various sugars.
Does not detect non reducing sugars such as sucrose.

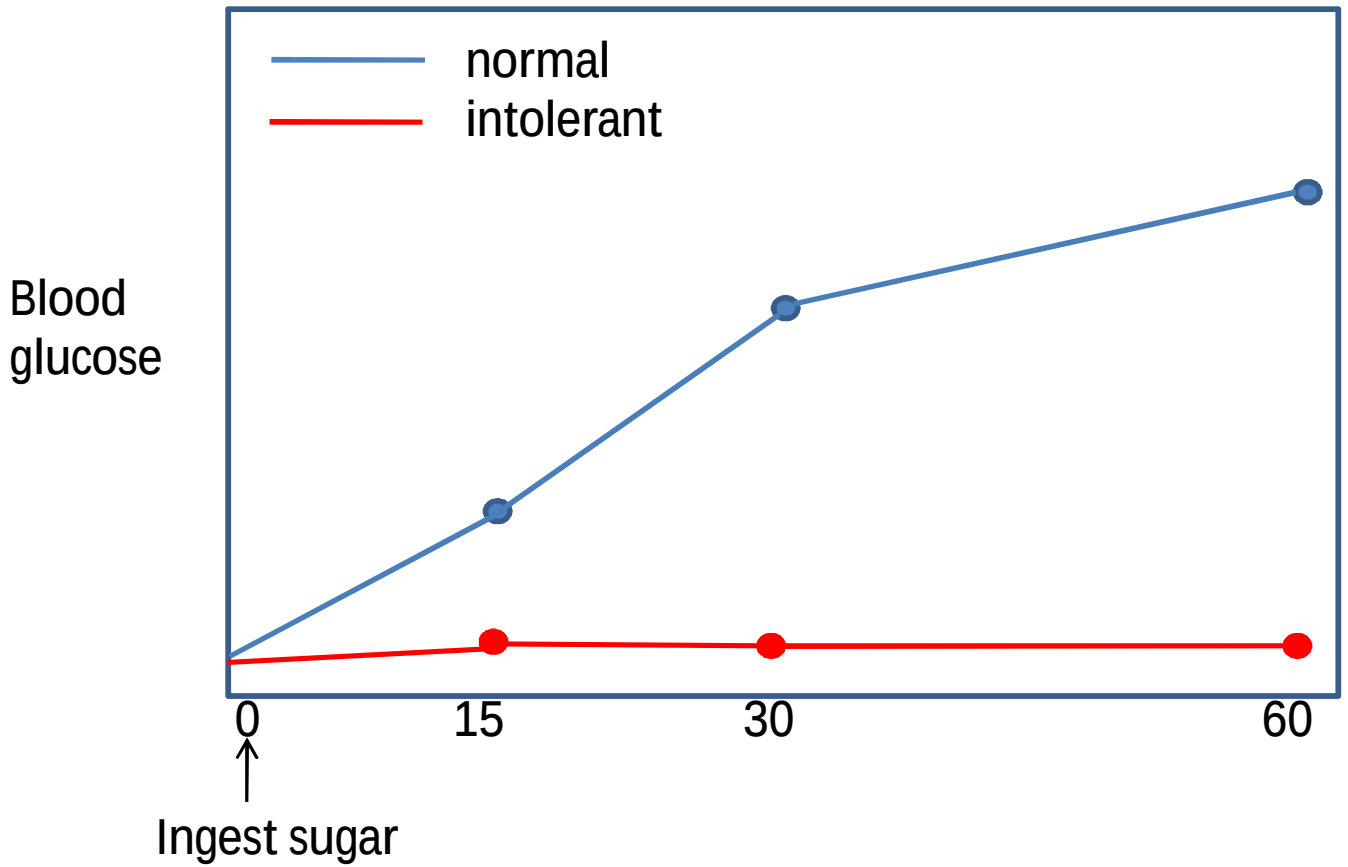
pH of faeces is normally >6.
Presence of lactic acid will give a pH <6.

2. Discussion on Stool analysis

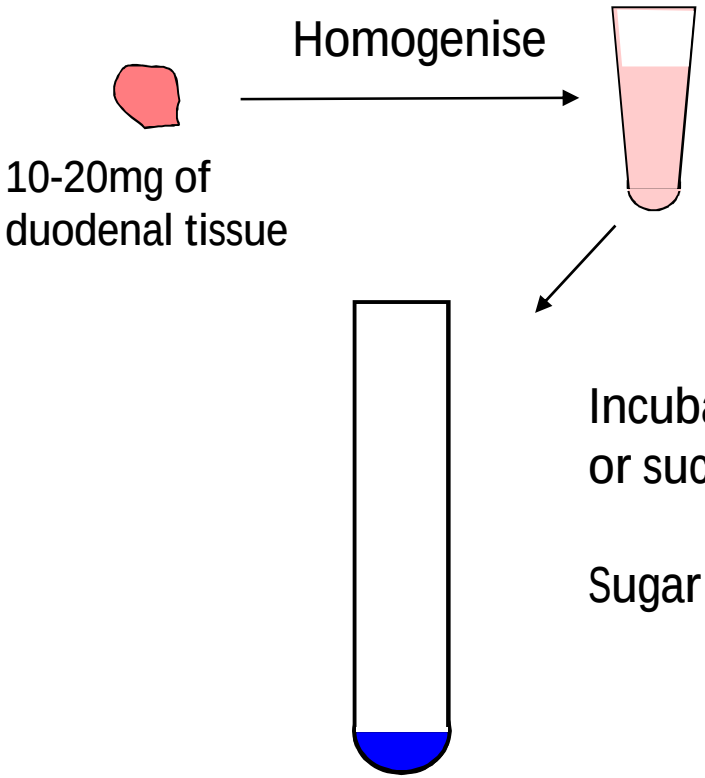
3. Hydrogen Breath Test



4. Sugar tolerance test



5. Enzyme analysis



Incubate at 37^0C, 1 hour, with lactose or sucrose

Sugar is broken down to glucose

Measure glucose

$$\beta\text{-D-Glucose} + O_2 \xrightarrow{\text{Glucose oxidase}} \text{D-gluconic acid} + H_2O_2$$

$$H_2O_2 + \text{Homovanillic acid} \xrightarrow{\text{Peroxidase}} \text{Dimeric Homovanillic acid}$$

Fluoresces at pH 8

Treatment

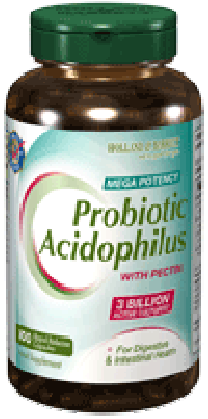
Remove offending sugars from the diet

Some products may be easier to digest.
e.g. hard cheeses, ice cream, fermented milk products such as yoghurt

ERT-

yoghurts contain microorganisms which help digest disaccharides

Brewer's yeast is rich in invertase (breaks down sucrose)



Summary

- Dietary carbohydrates are broken down by amylase and disaccharidases
- Main disaccharidases are lactase and sucrase-isomaltase
- Deficiency lead to diarrhoea, stomach pains, bloating
- Deficiency can be primary or secondary
  - 1y- congenital very rare, affect only one enzyme, irreversible
    Most children naturally switch off lactase activity.
  - 2y- more common, occur at any age, reversible if due to loss of duodenal brush border
- Many methods for diagnosis- some more invasive than others.
  Underlying cause can be difficult to establish
- Treatment is by dietary modification- either removal of offending sugars or use of enzymes to aid digestion


The good news is that you don't have mad cow's disease. The bad news is you're lactose intolerant.