Back to Basics:
Carbohydrate Digestion & Absorption

Ahmed Al-Sarkhy

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Objectives

- Review CHO chemistry
- **Review digestion & absorption mechanism**
- **Diagnostic tests of CHO malabsorption esp Hydrogen Breath test**
- Quick review of some malabsorption defects

CHO chemistry

- Carbohydrates are called carbohydrates because they are essentially hydrates of carbon (i.e. they are composed of carbon and water $(CH_2O)_{n.}$

- **Simple sugers = Monosaccharides :**
  - Glucose
  - Fructose
  - Galactose

- **Disaccharides :**
  - Sucrose: glucose + fructose
  - Lactose: glucose + galactose
  - Maltaose: Glucose + Glucose

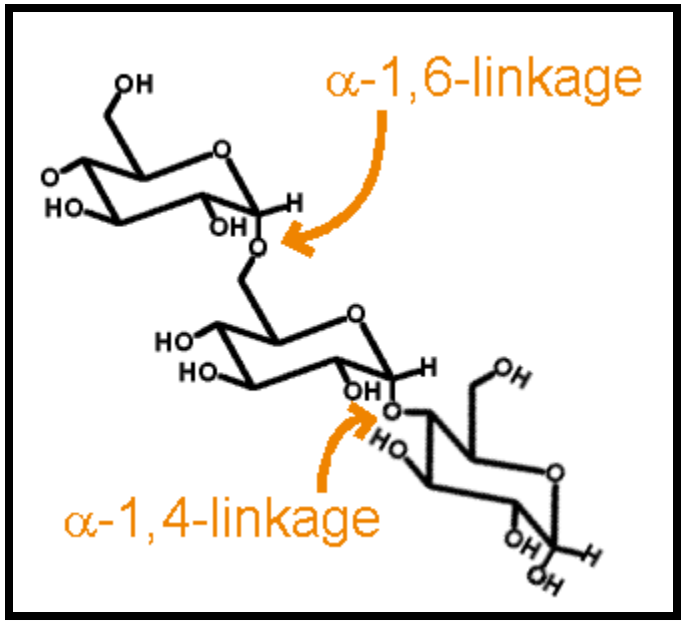
CHO chemistry

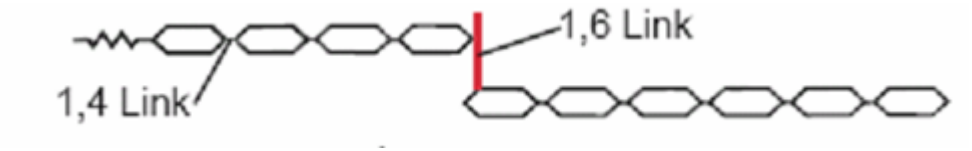
- **<u>Oligosaccharides: 2-10 monosaccharides:</u>**
  - Maltriose

- **<u>Polysaccharides (100-1000 monosaccharides) :</u>**
  - Starch (found in plants): amylose & amylopectin
  - Glycogen (found in animals)
  - Dietary fibers (non-starch polysaccharides)

Starch

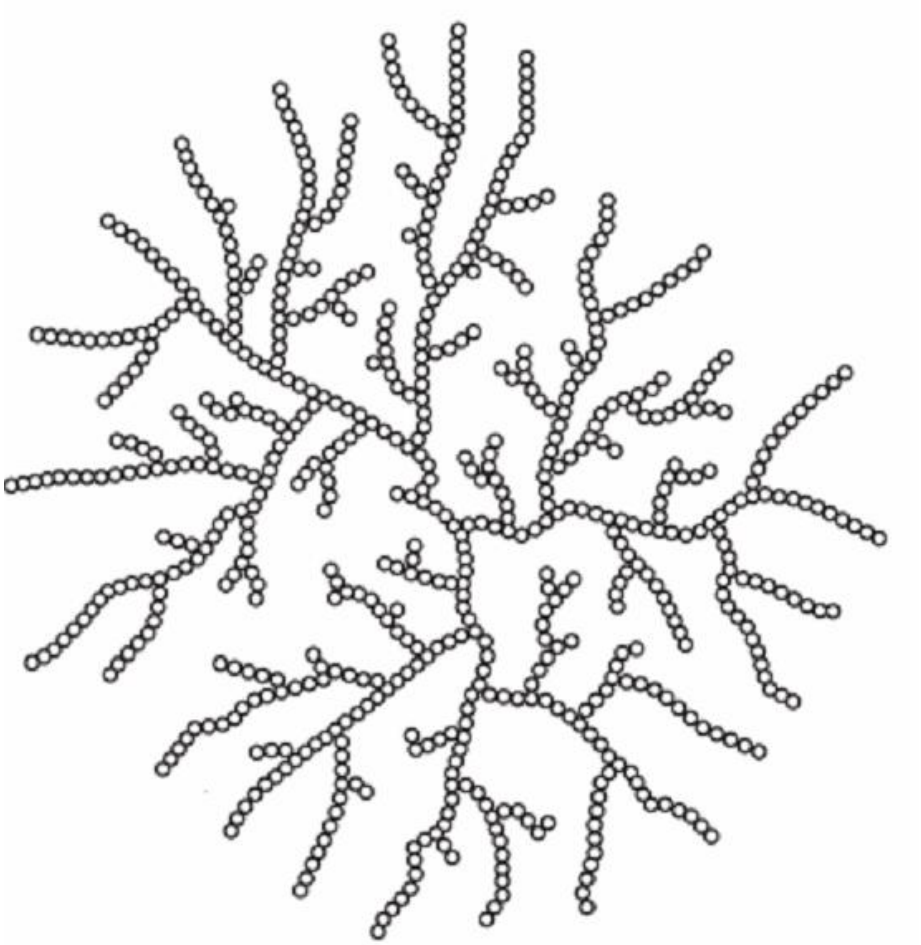
- ***Amylose*** → linear polymer of glucose connected by α-1,4 glycosidic linkage (unbranded)
- ***Amylopectin*** → linear polymer of glucose connected by α-1,4 linkage but also has branched-chain side chains connected by α-1,6 linkages q 30th glucose residue
- Most starches usually contain more amylopectin than amylase





