METABOLISM OF CARBOHYDRATES

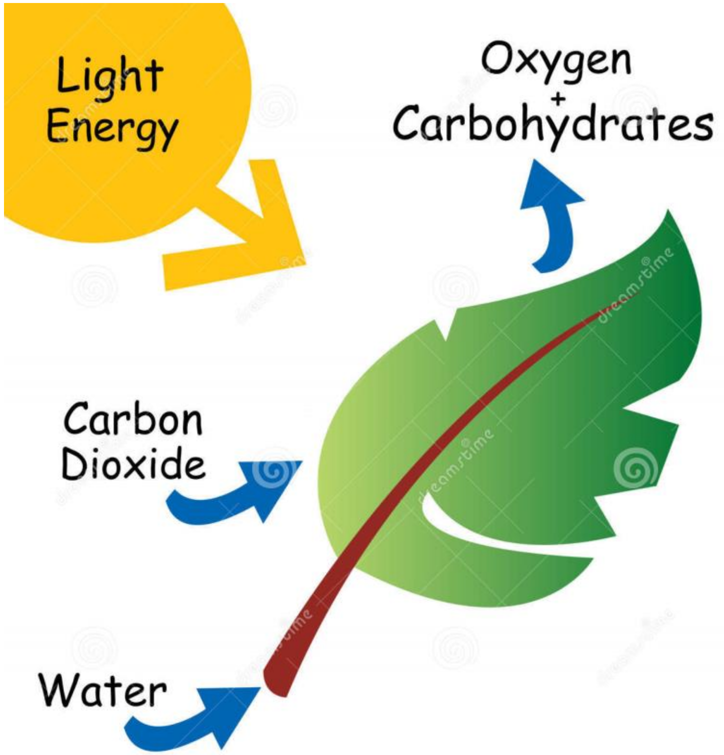
Lecture I

CARBOHYDRATES

aldehyde or ketone derivatives of the higher polyhydric alcohols, or compounds which yield these derivatives on hydrolysis

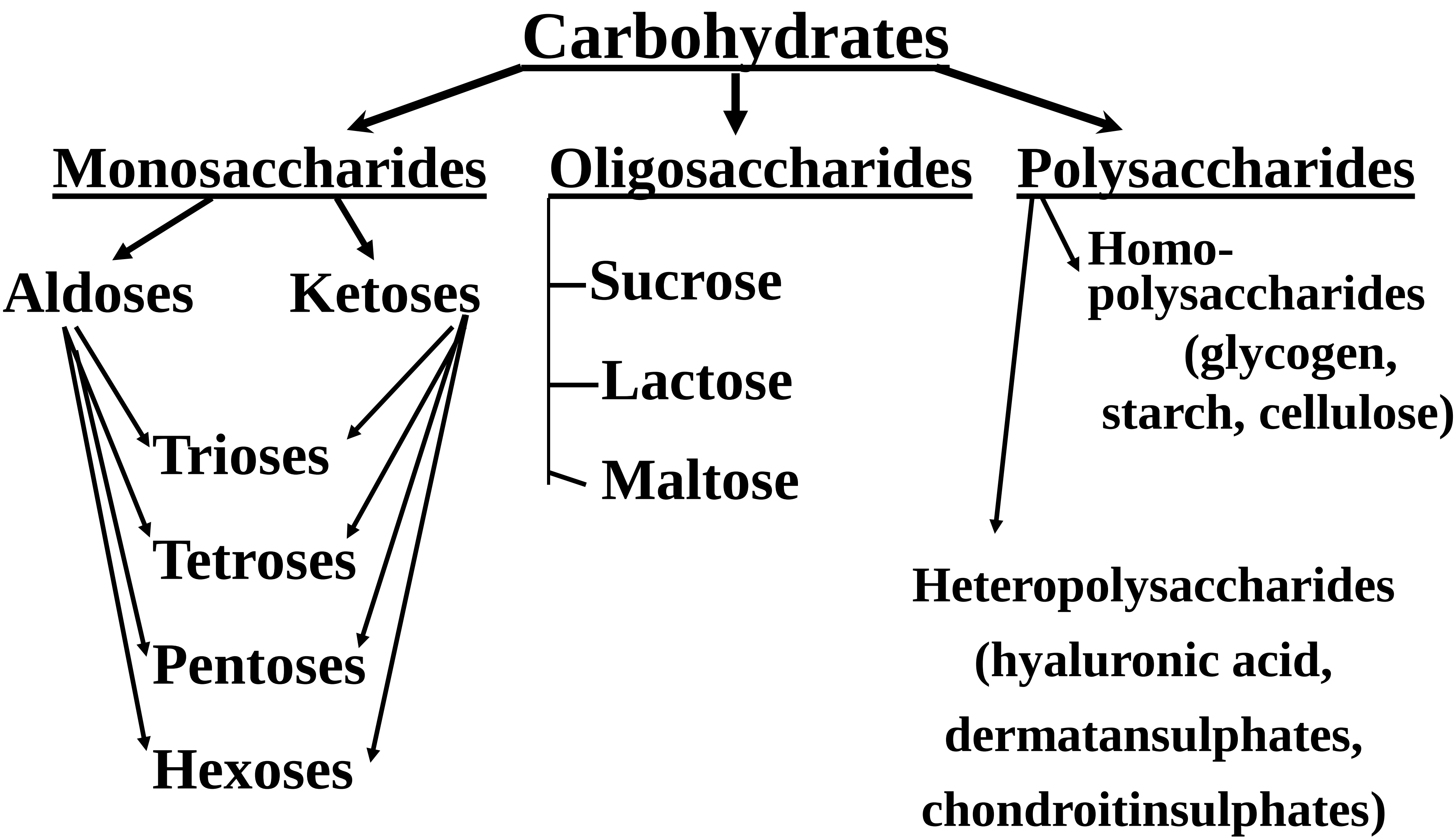
Carbohydrates are widely distributed in plants and animals.

In plants, glucose is synthesized from CO_2 and H_2O by photosynthesis and stored as starch or used to synthesize the cellulose of the plant cell walls.



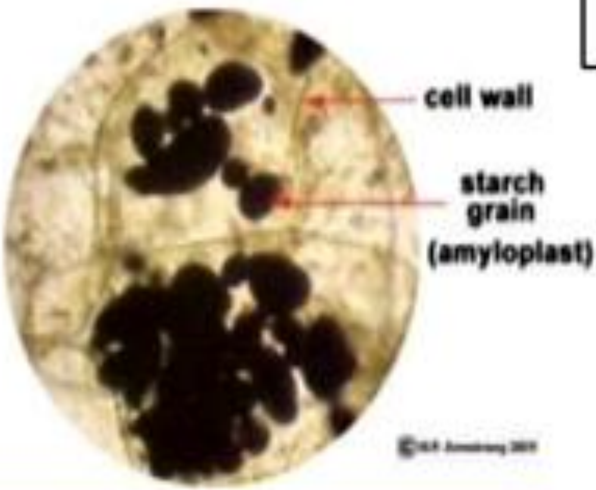
Animals can synthesize carbohydrates from amino acids, but most are derived ultimately from plants. Carbohydrates are major constituents of animal food.

Classification of carbohydrates

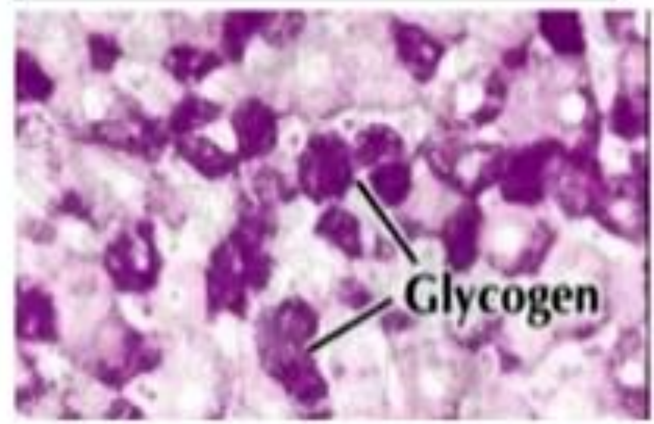


polysaccharides

starch	cellulose	glycogen
Found in Plants	Component of cell wall of plants	Found in Animals & yeast



Main carbohydrate reserve in plants



Main carbohydrate reserve in animals & yeast

<u>Harper's Illustrated Biochemistry</u>

structure of monosaccharides

importance of monosaccharides

structure of disaccharides

importance of disaccharides

structure of glycogen

FUNCTIONS OF CARBOHYDRATES

- **Energetic (major metabolic fuel)**
- **Structural (glycosaminoglycans of connective tissues, glycolipids in membranes)**
- **Metabolic (lipids and some aminoacids can synthesized from carbohydrates)**
- **Protective (components of immunoglobulins)**

FUNCTIONS OF CARBOHYDRATES

- **Receptative (glycoproteins of membraines)**
- **Antigenic (glycoproteins of erythrocytes define the group of blood)**
- **Plastic (elements in the structure of DNA, RNA, FAD, NAD(P),etc)**
- **Antitoxic**

Carbohydrates in human body

BLOOD:

glucose 3.3 – 6.4 mmol/L

TISSUES:

glycogen

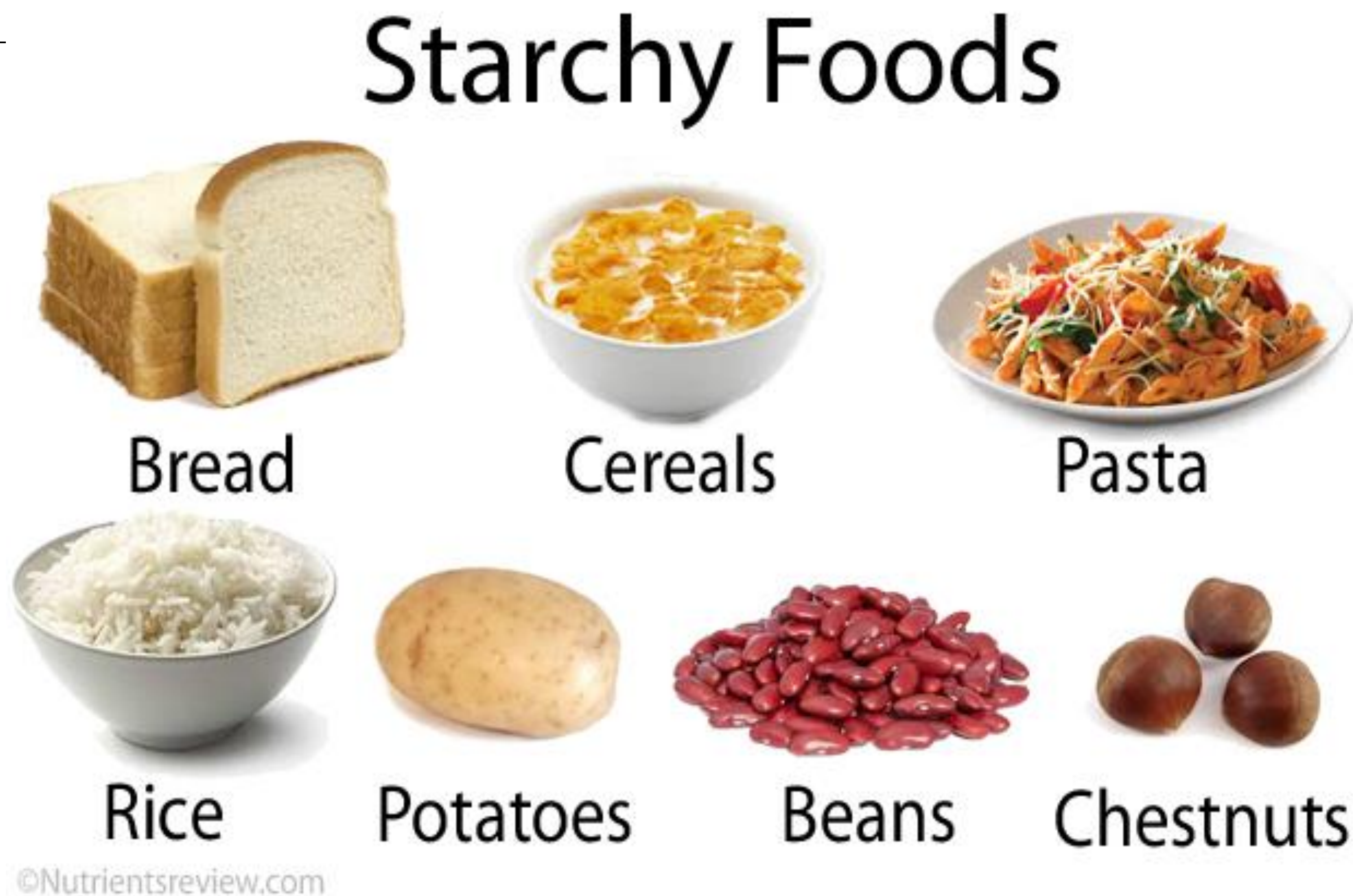
liver 2 - 5 %

muscle 0.5 - 1 %

brain 0.05 - 0.15 %

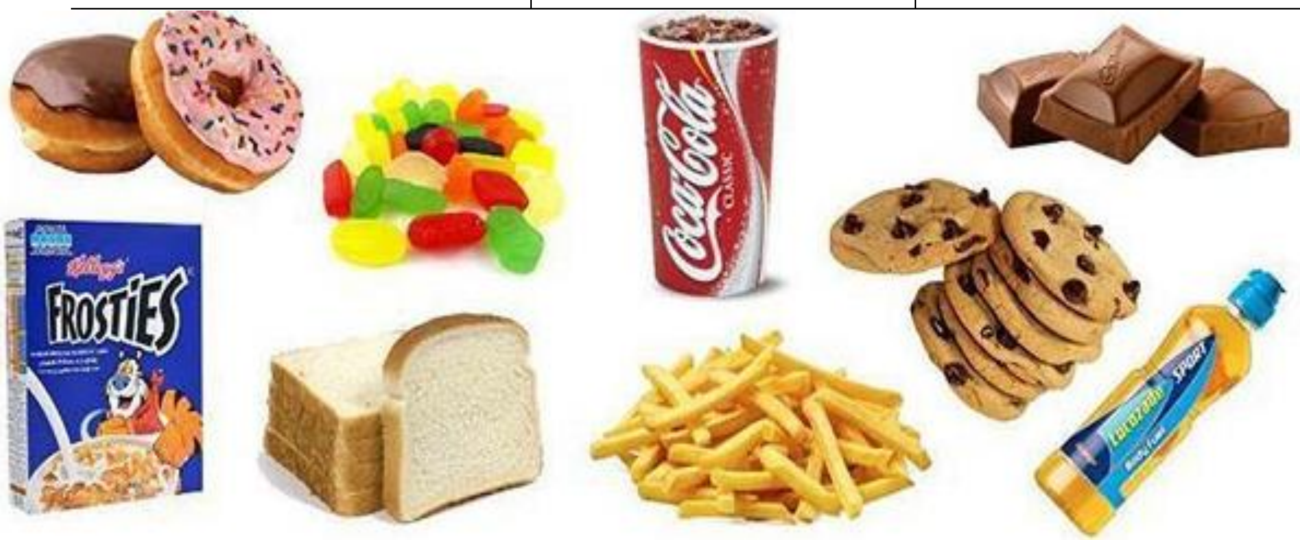
DIETARY CARBOHYDRATES

Poly-saccharides	**Starch**	**Bread, Potatoes, cereals**	**250-400 g/day**



DIETARY CARBOHYDRATES

Di-saccharides	Sucrose Lactose Maltose	Sugar, milk, sweets, cakes, etc	50-100 g/day



