DEFICIENCIES OF DUODENAL DI SACCHARI DASES
## Major Dietary Disaccharides

<table>
<thead>
<tr>
<th>Disaccharide</th>
<th>Structure</th>
<th>Natural occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maltose</td>
<td>Glcα(1→4)Glcα</td>
<td>Plants (starch) and animal (glycogen)</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Glcα(1→2)Fruβ</td>
<td>Many fruits, seeds, roots, honey</td>
</tr>
<tr>
<td>Lactose</td>
<td>Galβ(1→4)Glc</td>
<td>Milk, some plant sources</td>
</tr>
<tr>
<td>Trehalose</td>
<td>Glcα(1→1)Glcα</td>
<td>Mushrooms, yeast, insects, shrimp</td>
</tr>
<tr>
<td>Cellobiose</td>
<td>Glcβ(1→1)Glc</td>
<td>Plants (cellulose)</td>
</tr>
</tbody>
</table>
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

\[ \alpha_{1,4} \text{ glucose linkage} \]

\[ \text{AMYLOSE} \rightarrow \text{MALTOTRIOSE} + \text{MALTOSE} \]

\[ \alpha \text{ amylase} \]

\[ \text{AMYLOPECTIN} \rightarrow \alpha - \text{LIMIT DEXTRINS} \]

\[ \alpha_{1,6} \text{ glucose linkage} \]

**Figure 10.** The action of pancreatic \( \alpha \)-amylase on linear (amylose) and branched (amylopectin) starch. Circles indicate glucose residues and the reducing glucose unit.

Amylase

Polysaccharides (starch and glycogen)

Disaccharides

Monosaccharides

Dietary carbohydrates

Lactase

Maltase

Sucrase-isomaltase

Uptake into blood
## The Four Disaccharidase Complexes

<table>
<thead>
<tr>
<th>Enzyme or complex</th>
<th>Substrates include</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maltase-Glucoamylase complex</td>
<td>Maltose (1,4-(\alpha)-bonds)</td>
</tr>
<tr>
<td>Sucrase-isomaltase complex</td>
<td>Sucrose, isomaltose, maltose, maltotriose (1,4-(\alpha)-bonds)</td>
</tr>
<tr>
<td></td>
<td>Splits 1,6-(\alpha)-bonds from a-limit-dextrans</td>
</tr>
<tr>
<td>b-Glycosidase complex (Lactase-phlorizin hydrolase)</td>
<td>Lactose, cellobiose, cellotriose</td>
</tr>
<tr>
<td>Trehalase</td>
<td>Trehelose</td>
</tr>
</tbody>
</table>
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)
<table>
<thead>
<tr>
<th>Causes of disaccharidase deficiencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
</tr>
<tr>
<td>Hereditary</td>
</tr>
<tr>
<td>Very rare*</td>
</tr>
<tr>
<td>Usually only affects</td>
</tr>
<tr>
<td>1 disaccharidase</td>
</tr>
<tr>
<td>Presents at birth*</td>
</tr>
<tr>
<td>Not associated with intestinal disease</td>
</tr>
<tr>
<td>Irreversible</td>
</tr>
<tr>
<td>Managed by dietary control</td>
</tr>
</tbody>
</table>

*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

Intestinal lumen

Glucose, Galactose

SGLUT-1

Na

Fructose

GLUT-5

Glucose, Fructose, Galactose

GLUT-2

Blood

ADP

ATP

2K⁺

3Na⁺
# Disorders of Monosaccharide Transporters

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

Sucrose also glucose, fructose, etc.
4. Sugar tolerance test

Blood glucose

Ingest sugar

- **normal**
- **intolerant**
5. Enzyme analysis

Homogenise 10-20mg of duodenal tissue

Incubate at 37°C, 1 hour, with lactose or sucrose
Sugar is broken down to glucose

Measure glucose

Glucose oxidase

\[ \beta-D-Glucose + O_2 \rightarrow D-gluconic\ acid + H_2O_2 \]

Peroxidase

\[ H_2O_2 + Homovanillic\ acid \rightarrow \text{Dimeric\ Homovanillic\ acid} \]

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.