Glycogen structure

- Major storage carbohydrate in animals
- Long straight glucose chains (α 1-4)
- Branched every 8-10 glucose residues (α 1-6 linkage)
- More branched than starch



Non-starch polysaccharides

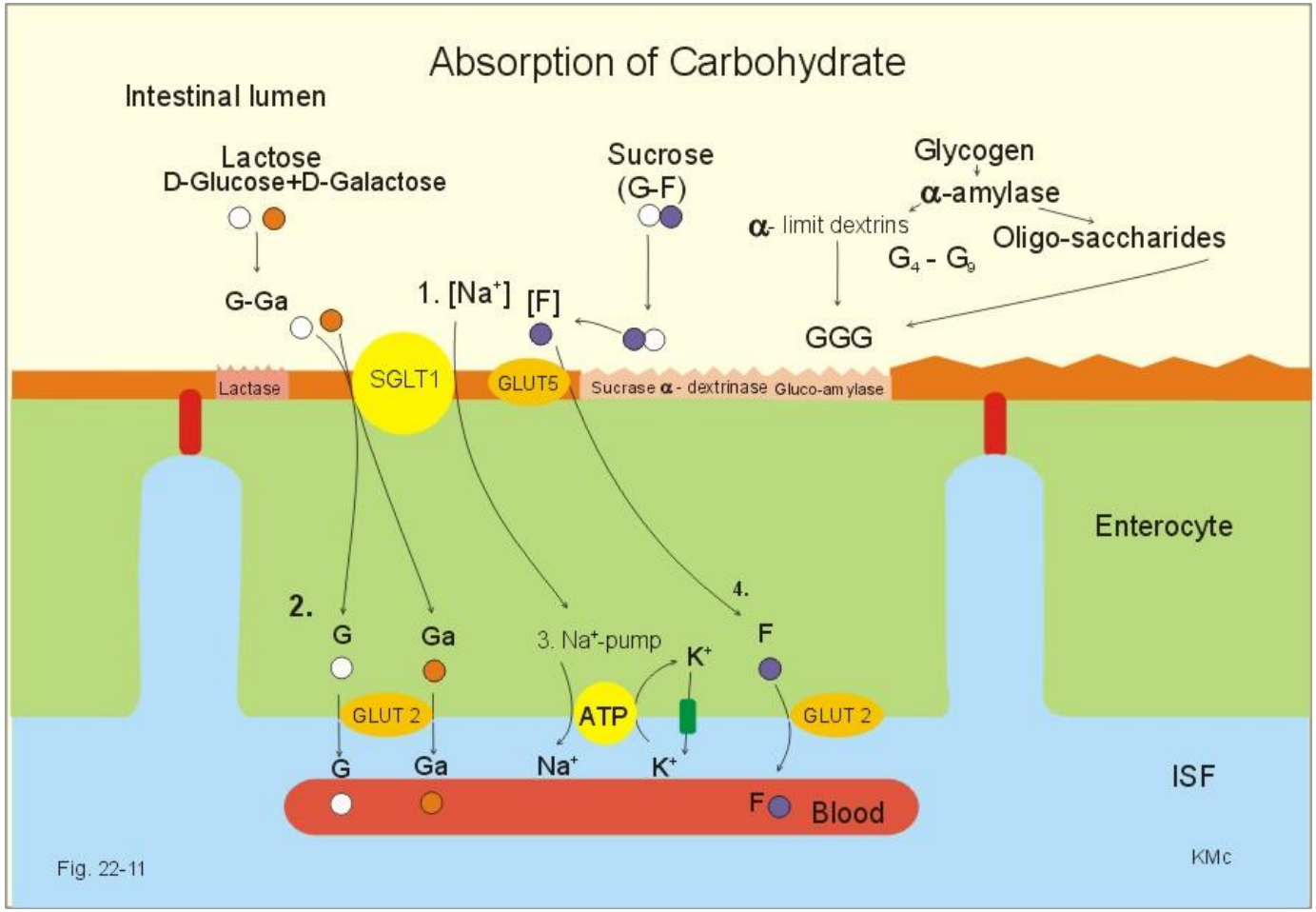
- Dietary fibers or "unavailable" CHO consisting predominantly of celluloses & hemicelluloses

- ***Cellulose*** → **β-1,4–linked** glucose molecules in straight chains
- ***Hemicelluloses*** → pentose & hexose polymers with both straight and branched chains

- Both forms are resistant to digestion in SB because β-1,4 bond is resistant to the digestive enzymes in human GIT.

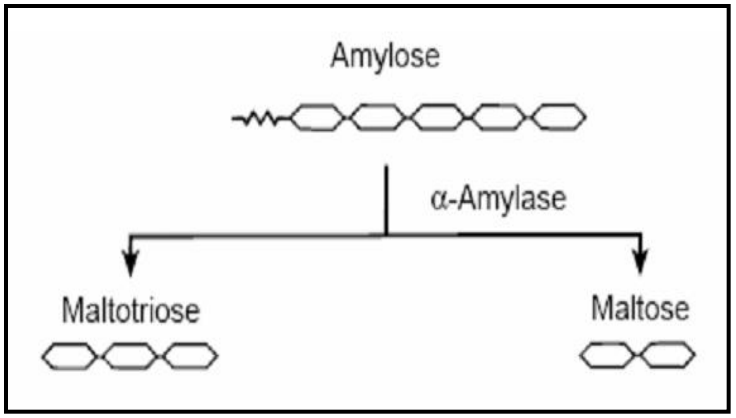
- They are broken down to some extent by colonic bacteria → SCFAs which are easily absorbed by colonic mucosa