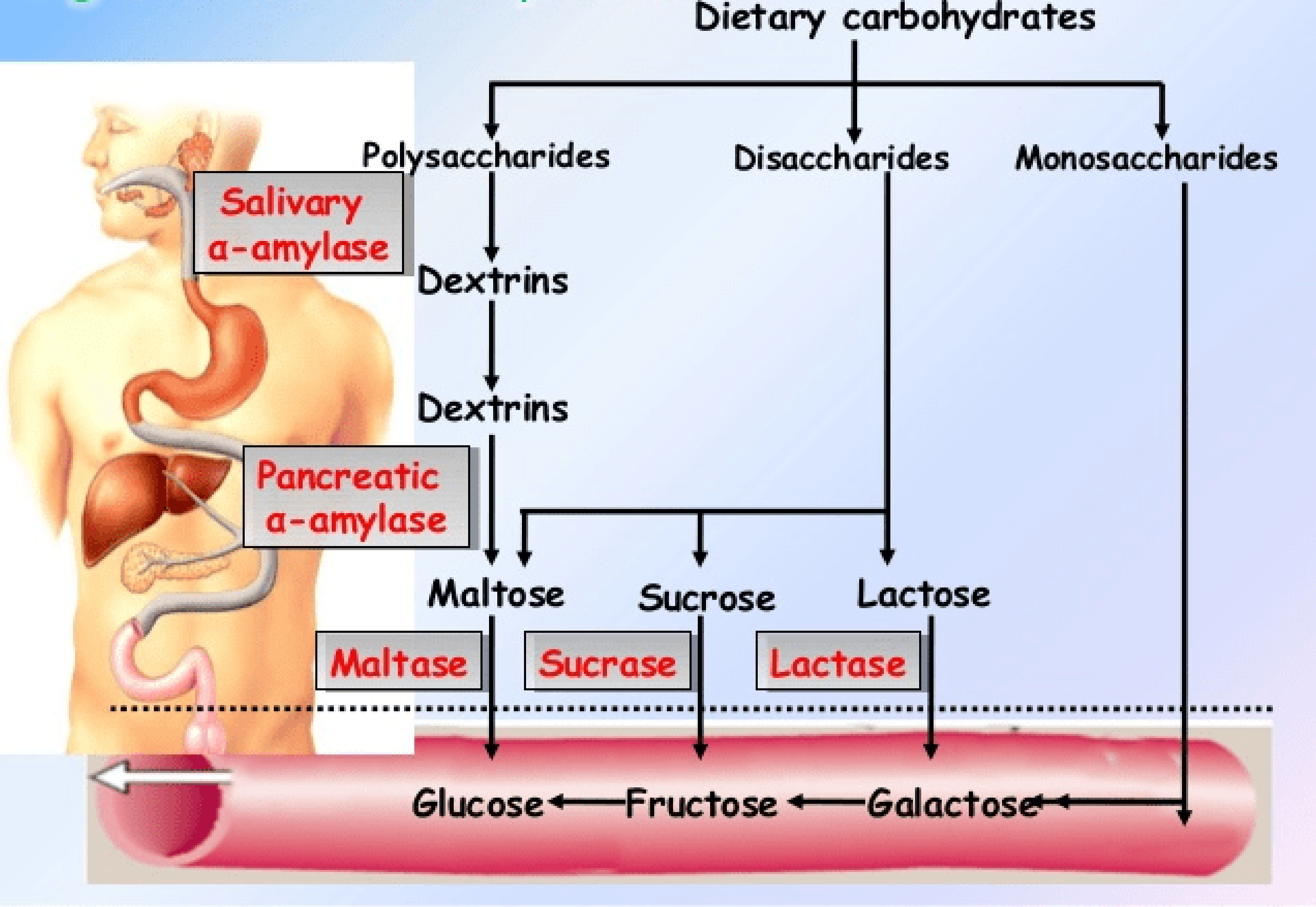
DIETARY CARBOHYDRATES

Mono-saccharides	Glucose, Fructose, galactose	Fuits, berryes	0-50 g/day

Digestion of carbohydrates

Section of GIT	*Enzymes*	*Localisation of enzymes*	*Products of hydrolysis*
Oral cavity	**amylase**	**saliva**	**Dextrins**
Duo-denum	**amylase**	**Pancreatic juice**	**Maltose, maltotriose, glucose, small branched dextrins**
Small intestine	**Oligo-1,6-glycosidase, amylo-1,6-glycosidase, maltase, lactase, sucrase**	**Brush border of the intestinal mucosal cells**	**Mono-saccharides**

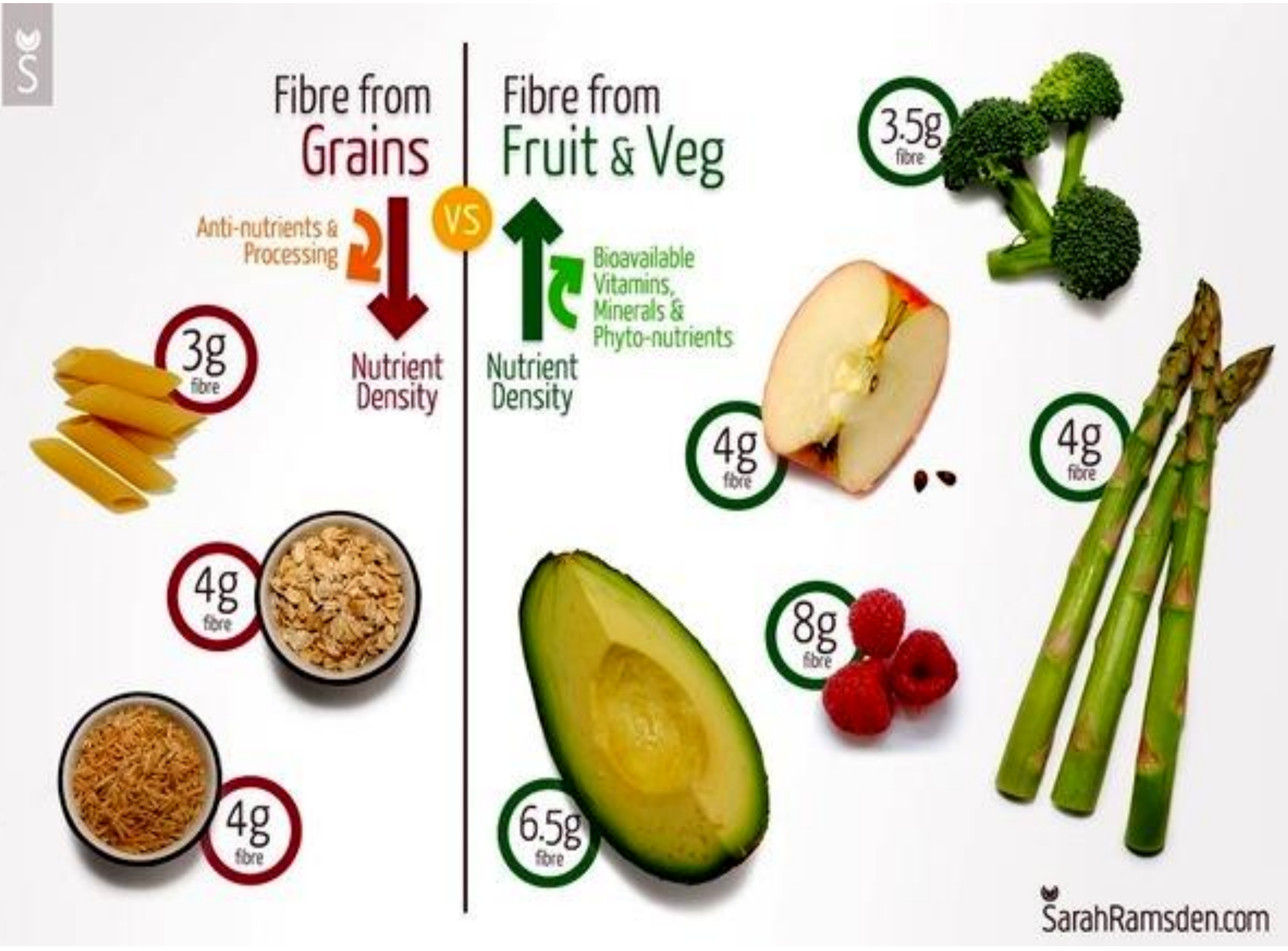
Digestion of Carbohydrates



Carbohydrates which are not hydrolysed in GIT(dietary fibre)

- **cellulose**
- **pectins**
- **lignins**

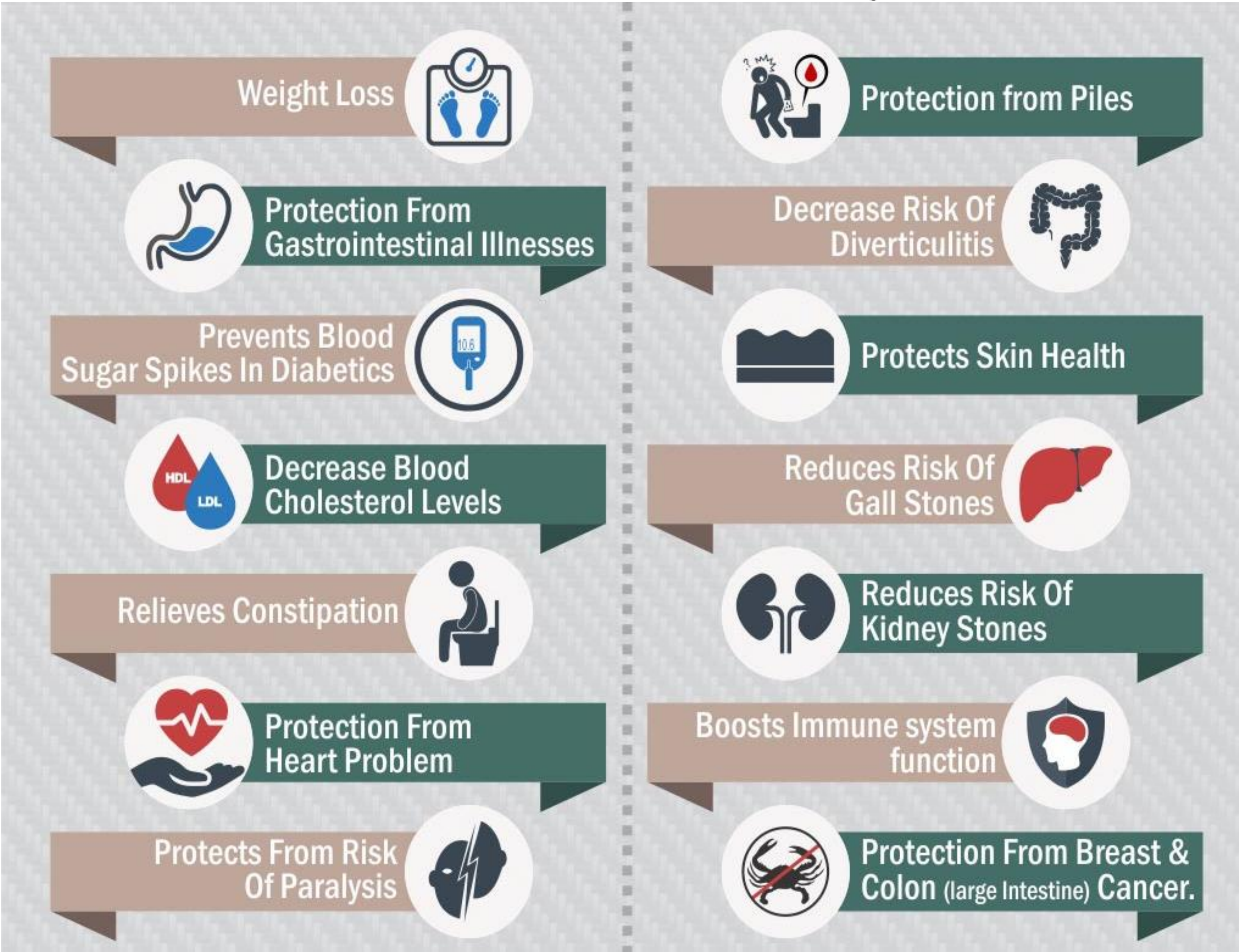
these compounds we receve from unprocessed cereals, vegetables and fruits.