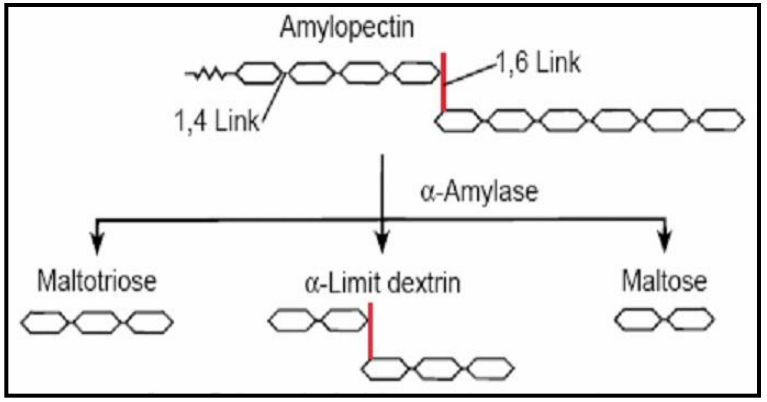
CHO Digestion & absorption



Intra-luminal digestion

- Salivary gland & pancreas secret α **amylases** that cleave ***α-1,4 links***
- Both of them work in an alkaline/natural pH values
- α 1,6 linkage in the branched oligo & polysaccharides in amylopectin & glycogen are broken by *intestinal isomaltase* → maltose & glucose
- Other enzymes : Gluco-amylase (Maltase)





Brush Border Membrane Hydrolases

- Disaccharides (sucrose, lactose, maltose) cannot be absorbed intact → hydrolyzed by specific brush border membrane hydrolases

- Disaccharidases are synthesized by both crypt & villous cells & **expressed only on villous cells**

- Maximally expressed in *villi* of **duodenum & jejunum**

Brush Border Membrane Hydrolases

Enzyme	Substarte	Products
Lactase	Lactose	Glucose + Galactose
Maltase (Glucoamylase)	Maltose	Glucose + Glucose
Sucrase - Isomaltase		
Sucrase	Sucrose	Glucose + Fructose
Isomaltase	Dextrin	Glucose

Transport across the mucosa

- Monosaccharides : *glucose*, *galactose*, *fructose* are absorbed by carrier-mediated transport systems located just adjacent to the enzymes at the brush border membrane

- **There are 2 types of monosaccharides transporters:**

  1- Na/Glucose Transporters (active Glucose Tp):

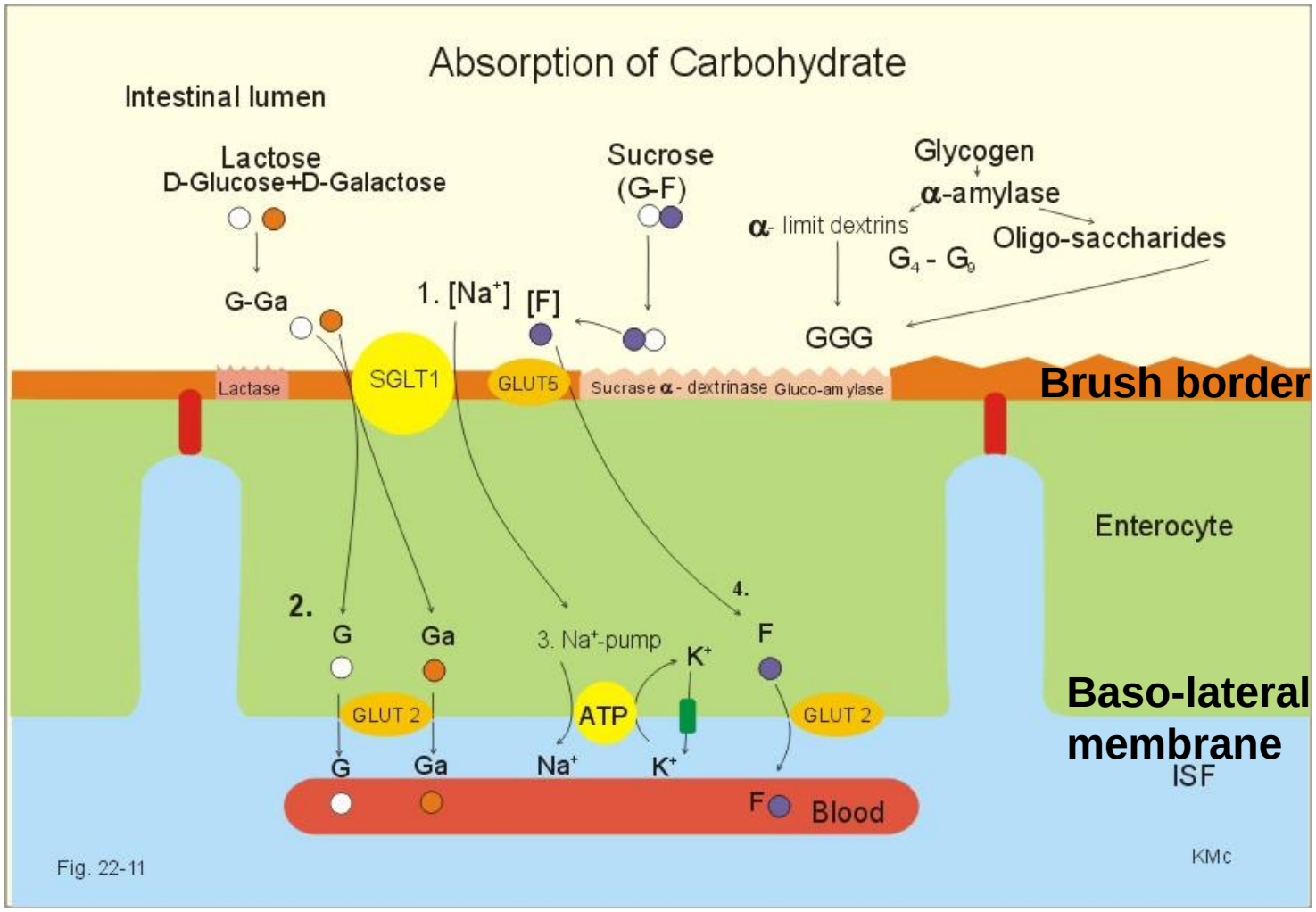
  absorption of glucose is stimulated by the presence of Na in the intestinal chyme

  - **SGULT-1** (at the tip of mature SB): SGULT-2 (SB ? function)

  2- Na independent facilitative Transporters :

  5 iso-forms: **GLUT-1, GLUT-2,** GLUT-3, GLUT-4 & **GLUT-5**

Transport across the mucosa



Facilitated diffusion

Transport across the mucosa

- Glucose & galactose absorption by secondary active transport driven by Na gradient across apical cell membrane = Na dependant Glucose Galactose Transporter (SGLT-1)

- Fructose absorption occurs by facilitated diffusion → not against concentration gradient but with a carrier protein to achieve transport rates greater than one would expect from simple diffusion

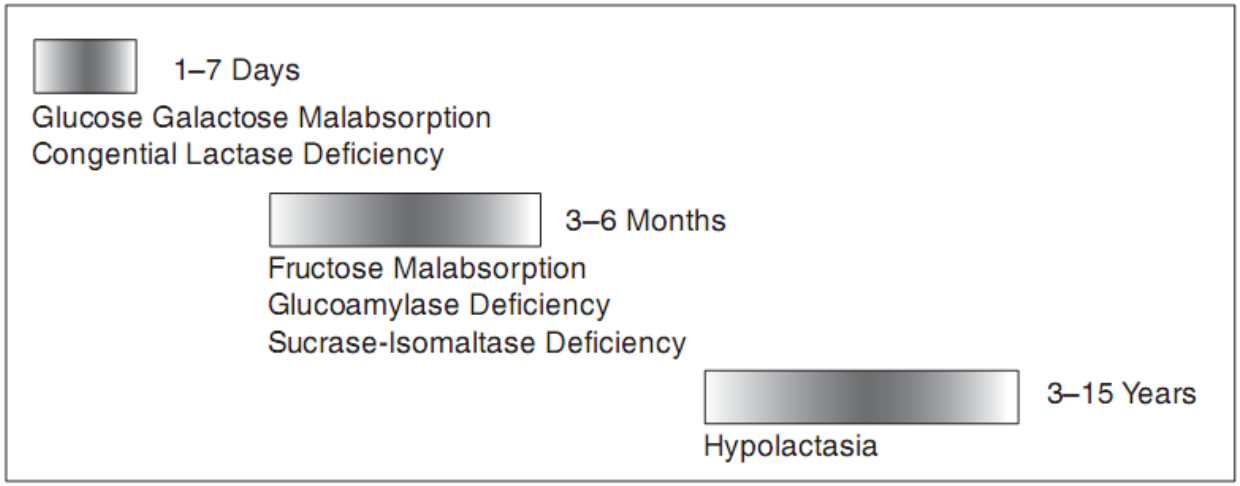
- Monosaccharides exit across the basolateral membrane depends on facilitated diffusion (not requiring energy) via a specific carrier

Causes of CHO malabsorption

- **<u>Primary CHO Malabsorption:</u>**

  - It result from congenital defects of single BB enzyme or transporter which lead to absence or marked decrease in the enzyme/transporter activity

  - Present early in life



- **<u>Secondary CHO malabsorption:</u>**

  - Defect from impairment of the epithelial surface of the small intestine (GE, celiac disease or Crohn's disease)

Clinical presentation of CHO malabsorption

- Symptoms; sever diarrhea with metabolic acidosis early in life.
- Later on, recurrent pain, bloating, flatus, diarrhea, distension on introducing the responsible diet

- Unabsorbed sugar → fluid shift → Increased osmotic load → diarrhea

- Unabsorbed sugar + colonic bacteria → Fermentation & Gas production (abdm distension, flatulence & cramps)

- Fermentation → SCFAs → Acidic stool (pH < 5)

Dx of CHO malabsorption

- **Direct tests:** invasive, measurement of enzyme activities in intestinal biopsies

- **Indirect:**

  1- Stool: acidic pH < 5.5, High stool osmotic gap (>40mOsm), +ve reducing substances

  2- Hydrogen Breath Test (HBT)…

  3- Xylose test: measurement of xylose in urine or blood…

  4- Measurement of glucose after lactose ingestion

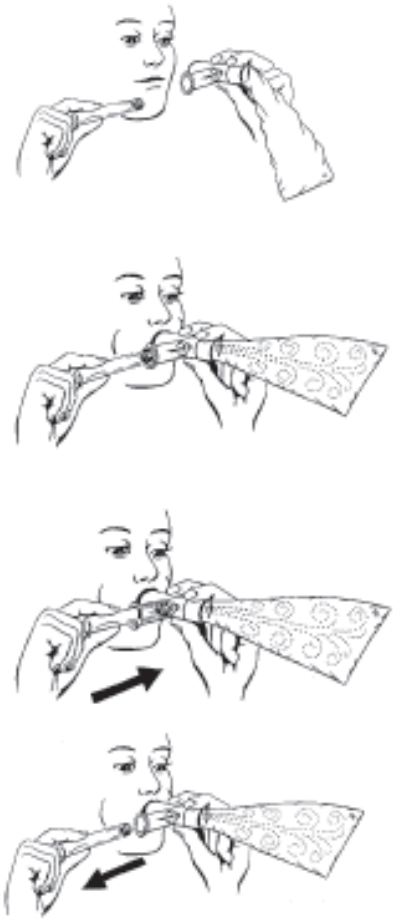
Dx of CHO malabsorption

Improvement after dietary adjustment and recurrence of symptoms when dietary exposure occur is still the best way of confirming the diagnosis.