Fibre from
Grains
VS
Fibre from
Fruit & Veg
Anti-nutrients &
Processing
Nutrient
Density
Bioavailable
Vitamins,
Minerals &
Phyto-nutrients
Nutrient
Density
3g
fibre
4g
fibre
4g
fibre
3.5g
fibre
4g
fibre
4g
fibre
8g
fibre
6.5g
fibre
SarahRamsden.com

Biological role of cellulose

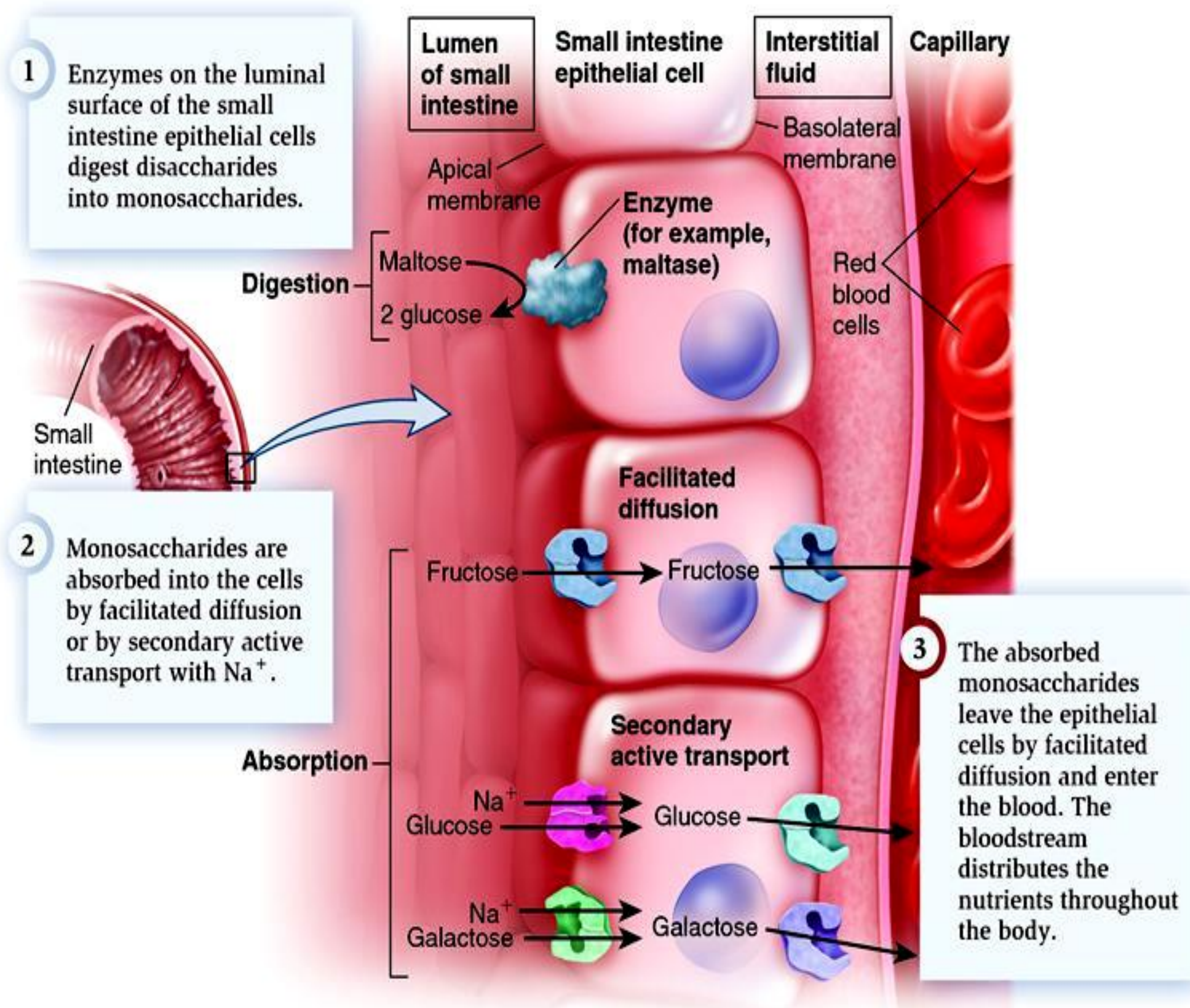
- bacterial medium
- intestinal peristalsis (regulation gut transit and motility)
- the basis of feces
- sorbent of different toxins

Health benefits of dietary fibers



Absorption of carbohydrates

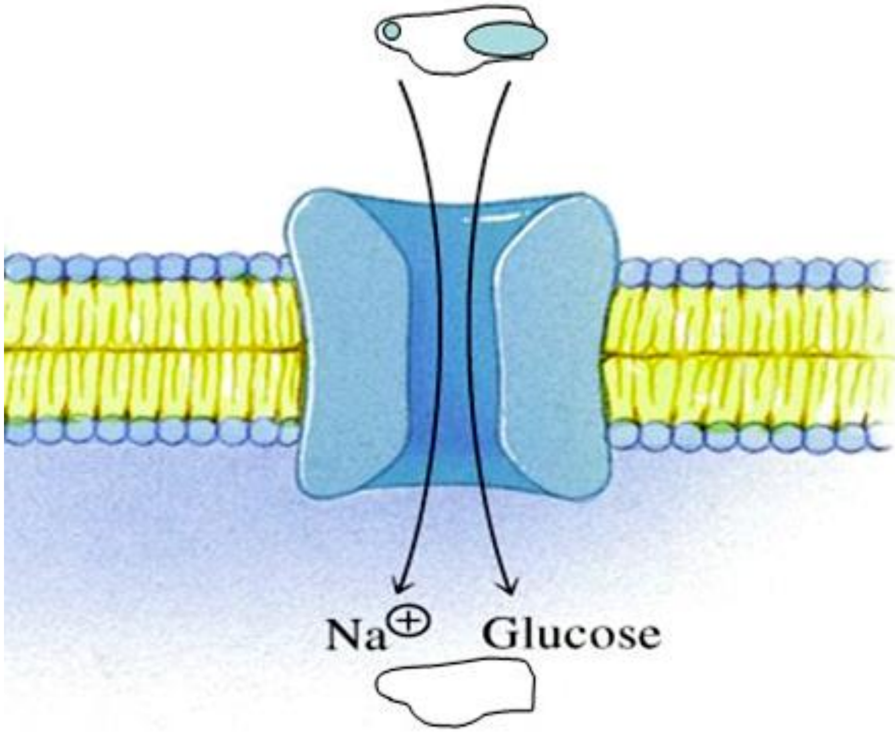
only monosaccharides are absorbed



1 Enzymes on the luminal surface of the small intestine epithelial cells digest disaccharides into monosaccharides.
Lumen of small intestine
Small intestine epithelial cell
Interstitial fluid
Capillary
Basolateral membrane
Apical membrane
Enzyme (for example, maltase)
Digestion
Maltose
2 glucose
Red blood cells
Small intestine
Facilitated diffusion
2 Monosaccharides are absorbed into the cells by facilitated diffusion or by secondary active transport with Na+.
Fructose
Fructose
3 The absorbed monosaccharides leave the epithelial cells by facilitated diffusion and enter the blood. The bloodstream distributes the nutrients throughout the body.
Secondary active transport
Absorption
Na+
Glucose
Glucose
Na+
Galactose
Galactose

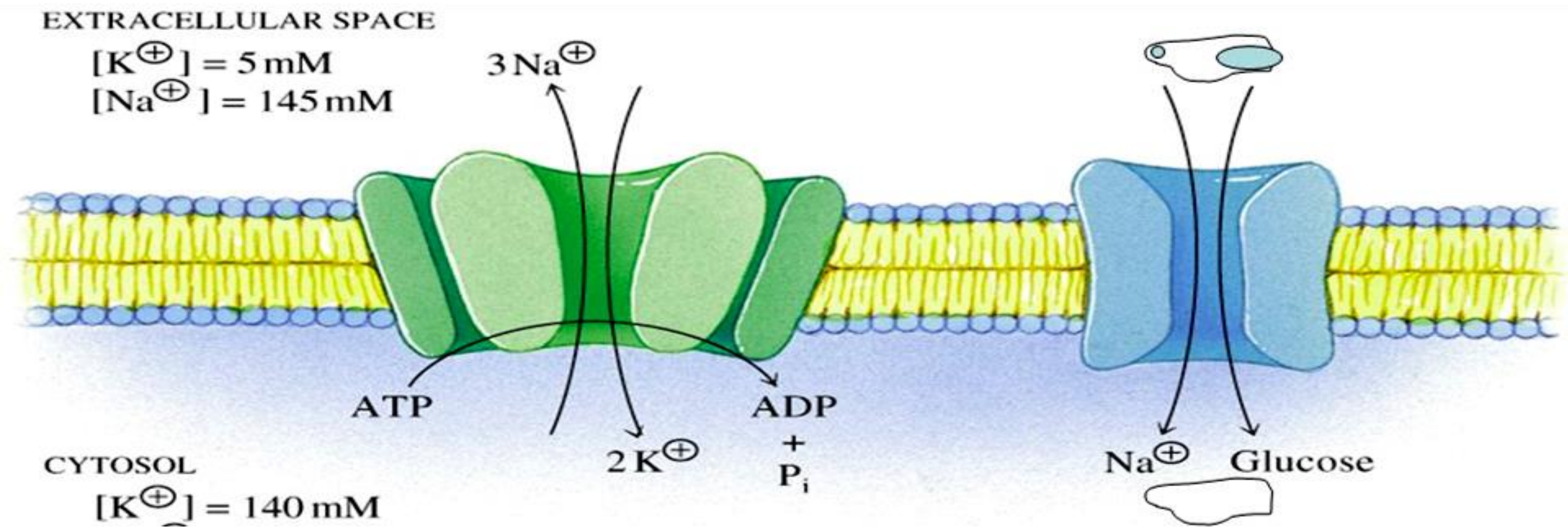
At the brush-border membrane glucose and galactose are transported by the Na^+-dependent glucose transporter.

This membrane-linked protein binds with glucose (galactose) and Na^+ and transports both into cytosol.



The Na^+ is thus transported down its concentration gradient, carrying glucose against its concentration gradient.

This transport mechanism is linked to Na^+-dependent ATPase, which then removes Na^+ from the cell in exchange for K^+, with the concomitant hydrolysis of ATP



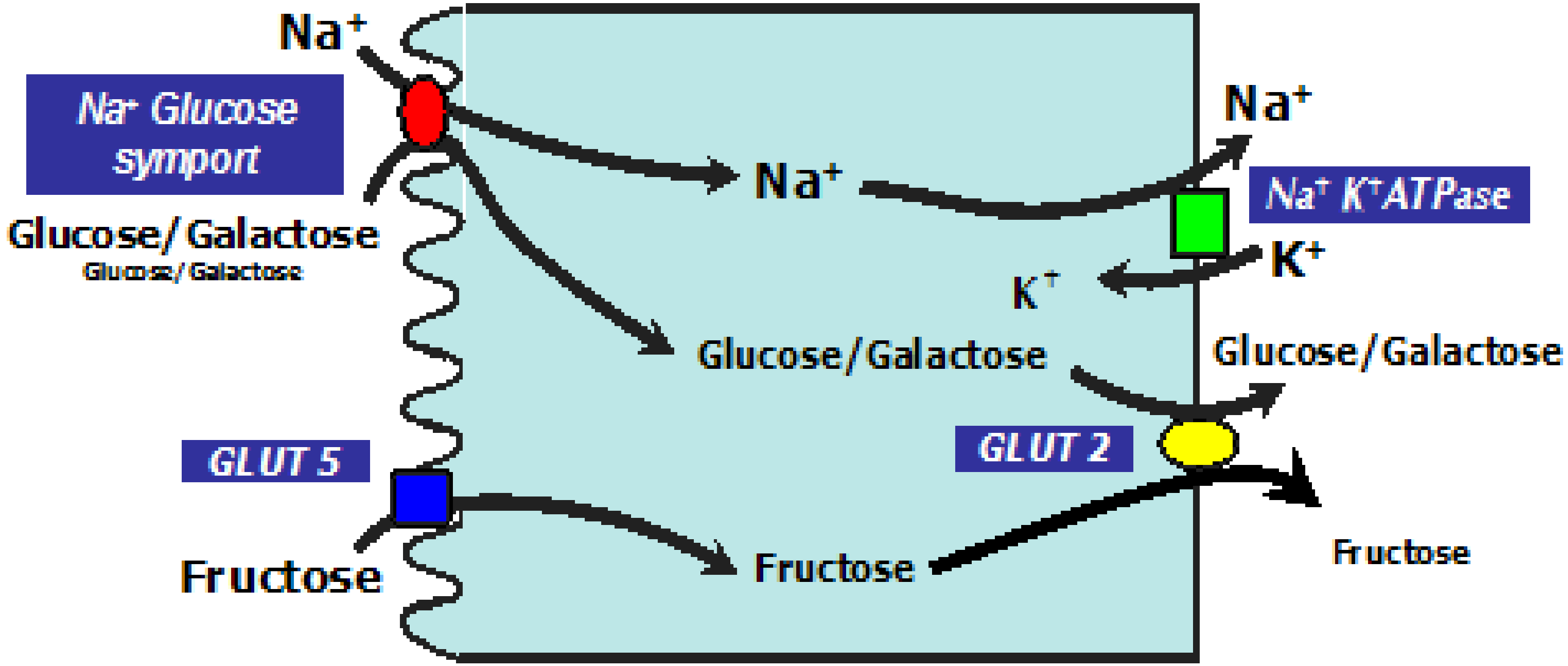
The transport of glucose (galactose) is thus an indirect active process (secondary active transport).