World J Gastroenterol 2007 November 21; 13(43): 5687-5691

HBT

- After ingestion of the test sugar (eg: lactose, fructose, sucrose), the amount of hydrogen in the exhaled gas is measured.
- All of these breath tests rely on bacterial fermentation of nonabsorbed carbohydrate → **hydrogen, methane, carbon dioxide → exhaled & measured from breath samples**
- H2 not produced by mamillian , only by bacteria.
- **An increase in hydrogen of more than 20 parts per million from the baseline** is considered to indicate malabsorption.
- The extent of the hydrogen increase **does not correlate** either with the patients' symptoms or with the degree of malabsorption



Symons P, Jones MP, Kellow JE. *Scand J Gastroenterol* 1992; 27: 940-944

HBT

Test	Disorder
Lactose H2 breath test	Lactose intolerance
Glucose H2 breath test	→ Any peak is abnormal - Rapid transit (single peak) or - SBBOG (double peak)
Lactulose H2 breath test	- Normally, it shows 1 peak after 120 mints 2ndry to colonic bacteria fermentation - SBBOG (double peak)

Preparation for HBT

- **NPO** 12 hrs prior to the test
- **No fiber** diet 24 hrs prior
- **Consider LF** diet 1wk prior to the test for patients suspected to have LI
- No recent use of **ABx**
- **Anti-bacterial mouth** wash prior to the test to prevent premature H_2/CO_2 production by oral flora

FN;

1- If no H_2 producing bacteria

(measuring methane will increase the test sensitivity)

2- Recent ABx use

3- Rapid ventilation (clear it out quickly)

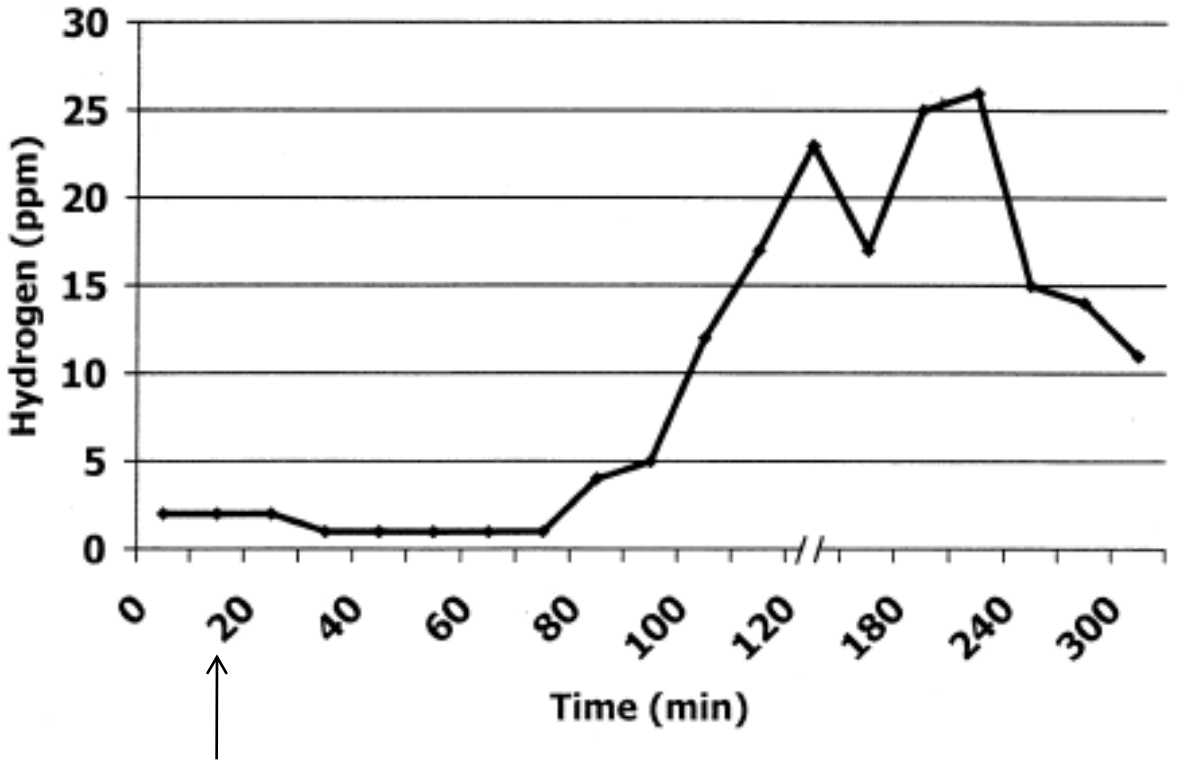
FP;

1- Improper fasting before the test

2- High fiber diet 24 hrs prior

3- Cigarette smokin

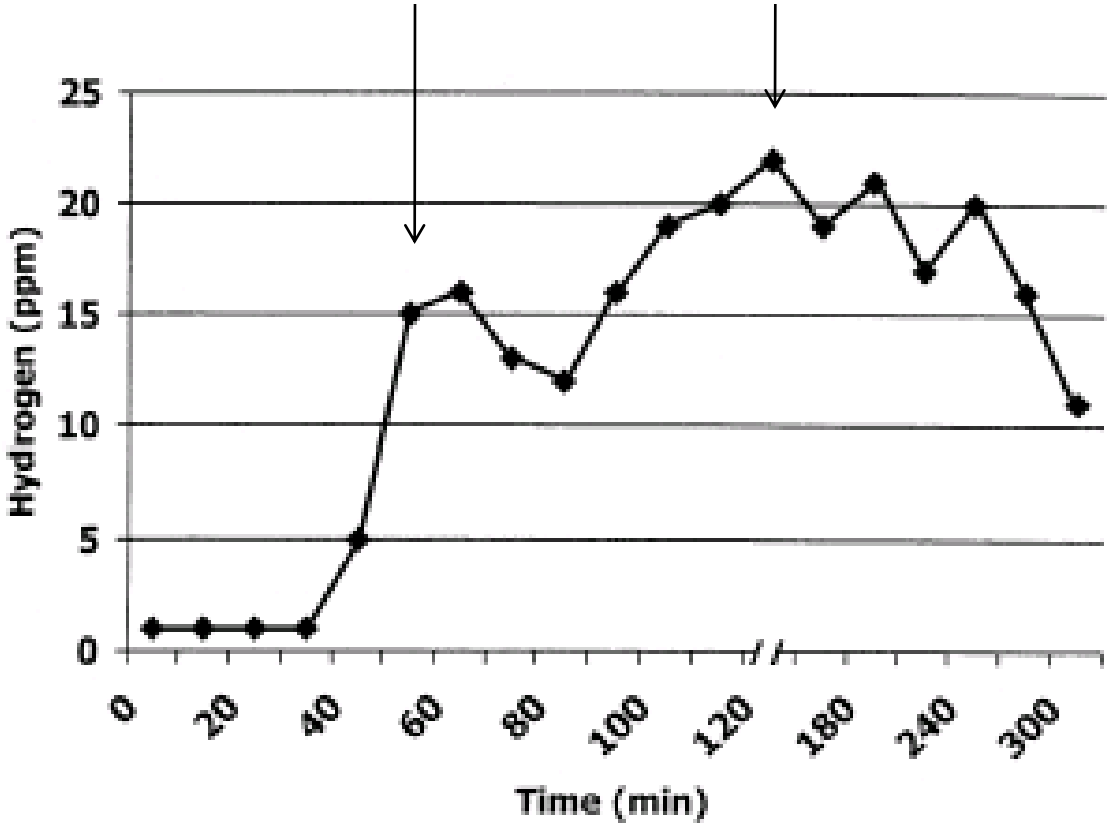
Normal Lactulose-Hydrogen breath test



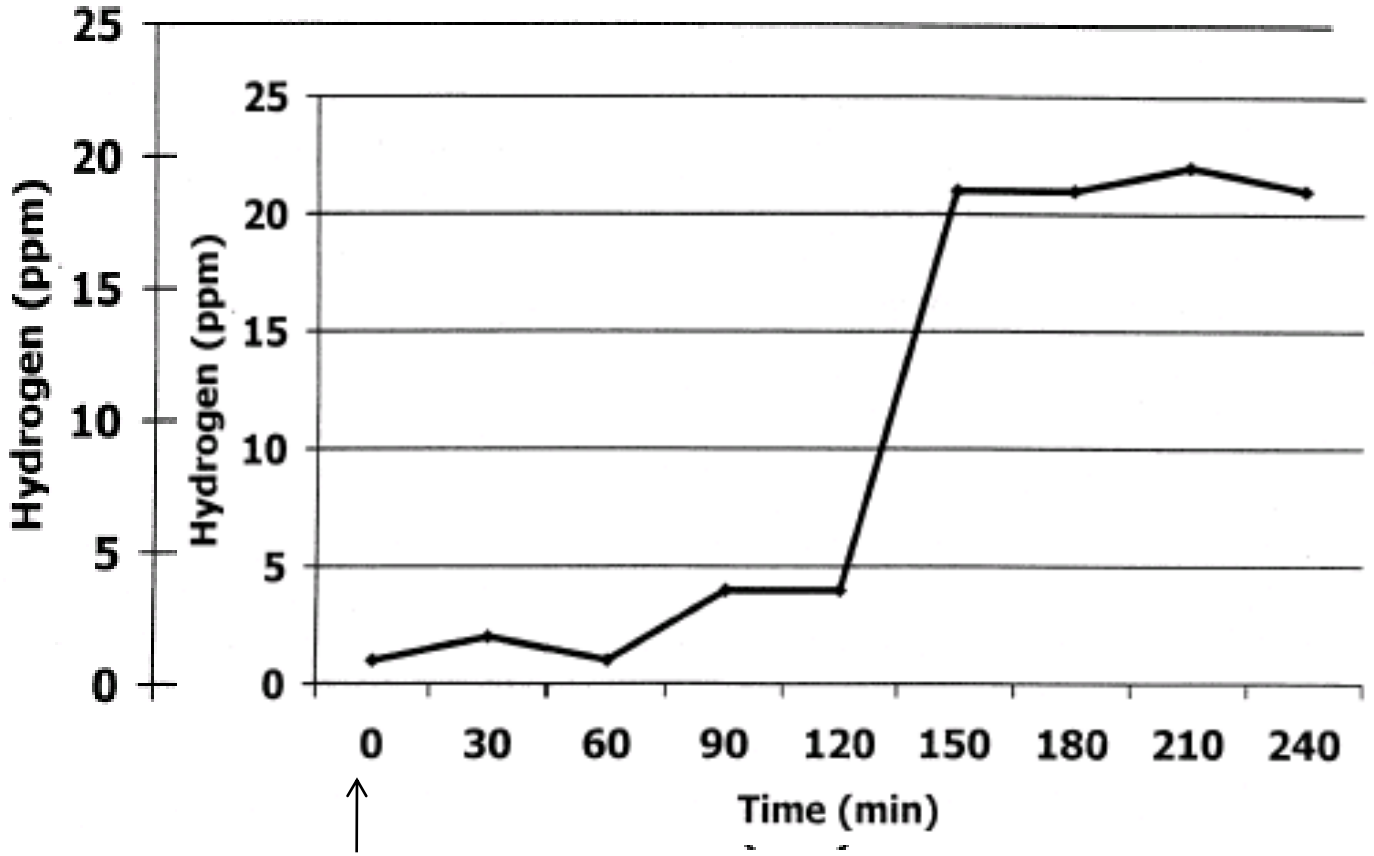
Normal baseline

Romagnuolo et al. Am J Gastr. 2002

Lactulose Breath test in pat with SBBOG



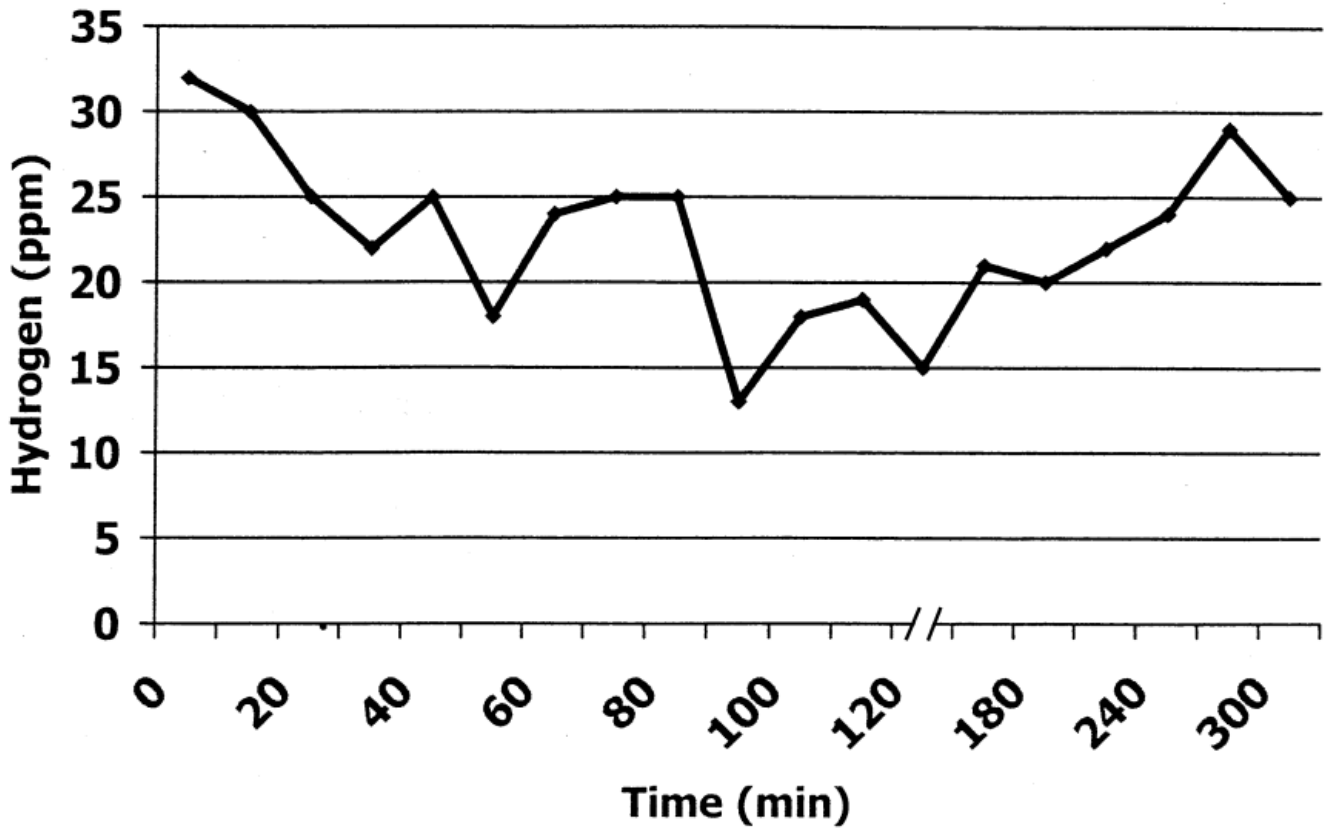
Lactose intolerance



Normal baseline
Before giving
lactose

Romagnuolo et al. Am J Gastr. 2002

Glucose H2 BT?.. DDx



D-Xylose test

- D-xylose is a pentose monosaccharide (absorbed both by an active sodium transporter and by **passive diffusion**
- The D-xylose test measures the absorptive capacity of the proximal small intestine rather than a specific defect in D-xylose absorption
- **Low blood levels and urinary excretion** suggests mucosal disease such as celiac but it does not tell about the specific defect