Glucose also can be transported by facilitated diffusion process involving a specific membrane-associated protein (GLUT)

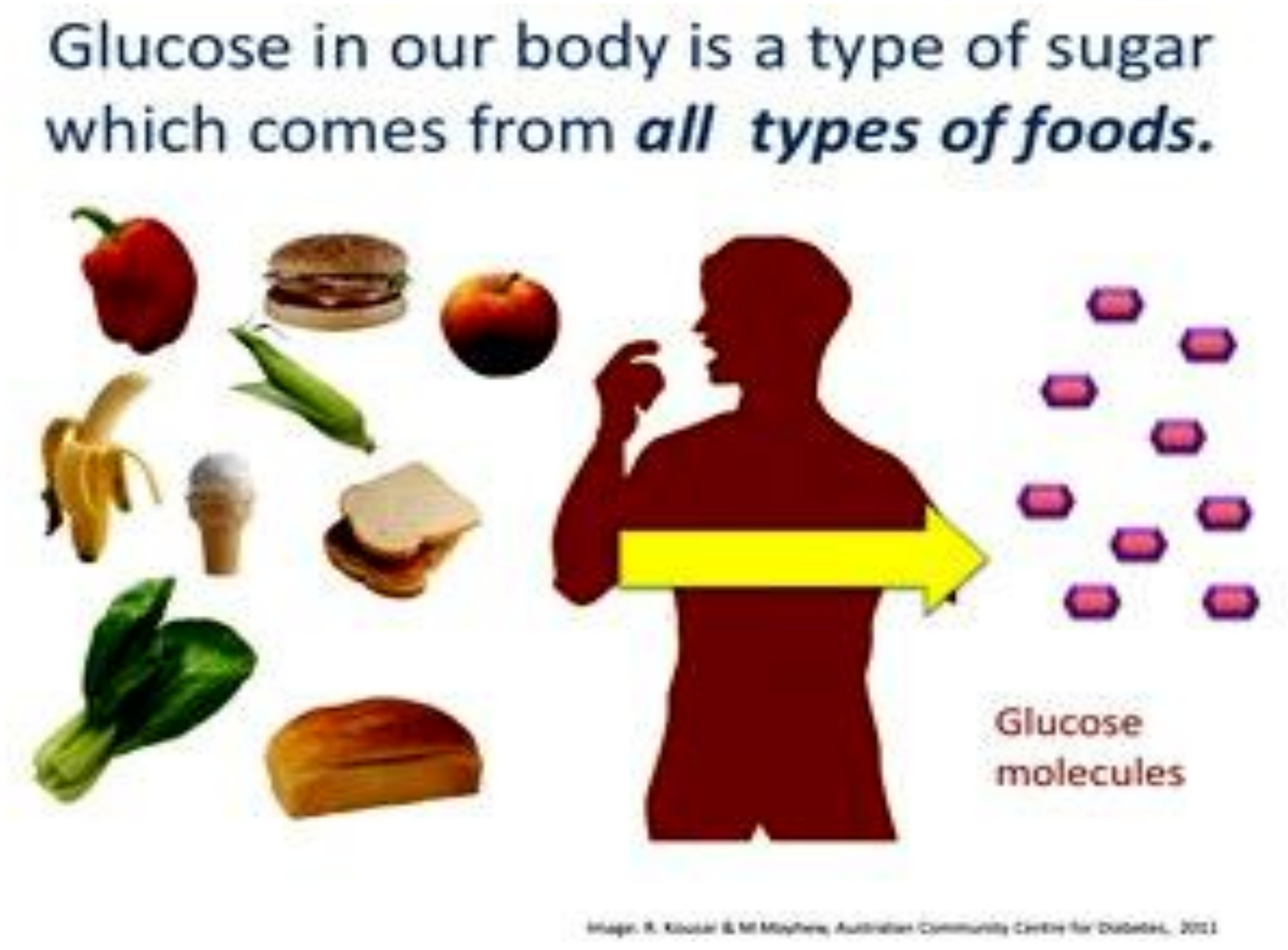
Other monosaccharides (**fructose, pentoses**) are absorbed by a **carrier-mediated diffusion**

Fructose is transported across the brush-border membrane by a facilitated diffusion process involving a specific membrane-associated protein, possibly glucose transporter (GLUT 5), which is present on the luminal side of the enterocyte, and GLUT 2 present on the antiluminal side.

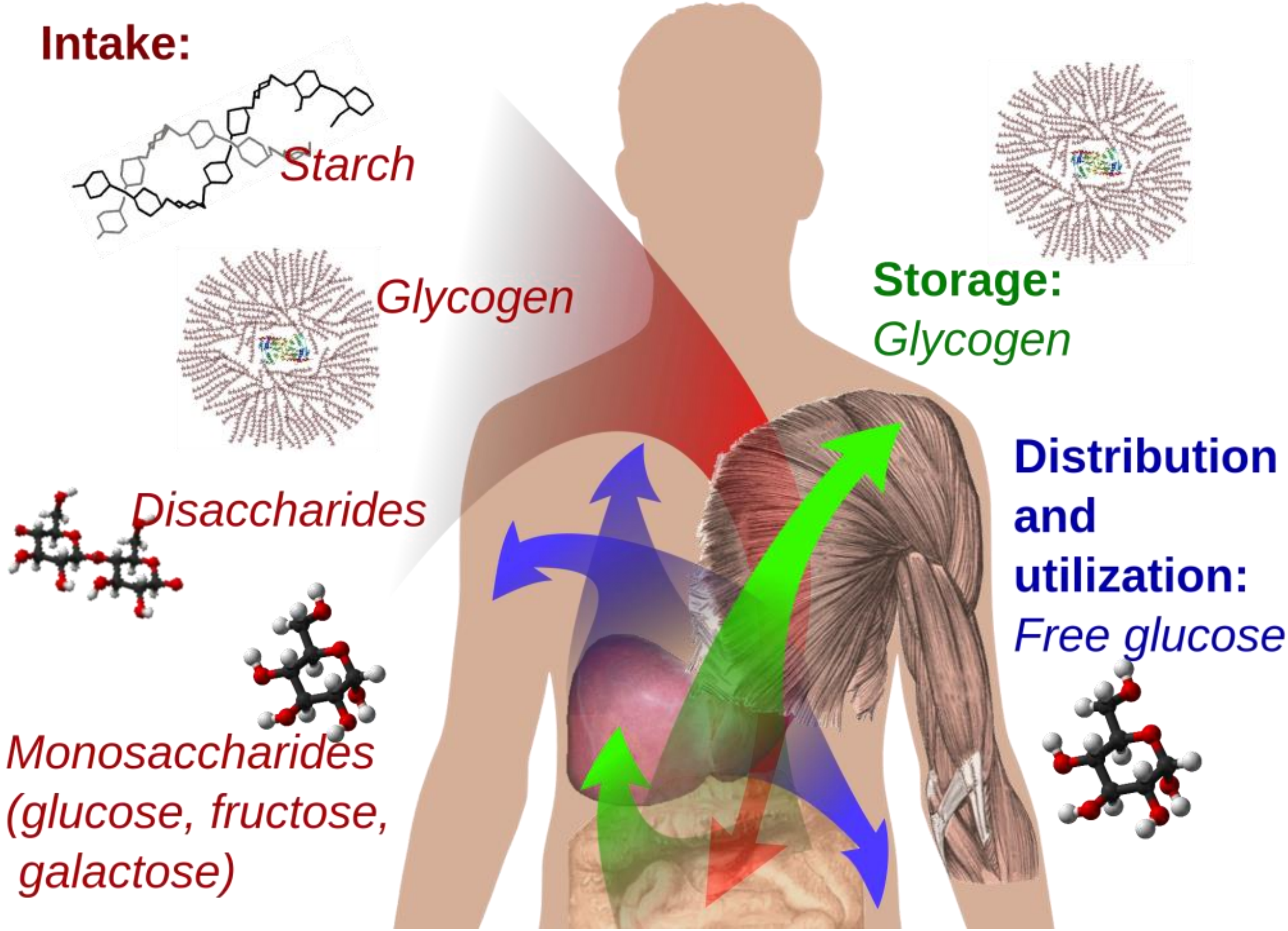
Intestinal Monosaccharide Transport



Glucose metabolism



Glucose metabolism



Entry of Glucose into cells

Glucose transporters are essential for facilitated diffusion of glucose into cells. The glucose transporter family comprises five major species, named GLUT 1 to GLUT 5

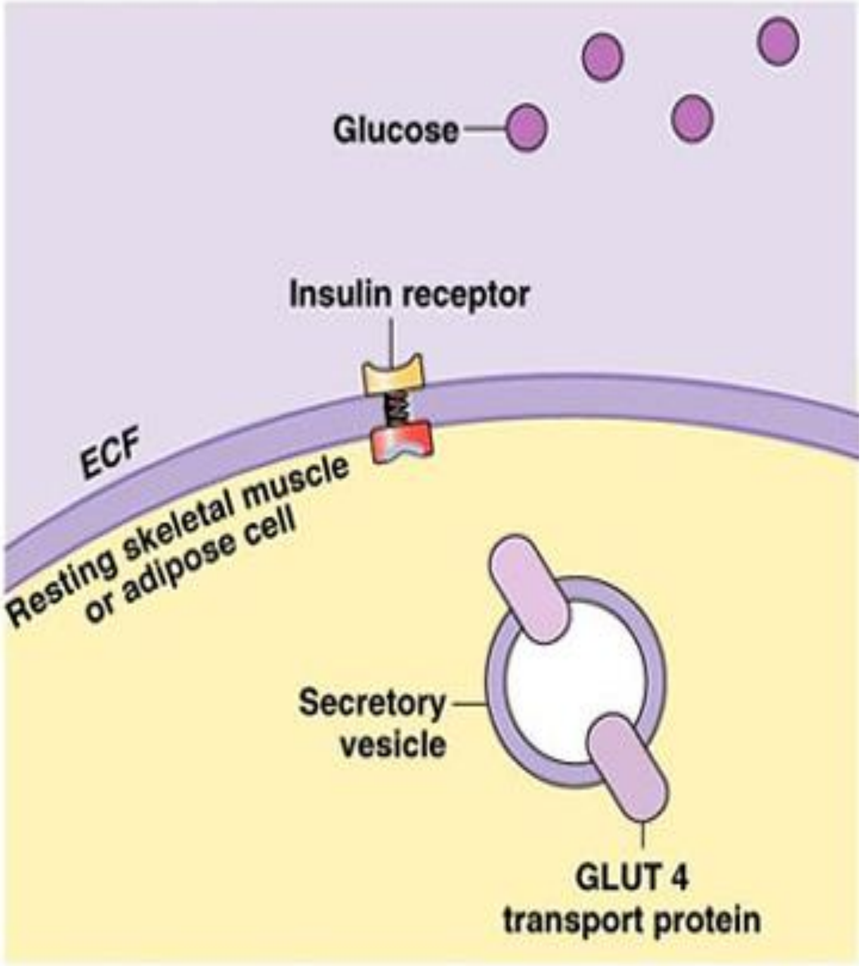
Glucose transporters

	Tissue Location	*Functions*
GLUT 1	Brain, kidney, colon, placenta, erythrocytes	Uptake of glucose
GLUT 2	Liver, pancreatic β cell, small intestine, kidney	Rapid uptake and release of glucose
GLUT 3	Brain, kidney, placenta	Uptake of glucose
GLUT 4	Heart and skeletal muscle, adipose tissue	Insulin-stimulated uptake of glucose
GLUT 5	Small intestine	Absorption of fructose

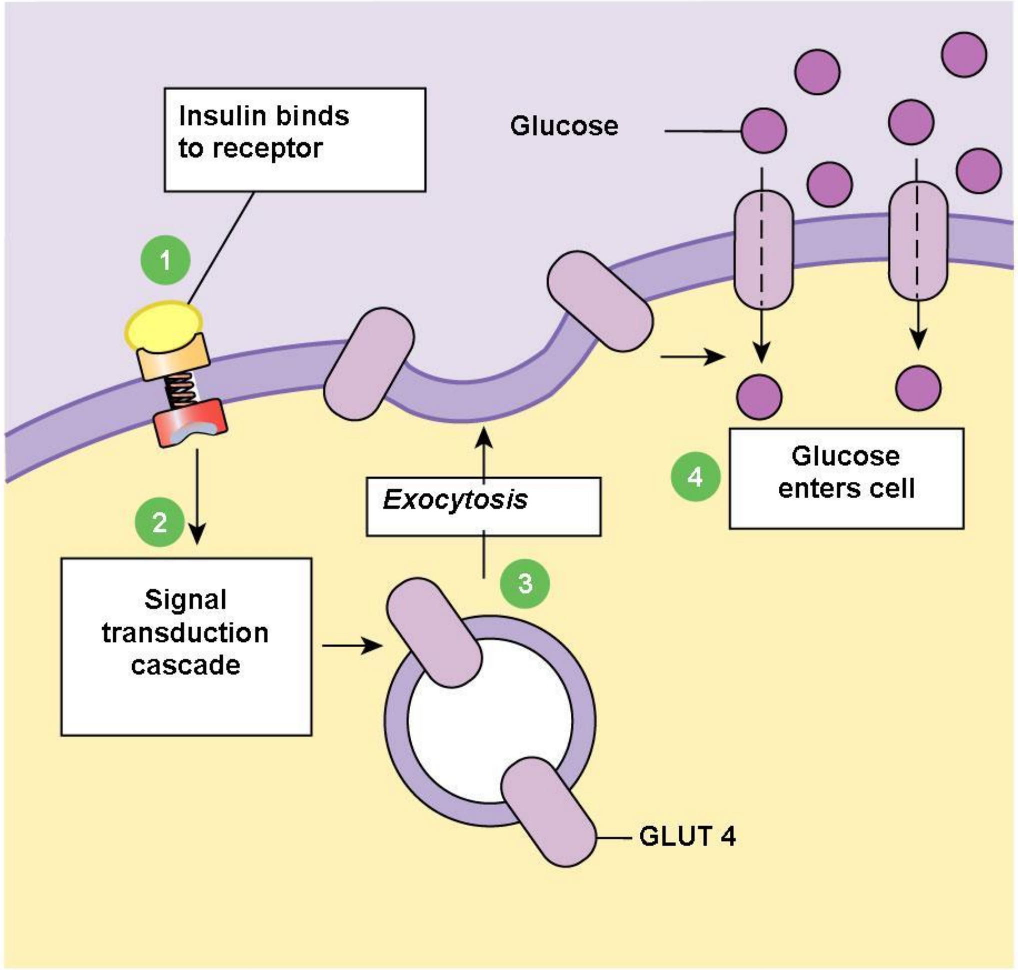
According latest data 15 GLUTS are encoded by human genome

Entry of Glucose into cells

1) **Insulin-independent transport system of glucose: not dependent on hormone insulin. This is operative in – hepatocytes, erythrocytes and brain.**
2) **Insulin-dependent transport system: muscles and adipose tissue (GLUT 4).**

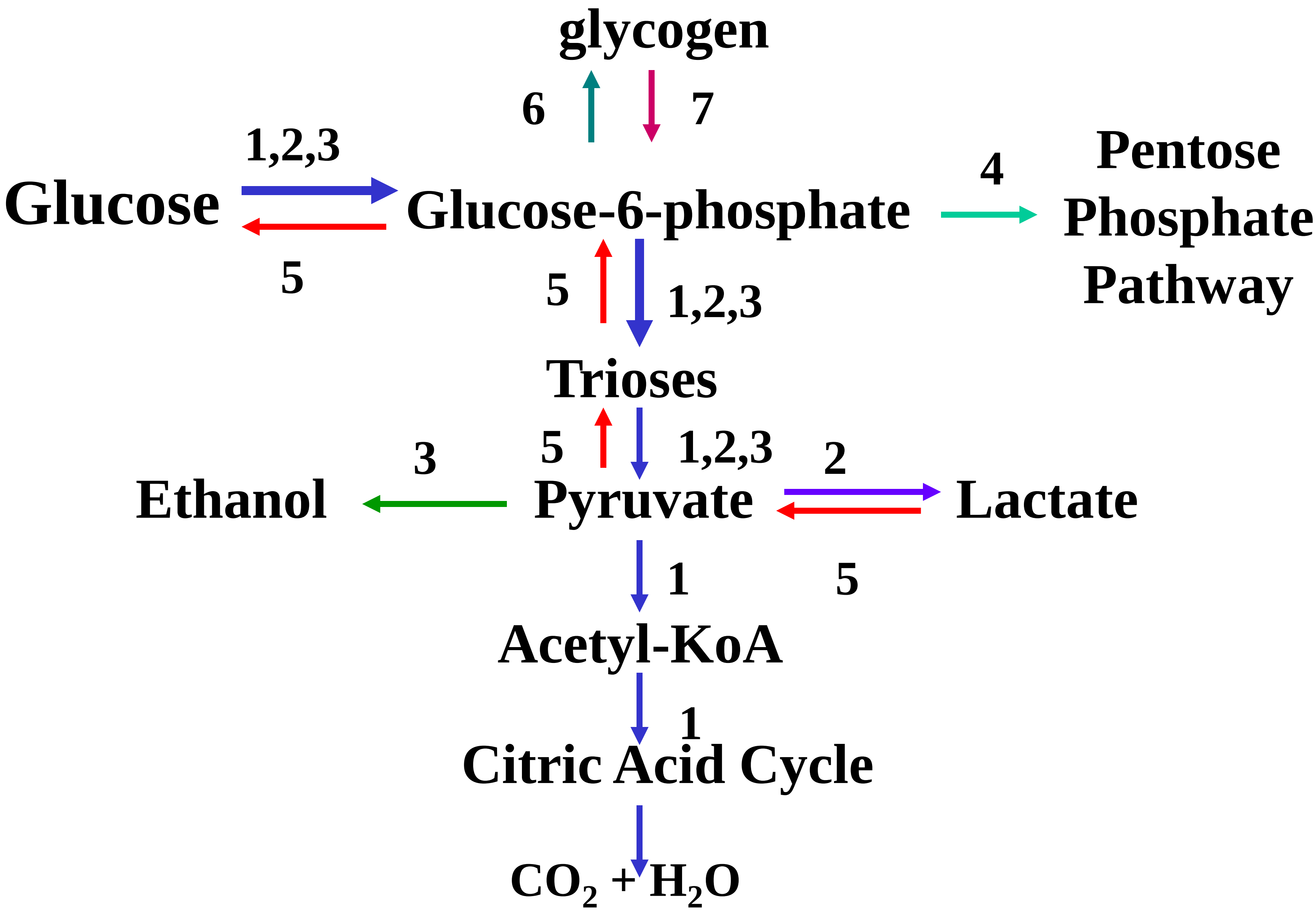


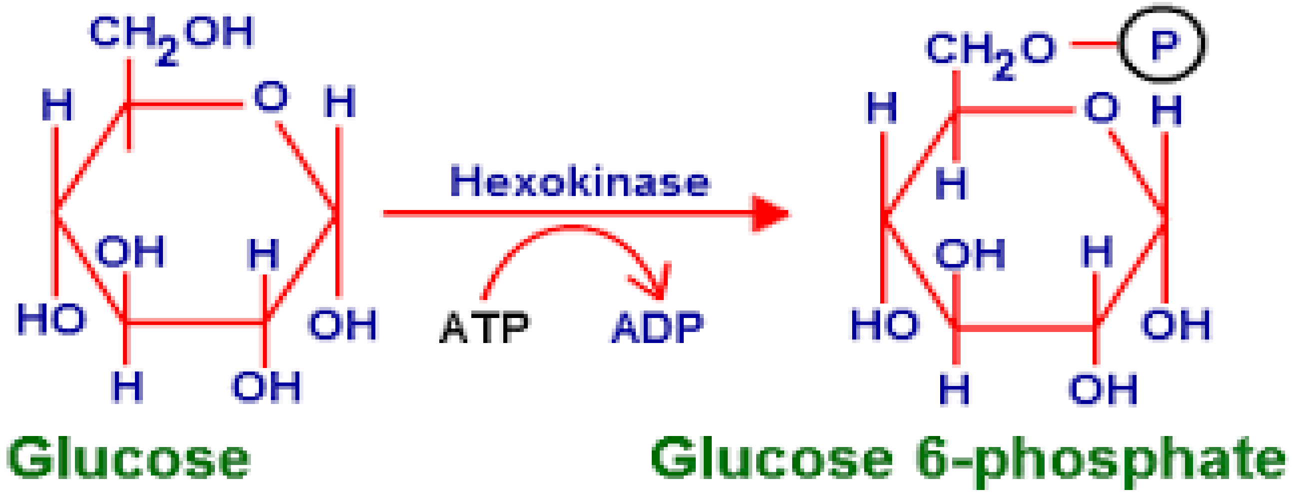
In the absence of insulin, glucose cannot enter the cell



Insulin signals the cell to insert GLUT 4 transporters into the membrane, allowing glucose to enter cell

The general scheme of glucose metabolism





CH2OH
H
O
H
OH
H
HO
OH
H
OH
Hexokinase
ATP
ADP
CH2O
P
H
O
H
H
OH
H
HO
OH
H
OH
Glucose
Glucose 6-phosphate

Phosphorylation of glucose is catalyzed by **hexokinase**

Hexokinase has a high affinity (low Km) for glucose, and is saturated under all normal conditions and so acts at a constant rate to provide glucose 6-phosphate to meet the cell's need.

Hexokinase is inhibited allosterically by its product, glucose 6-phosphate. Liver and pancreatic β islet cells also contain an isoenzyme of hexokinase, **glucokinase**.

The glucokinase differs from hexokinase:

- the glucose concentration at which glucokinase is half-saturated is higher than the usual concentration of glucose in the blood
- glucokinase is not inhibited by glucose 6-phosphate
- glucokinase is subject to inhibition by the reversible binding of a regulatory protein specific to liver.

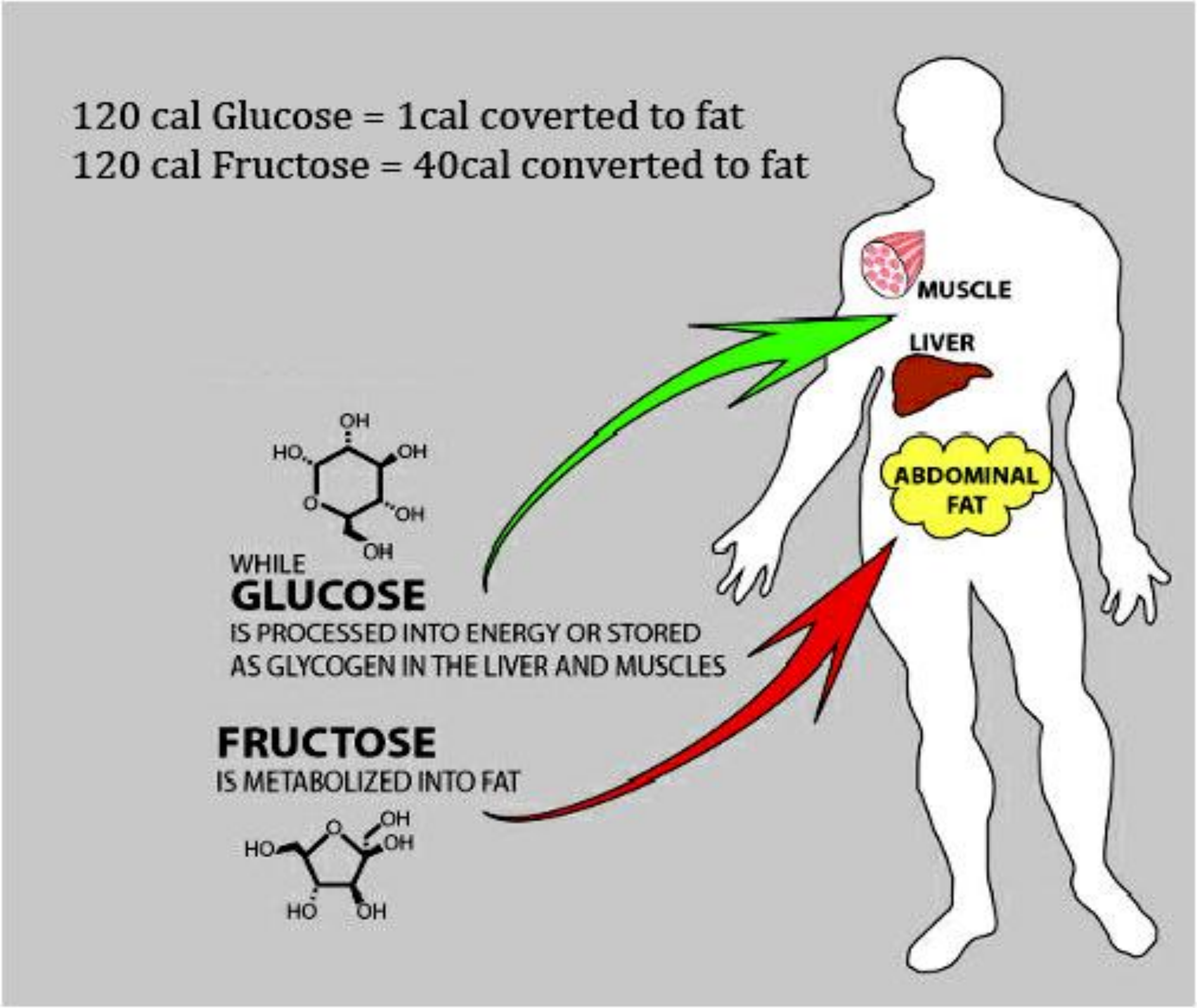
Metabolism of fructose

Fructose is present in fruit juices and honey.

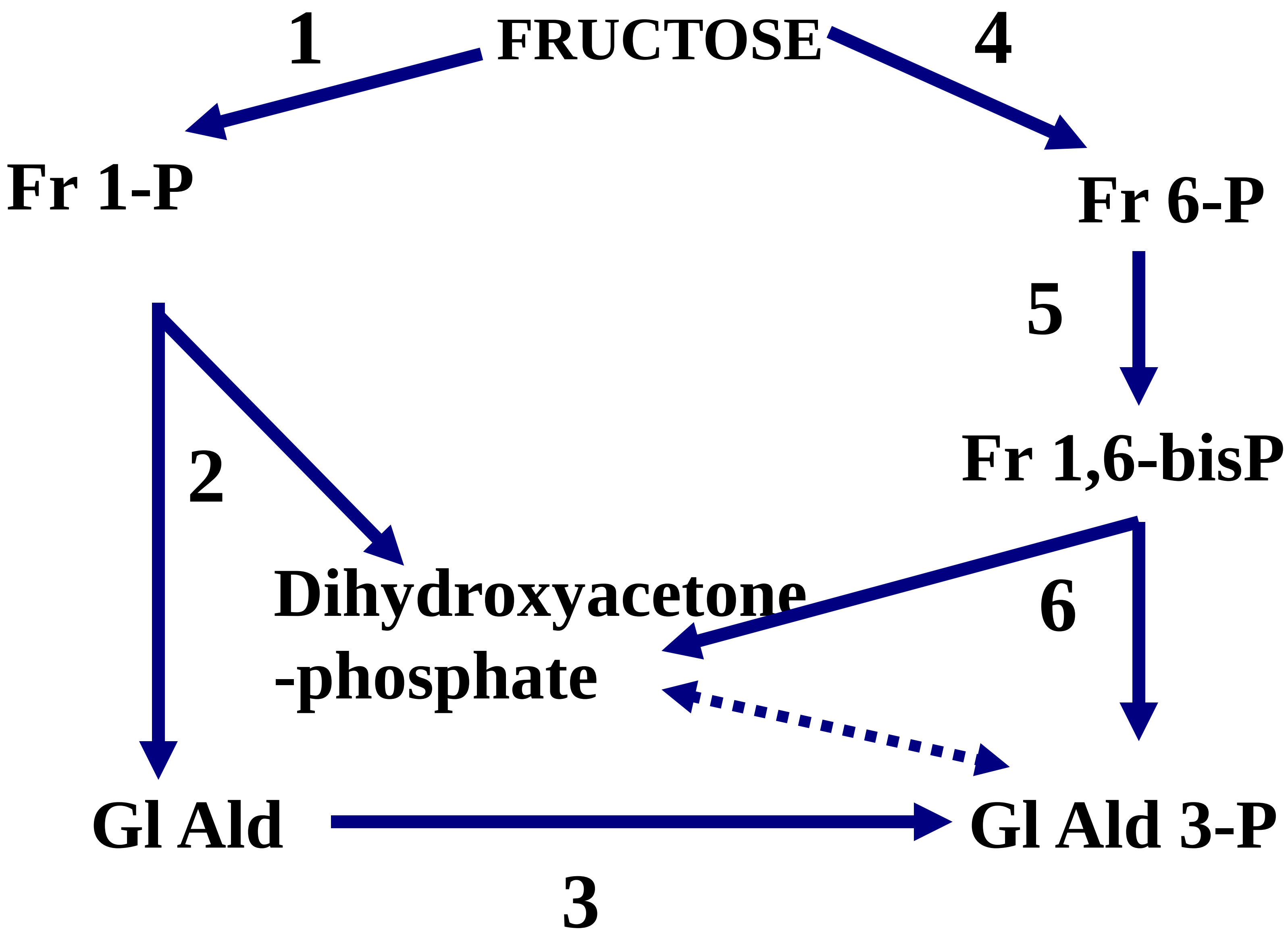
Chief dietary source is sucrose.