- Absorption is usually normal in pancreatic insufficiency since pancreatic enzymes are not required for xylose absorption.

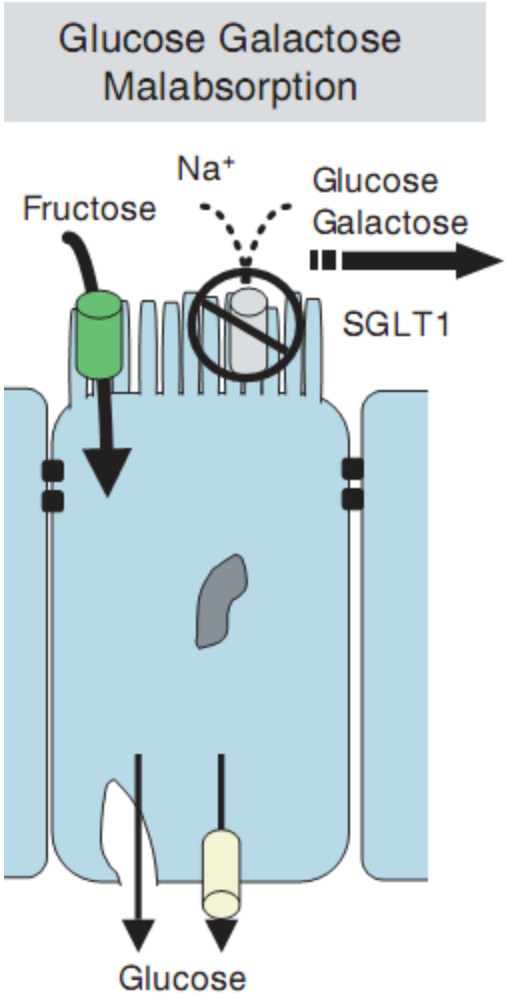
Glucose -Galactose malabsorption (GGM)

- AR, rare, life threatening diarrhea with metabolic acidosis early in life
- Defect in **SGLT-1** (SLC5A1 mutation)

- **Dx: 3 key features:**
  1- Elimination of Glucose & Galactose from diet → disappearance of sx
  2- +ve Glucose H2 BT
  3- Normal intestinal Bx- no mucosal disease

- Intestinal Bx can be used to measure Lactase & Sucrase activities to differentiate GGM from primary lactase or sucrose deficiency

- Responding well to fructose containing formula or diet
- Sx improve with age despite persistence of the Tp defect.