Metabolism of fructose

- **Fructose is easily metabolised and a good source of energy.**
- **Seminal fluid is rich in fructose and spermatozoa utilises fructose for energy.**
- **In diabetics, fructose metabolism through 'sorbitol' pathway may account for the development of cataract.**
- **Excess dietary fructose is harmful - leads to increased synthesis of TAG.**

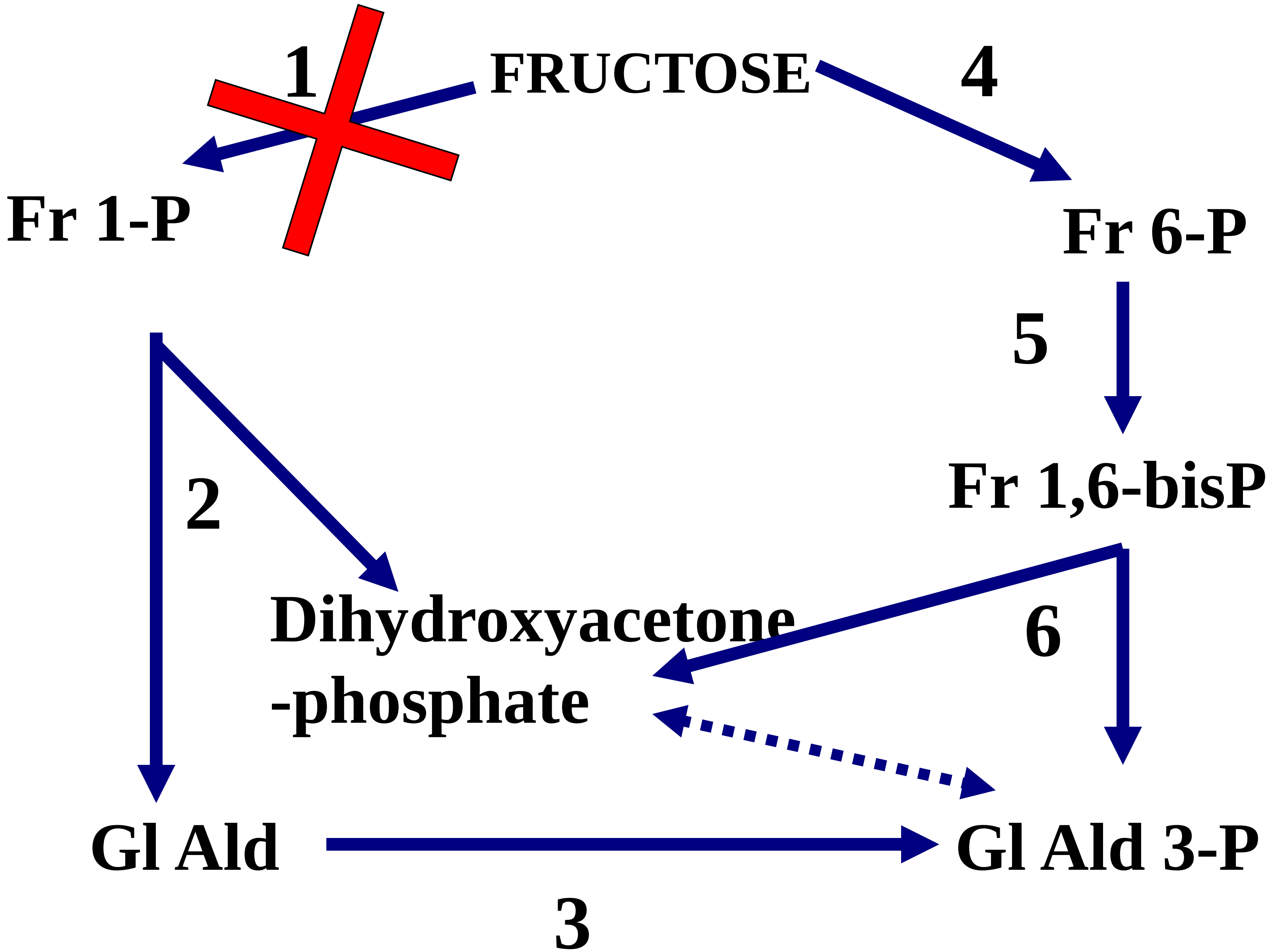

120 cal Glucose = 1cal coverted to fat
120 cal Fructose = 40cal converted to fat
MUSCLE
LIVER
ABDOMINAL FAT
OH
HO
OH
O
OH
OH
WHILE
GLUCOSE
IS PROCESSED INTO ENERGY OR STORED AS GLYCOGEN IN THE LIVER AND MUSCLES
FRUCTOSE
IS METABOLIZED INTO FAT
O
OH
HO
OH
HO
OH

Metabolism of fructose

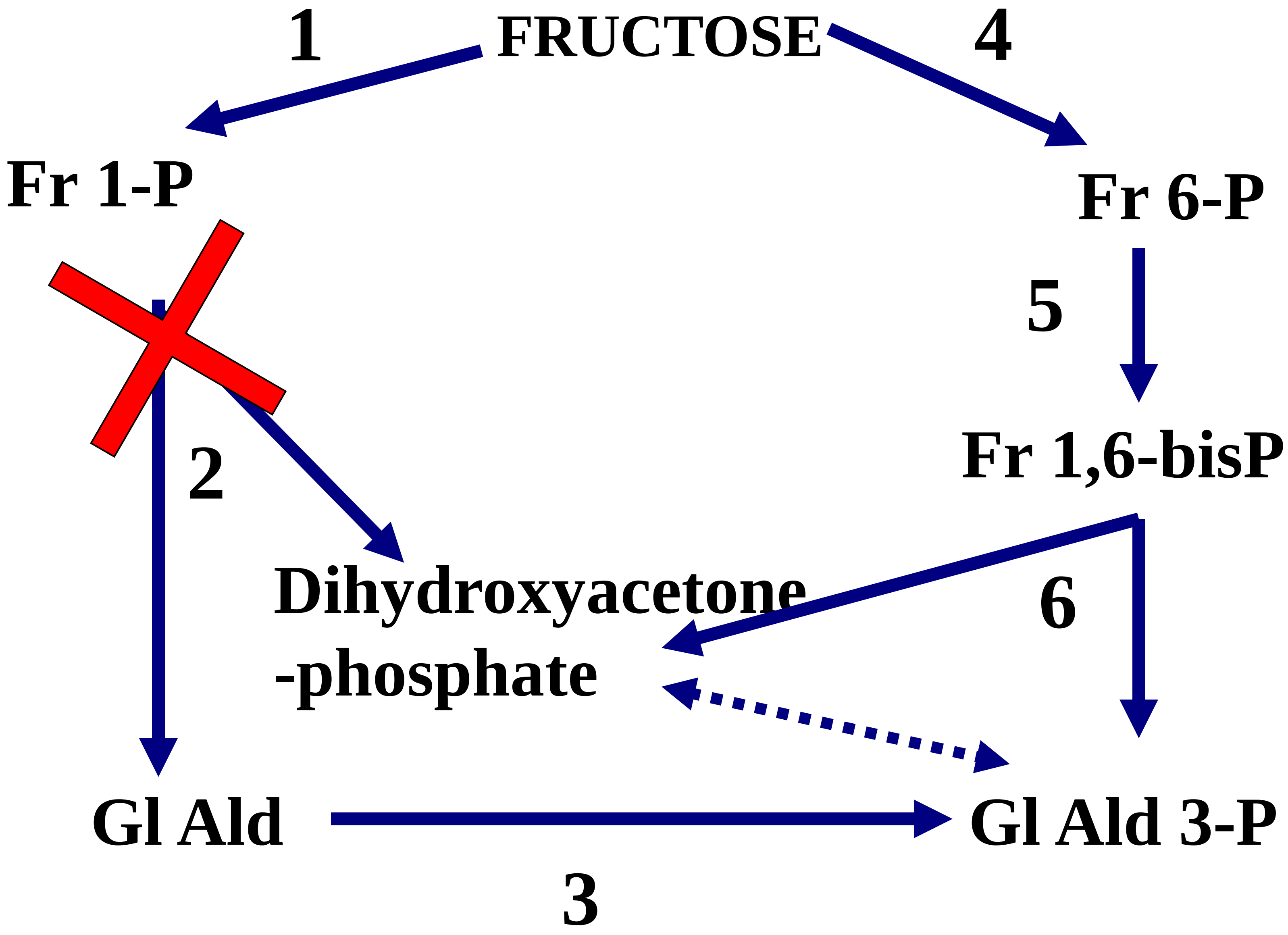


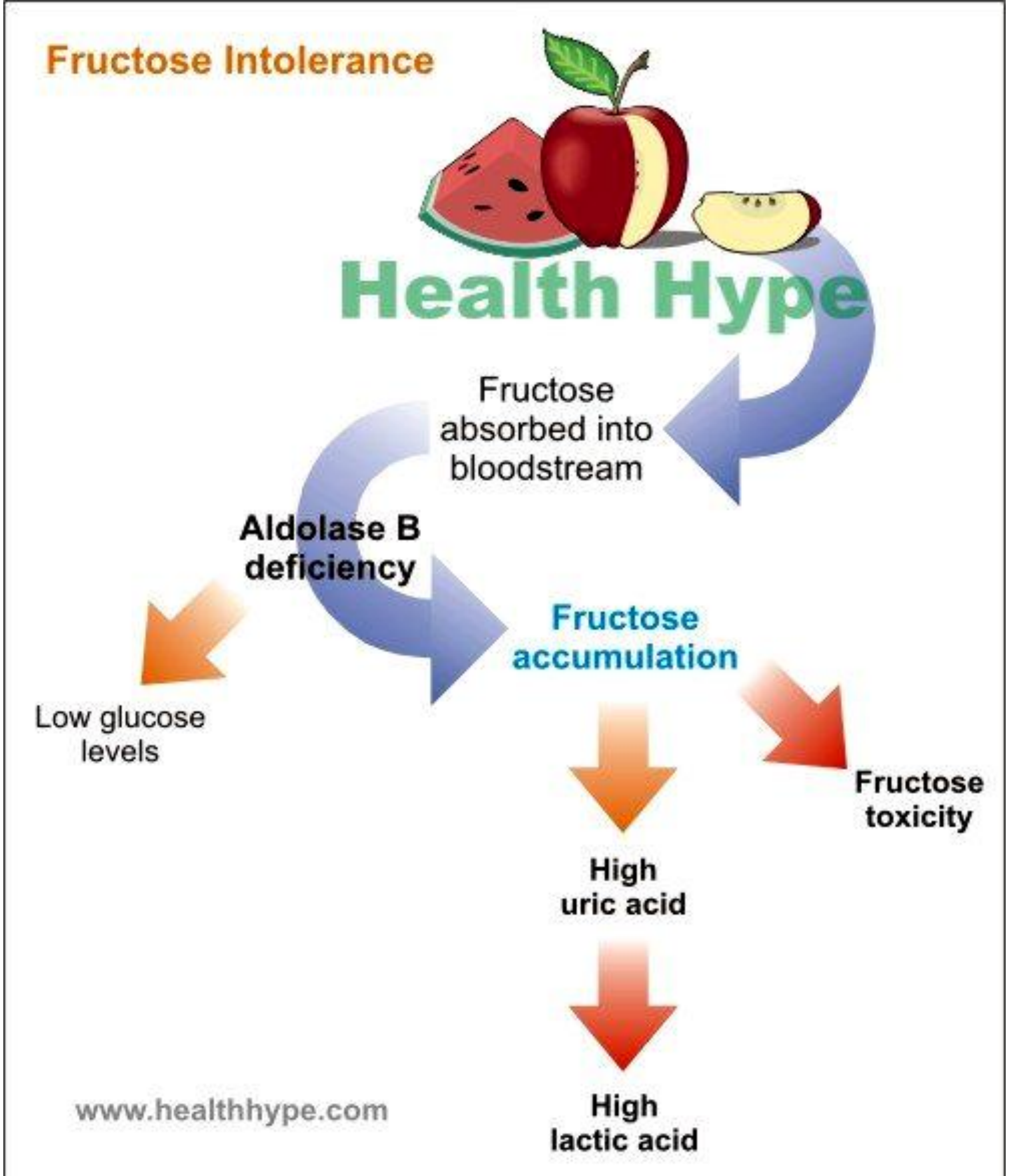
1. **Fructokinase**
2. **Fructose 1-phosphate aldolase (Aldolase B)**
3. **Triokinase**
4. **Hexokinase**
5. **Phosphofructokinase**
6. **Fructose 1.6-bisphasphate aldolase (Aldolase A)**

Essential fructosuria



Hereditary fructose intolerance




Fructose Intolerance
Health Hype
Fructose absorbed into bloodstream
Aldolase B deficiency
Fructose accumulation
Low glucose levels
High uric acid
Fructose toxicity
High lactic acid
www.healthhype.com

Hereditary Fructose Intolerance:

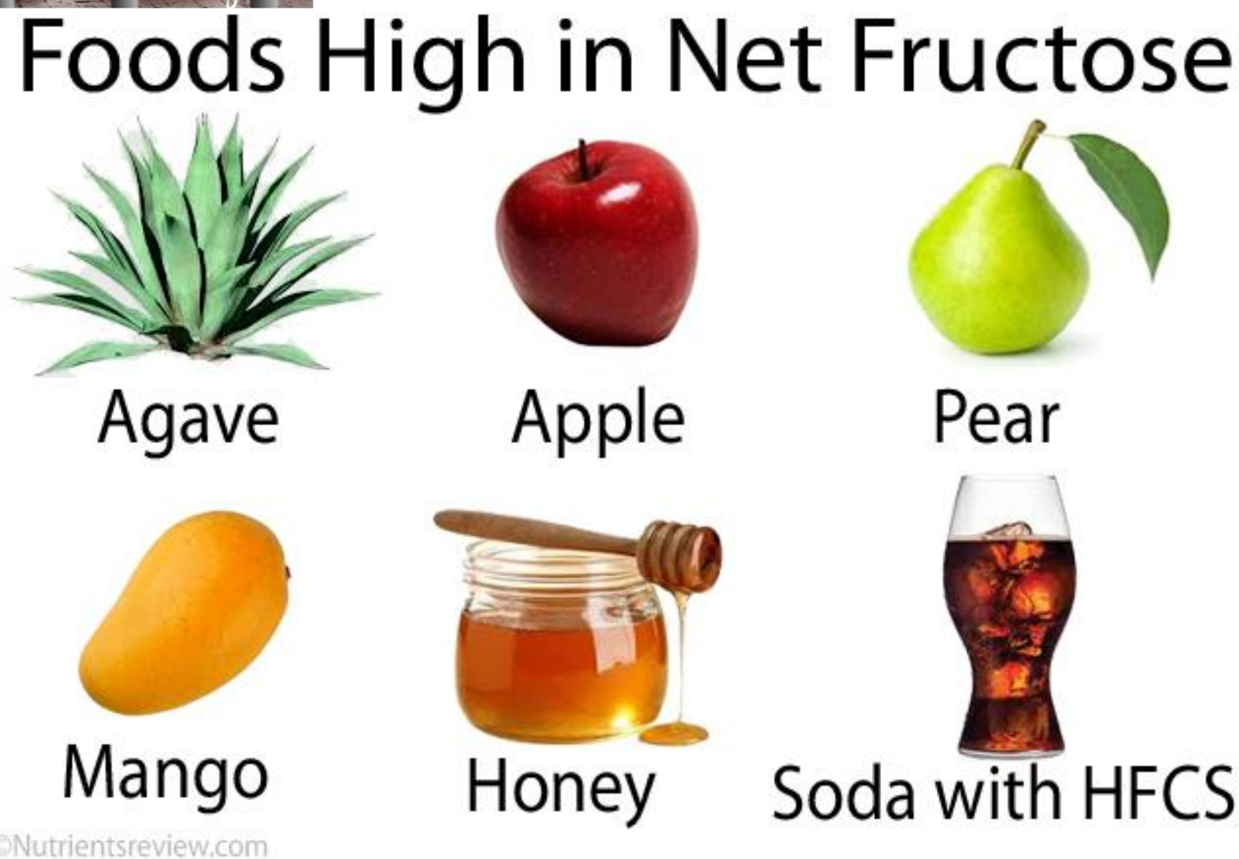
manifesting with severe clinical features.

- excessive and prolonged rise of fructose and fructose-1-P (↑) in blood;
- blood glucose falls (↓) **(hypoglycaemia). Accompanied by:**
- nausea and vomiting (may be haemorrhagic),
- profuse sweating

After cessation of symptoms,

- slight icterus, albuminuria, and aminoaciduria.

	Fructose Disorders	
	Essential Fructosuria	Hereditary Fructose Intolerance
Deficiency	Fructokinase	Aldolase B
Symptoms	None	Hypoglycemia Hepatomegaly Jaundice Vomiting
Treatment	None Needed	Avoid Sucrose & Fructose


Foods High in Net Fructose
Agave
Apple
Pear
Mango
Honey
Soda with HFCS
©Nutrientsreview.com

Galactose metabolism

Disaccharide lactose present in milk – principle source of of galactose.

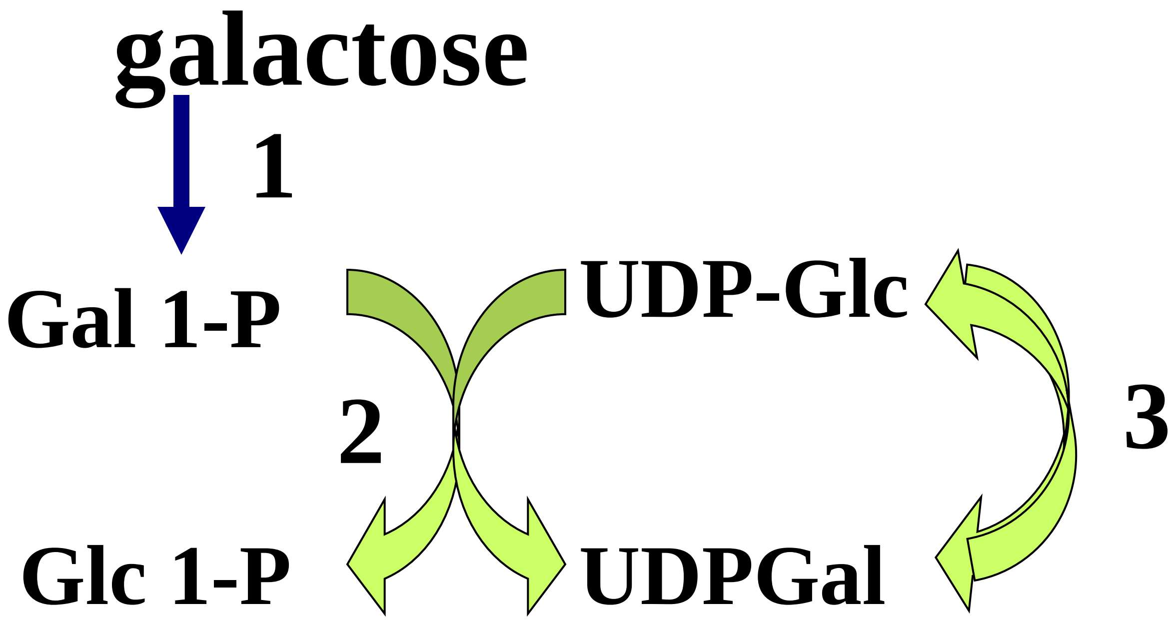
Lactase of intestinal mucosal cells hydrolyses lactose to galactose and glucose.

Within cell galactose is produced by lysosomal degradation of glycoproteins and glycolipids.

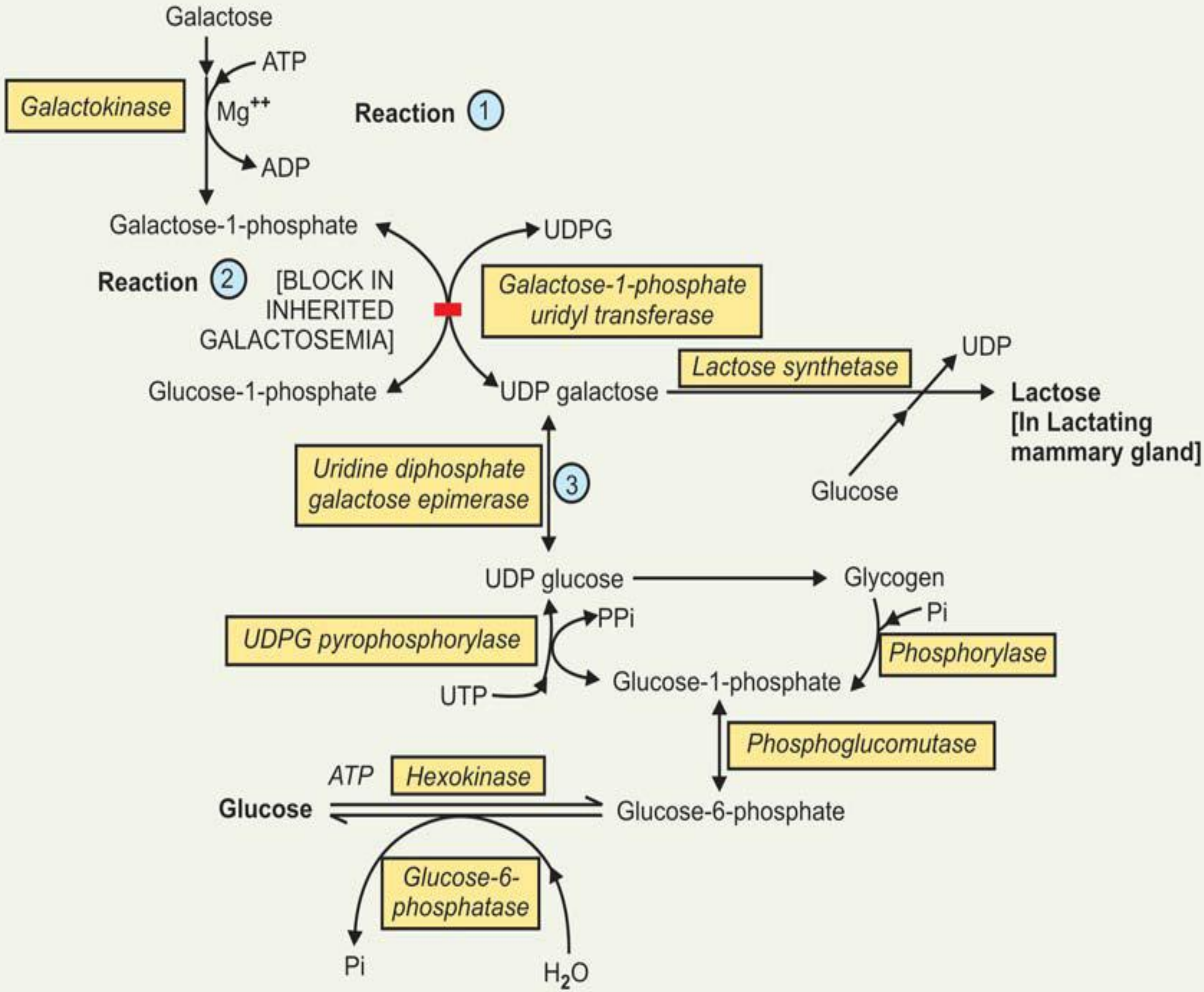
Galactose metabolism

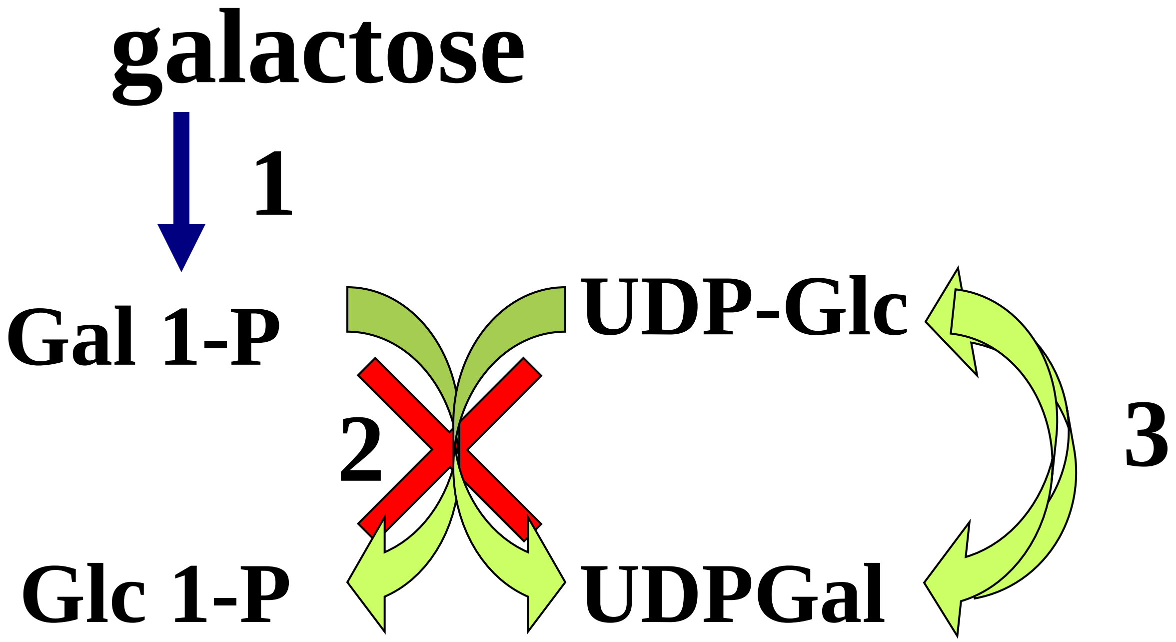
- **Galactose is required in lactating mammary gland for synthesis of lactose for breast milk.**
- **Galactose is utilised in brain and nervous tissues for synthesis of glycolipids (cerebrosides and gangliosides).**
- **Galactose is required for synthesis of chondromucoids and mucoproteins.**

Metabolism of galactose



1. **Galactokinase**
2. **Galactose 1-phosphate uridyl transferase**
3. **Uridine diphosphogalactose 4-epimerase**


Galactose
ATP
Galactokinase
Mg++
Reaction 1
ADP
Galactose-1-phosphate
UDPG
Reaction 2
[BLOCK IN INHERITED GALACTOSEMIA]
Galactose-1-phosphate uridyl transferase
UDP
Lactose synthetase
Glucose-1-phosphate
UDP galactose
Lactose [In Lactating mammary gland]
Uridine diphosphate galactose epimerase
3
Glucose
UDP glucose
Glycogen
PPi
Pi
UDPG pyrophosphorylase
Phosphorylase
UTP
Glucose-1-phosphate
Phosphoglucomutase
ATP
Hexokinase
Glucose
Glucose-6-phosphate
Glucose-6-phosphatase
Pi
H2O



Inherited deficiency of certain enzymes in pathway of galactose metabolism produces inherited disorder **“Galactosemia”**

Galactosemia:

An inherited disorder, in which there is inability to convert galactose to glucose in normal manner.