Fructose Malabsorption

- AR, isolated Fructose malabsorption (SLC 2A5 gene) , ? Toddler diarrhea
- SX: diarrhea if daily juice consumption > 15 cc/kg (dose dependant)
- Dx: features:
  1- Elimination of Fructose from diet → disappearance of sx
  2- +ve Fructose BT
  3- Normal intestinal histology

SUCARASE- ISOMALTASE (SI) Deficiency

- Need pancreatic protease to cleave them in the intestinal lumen
- Sucarase hydolyse α1,4 glucosidic bonds while Isomaltase hydrolyse α 1,6 bonds
- Deficiency of one of them is associated with abnormal activity of the other

- C/P: varies: chronic diarrhea with FTT in infants, chronic diarrhea with normal growth in preschool children, IBS-like sx in older children & adults

- Diet: exclude sucrose ,starch & glucose polymer, Sucrase replacement is available
- Tolerance to starch improve during the 1st 3-4 yrs
- Probiotics (Saccharomyces Cerevisiae) may help bc it possesses sucrase activity

LACTASE deficiency

- 3 types: congenital, acquired & primary hypolactasia

1- CONGENITAL LACTASE DEFICIENCY;

- AR, very rare with complete absence of lactase expression.
- 1st week of life with onset of breast feeding or lactose formula:
- rare – sever acidic diarrhea
- Associated with hypercalcemia & nephrocalcinosis (? 2ndry to Metabolic acidosis or Ca -absorption effect of the lactose)
- need strict LF diet (replaced by sucrose or fructose formula)

2- Acquired lactose deficiency; post SB inflammatory/infectious/allergic illness

LACTASE deficiency

3- ADULT type hypolactasia

- Genetically determined
- Lactase level decrease by age, starting at age of 5 yrs (> 75% of adults have a level of 5-10% of the birth level)

- Incidence varied widely between different populations (higher in the Mediterranean & oriental races, Scandinavians 2-15 %, Caucasians 20 %& Native Americans, Asians 80-100%)

- Rx; lactase supplementation or LF diet + Ca supplementation
- Those who tolerate small amount ; recommend cheese & yogurt

Glucose fate

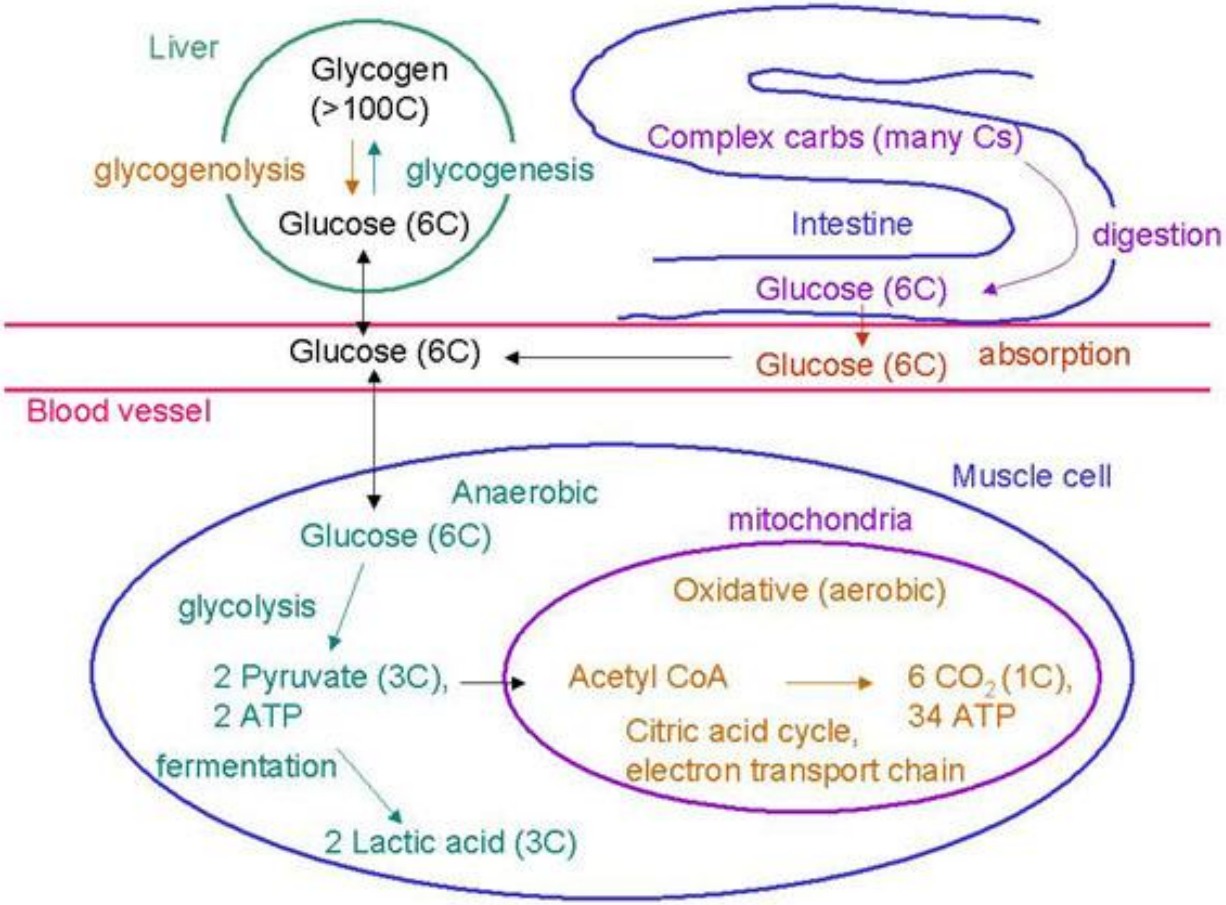
- **Glucose in the body undergoes one of three metabolic fates** :

  1- The majority of glucose is catabolized to produce ATP (in brain, muscle and kidney)

  2- it is stored as glycogen (in liver and muscle)

  3- it is converted to fatty acids → stored in adipose tissue as triglycerides & some stored in the liver.

CHO Metabolism



The End


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