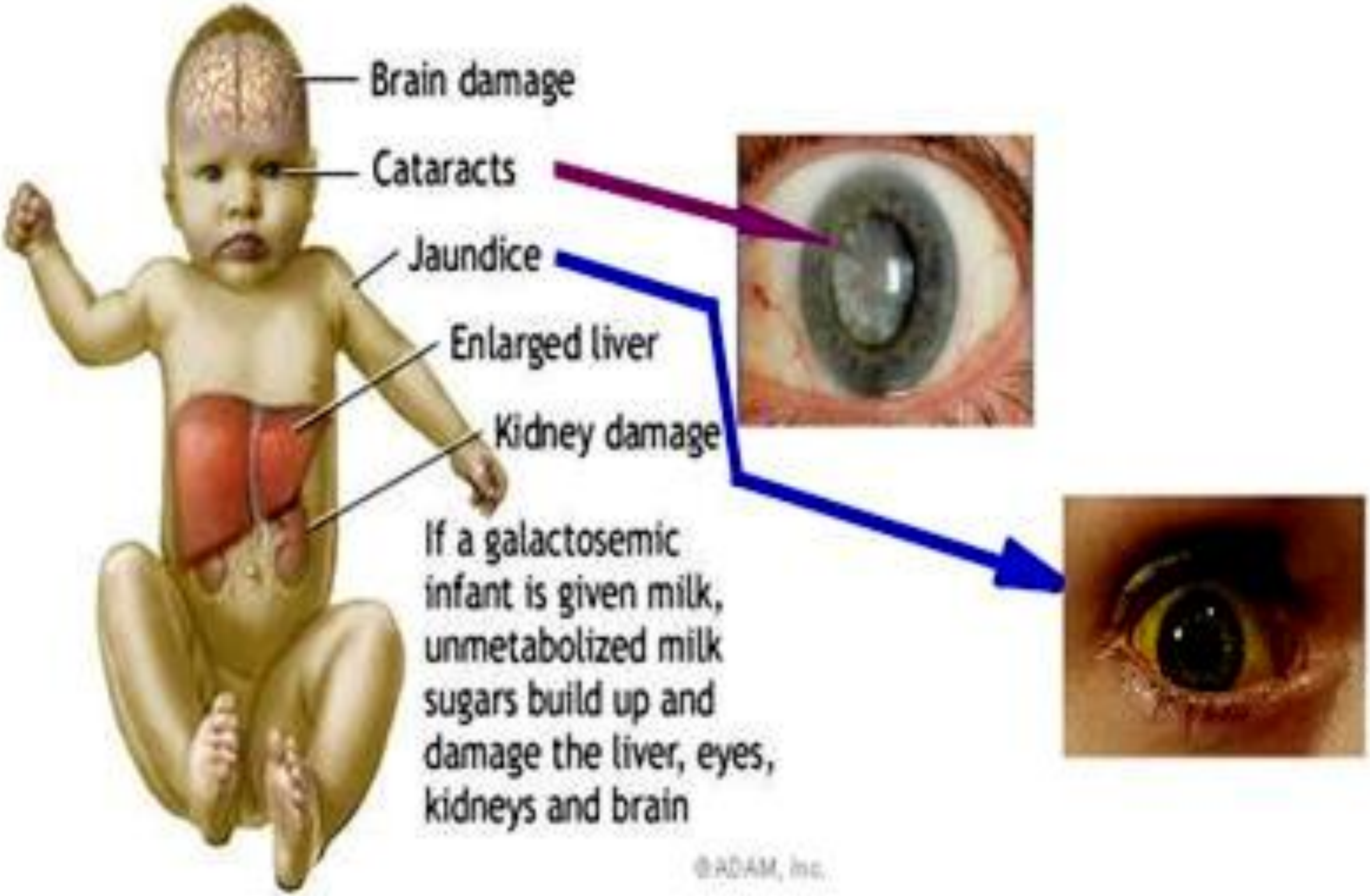
Infants appear normal at birth but later:

- **failure to thrive, becomes lethargic, may vomit, hypoglycaemia.**
- **may manifest jaundice, which may be prolonged in neonatal period**

Galactosemia:

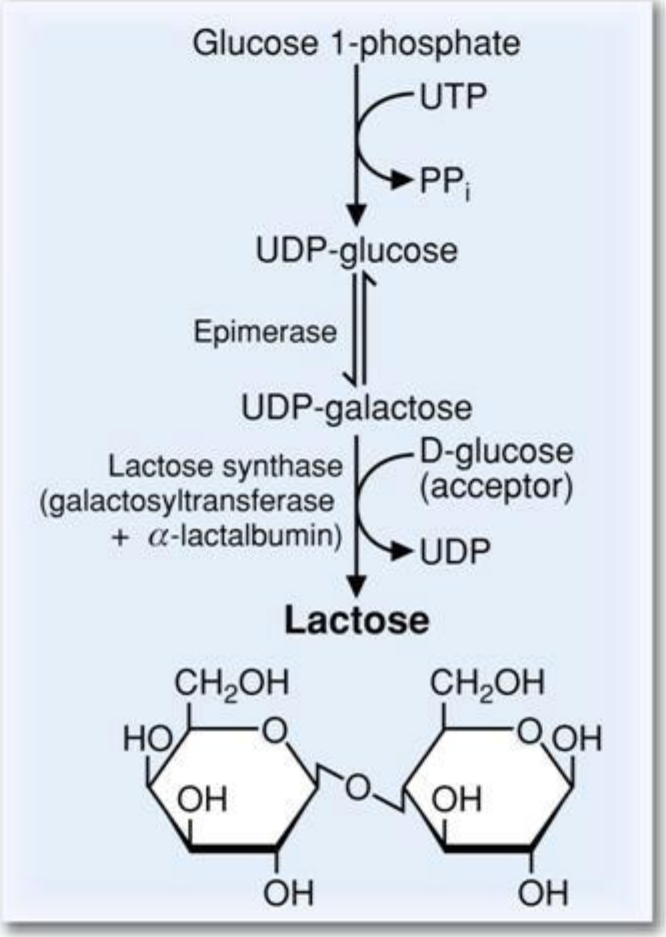
After 2 to 3 months:

- **Liver: may show fatty infiltration and lead to cirrhosis liver.**
- **Mental retardation: due to accumulation of galactose and galactose-1-P in cerebral cortex.**
- **Development of cataracts.**

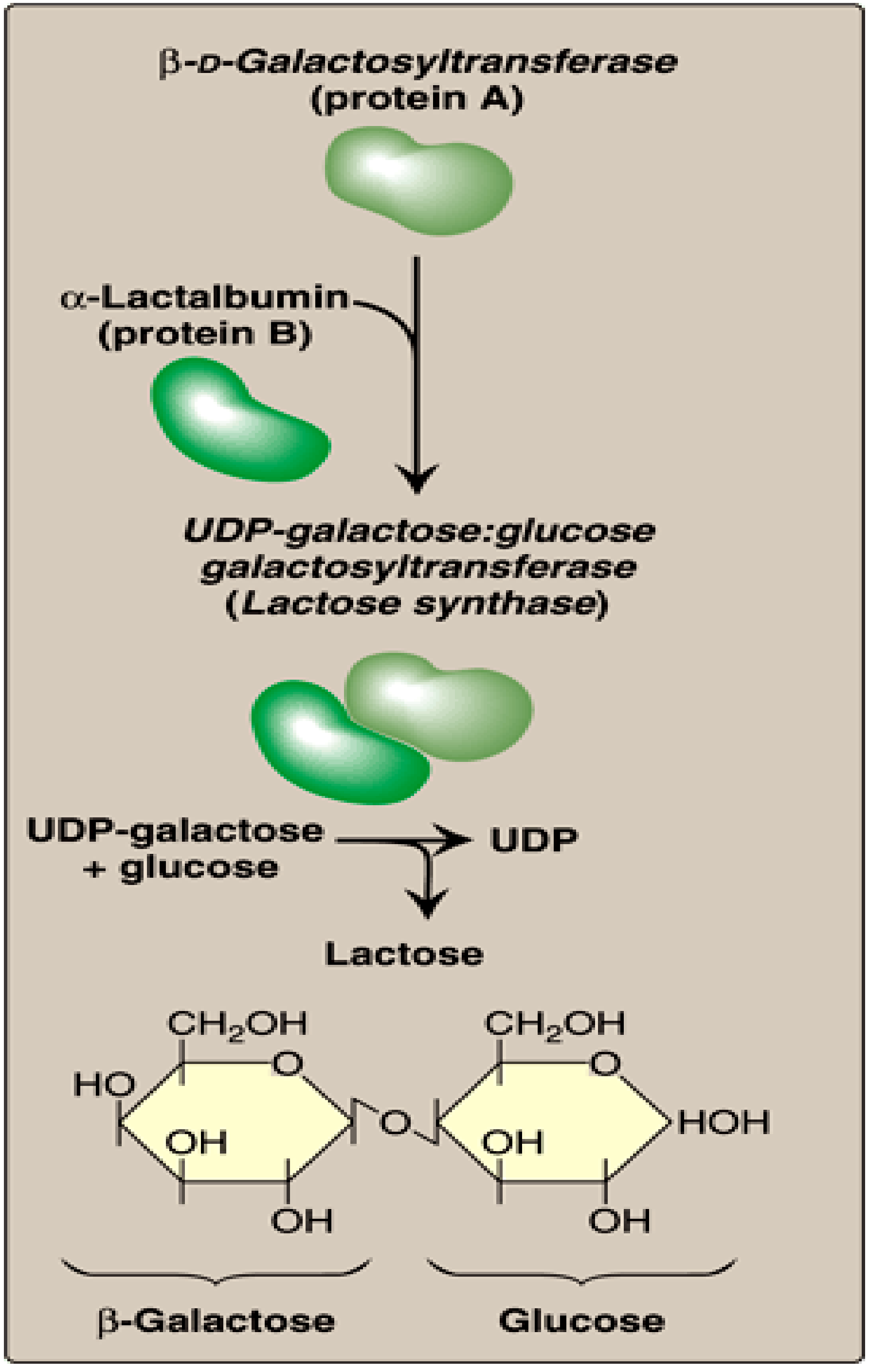

Brain damage
Cataracts
Jaundice
Enlarged liver
Kidney damage
If a galactosemic infant is given milk, unmetabolized milk sugars build up and damage the liver, eyes, kidneys and brain
©ADAM, Inc.

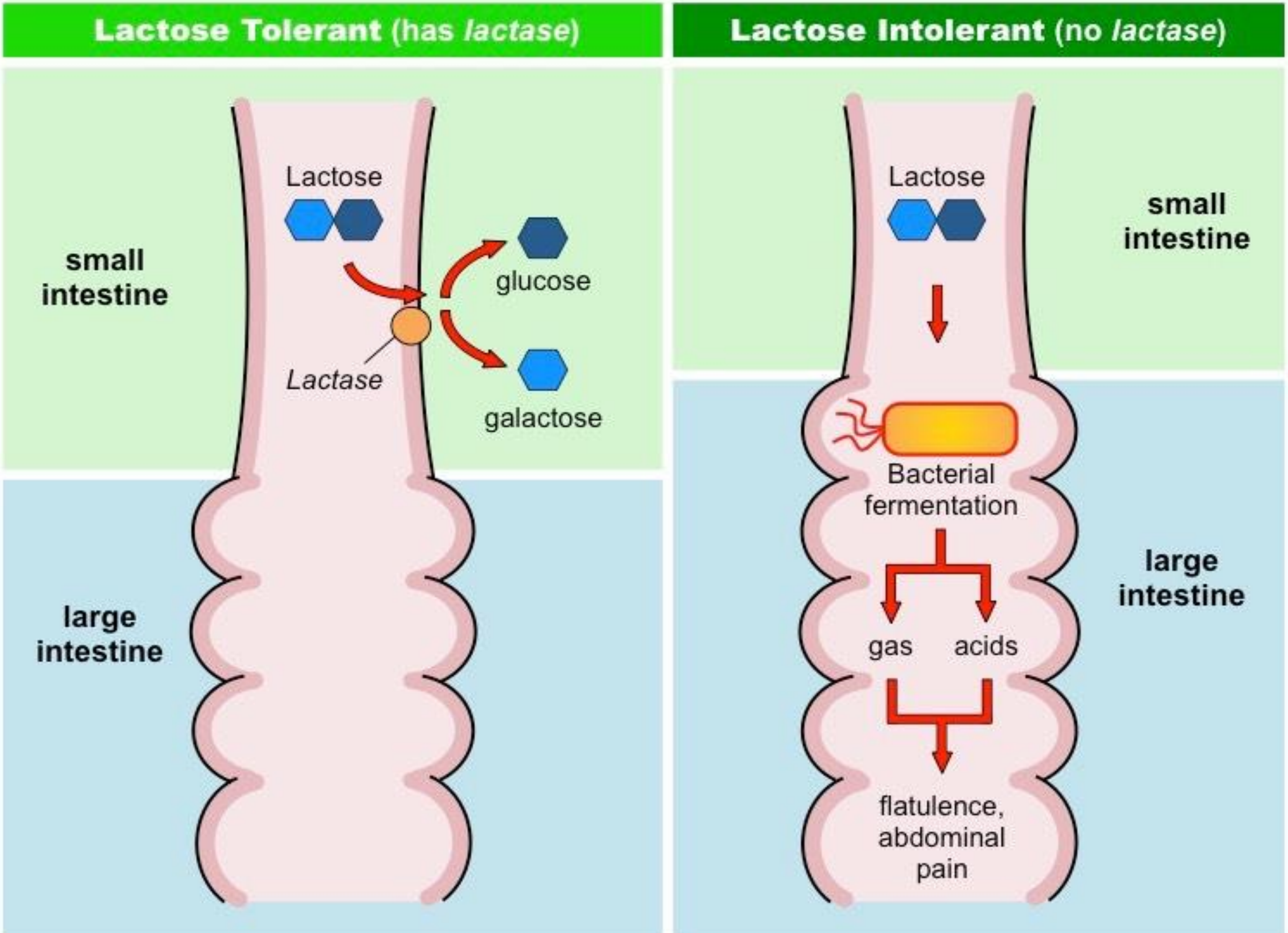
Lactose metabolism

Synthesis of Lactose



- Lactose = **glucose** + **galactose**
- Only synthesized in mammary for short periods during lactation
- **Lactose synthase** catalyzes transfer of galactose from UDP-galactose to glucose (NOT UDP-glucose) to form glycosidic bond
- Lactose synthase has 2 subunits
  1. **Galactosyltransferase** (enzyme)
  2. **α-Lactalbumin** (regulatory subunit)
     - Synthesized after childbirth in response to **prolactin**
     - Lowers K_m of galactosyltransferase for glucose (1200 mM → 1 mM) to increase rate of lactose synthesis
- Without α-lactalbumin, **Galactosyltransferase** normally transfers galactosyl units to glycoproteins
- α-Lactalbumin acts as **"specifier"** protein by altering substrate specificity


β-D-Galactosyltransferase
(protein A)
α-Lactalbumin
(protein B)
UDP-galactose:glucose
galactosyltransferase
(Lactose synthase)
UDP-galactose
+ glucose
UDP
Lactose
CH2OH
O
HO
OH
OH
O
CH2OH
O
OH
HOH
OH
β-Galactose
Glucose



Lactose Tolerant (has *lactase*)
Lactose Intolerant (no *lactase*)
small intestine
Lactose
glucose
Lactase
galactose
large intestine
Lactose
small intestine
Bacterial fermentation
large intestine
gas
acids
flatulence, abdominal pain