Metabolism of mono and disaccharide

fructose / galactose

Metabolism of fructose

table sugar α(1,2) linkage

- The major source of fructose is the disaccharide sucrose, which, when cleaved in the intestine, releases equimolar amounts of fructose and glucose

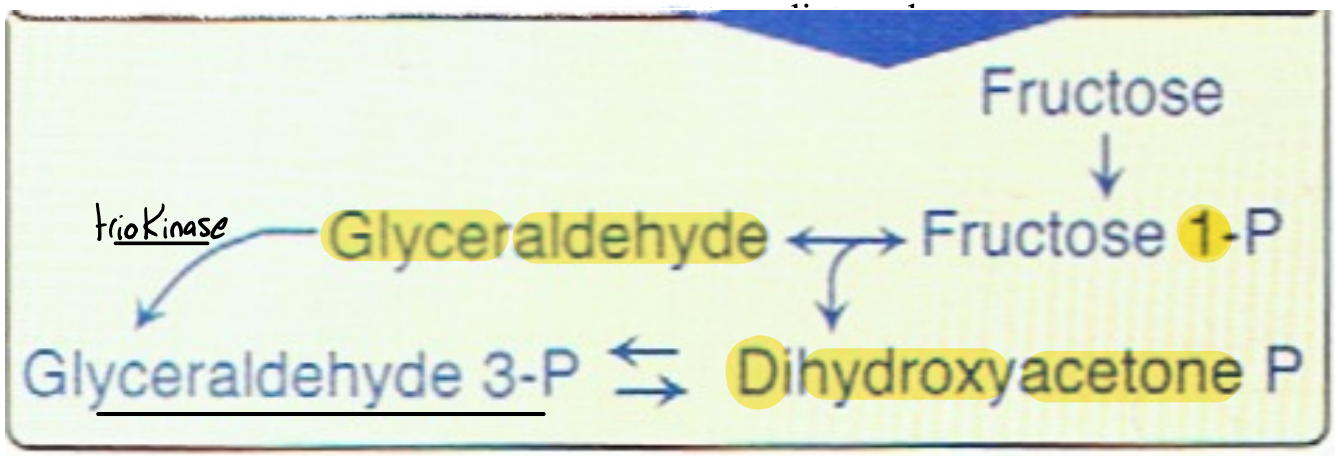
- fructose is also found as a free monosaccharide in high-fructose corn syrup (55 percent fructose/45 percent glucose, which is used to sweeten most cola drinks), in many fruits, and in honey.

Glut 5

- Entry of fructose into cells is not insulin-dependent and, in contrast to glucose, fructose does not promote the secretion of insulin.

glut4

GLUT-5 is the primary transporter for fructose in the small intestine and the testes



اللي عندهم تراكم فركتوز ايش ياكلو

1 sucrose

2 honey

3 fruit

4 milk

5 cola

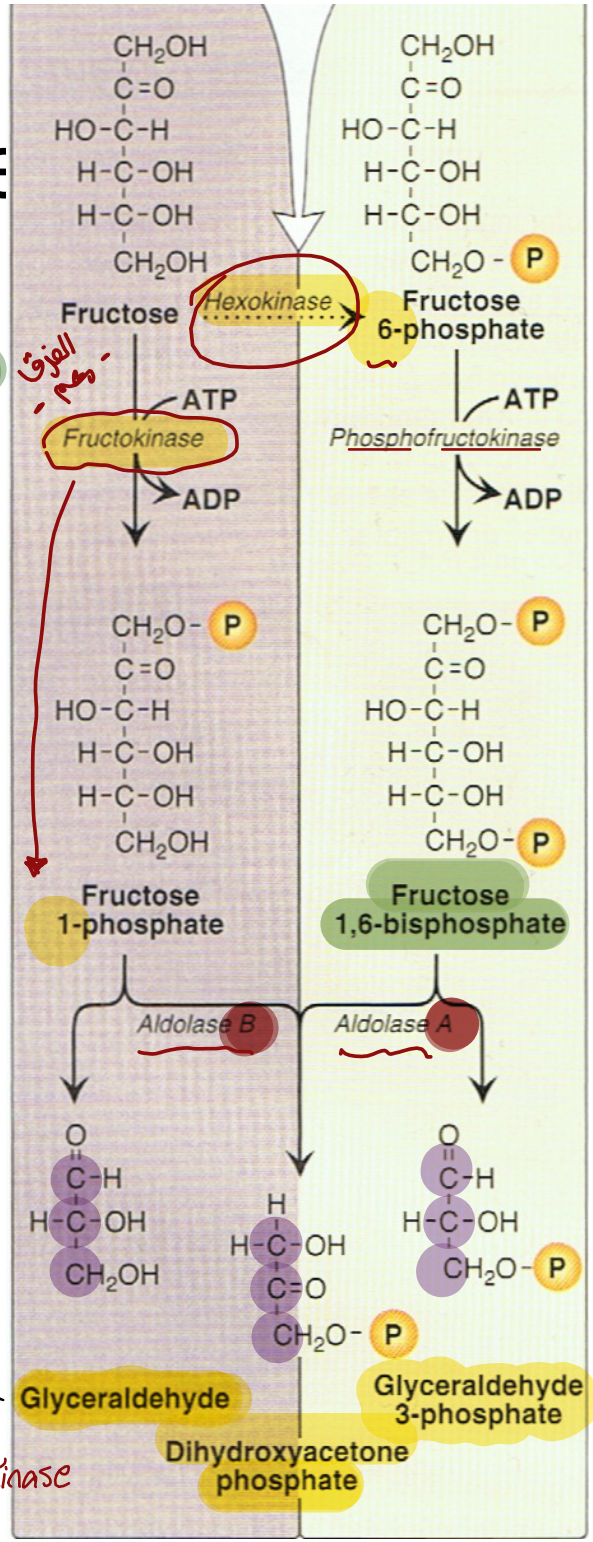
فيه fructose

فيه lactose ✓

Metabolism of fructose

A. Phosphorylation of fructose: by hexokinase or fructokinase (found in the liver, kidney, and the small intestinal mucosa). and converts fructose to fructose 1-phosphate, using ATP as the phosphate donor

B. Cleavage of fructose 1-phosphate (by aldolase B) to dihydroxyacetone phosphate (DHAP) and glycerolaldehyde. DHAP can directly enter glycolysis or gluconeogenesis, whereas glyceraldehyde can be metabolized by other pathways



Metabolism of fructose

A. Kinetics of fructose metabolism

A. The rate of fructose metabolism is more rapid than that of glucose because the trioses formed from fructose 1-phosphate bypass phosphofructokinase (the major rate-limiting step in glycolysis).

B. Intravenous infusion of fructose elevate the rate of lipogenesis caused by the enhanced production of acetyl CoA.

Acetyl CoA ↑ lipogenesis =

B. Disorders of fructose metabolism

harmless

A. Fructosuria ← fructokinase deficiency: benign condition

B. Hereditary fructose intolerance (HFI): a severe disturbance of liver and kidney metabolism as a result of aldolase B deficiency. Fructose 1-phosphate accumulates, and ATP and inorganic phosphate levels fall significantly, causing hyperuricemia, hypoglycemia, vomiting, jaundice, hemorrhage and hepatomegaly.

Aldose B deficiency

low ATP no glyconeogenesis no glucose

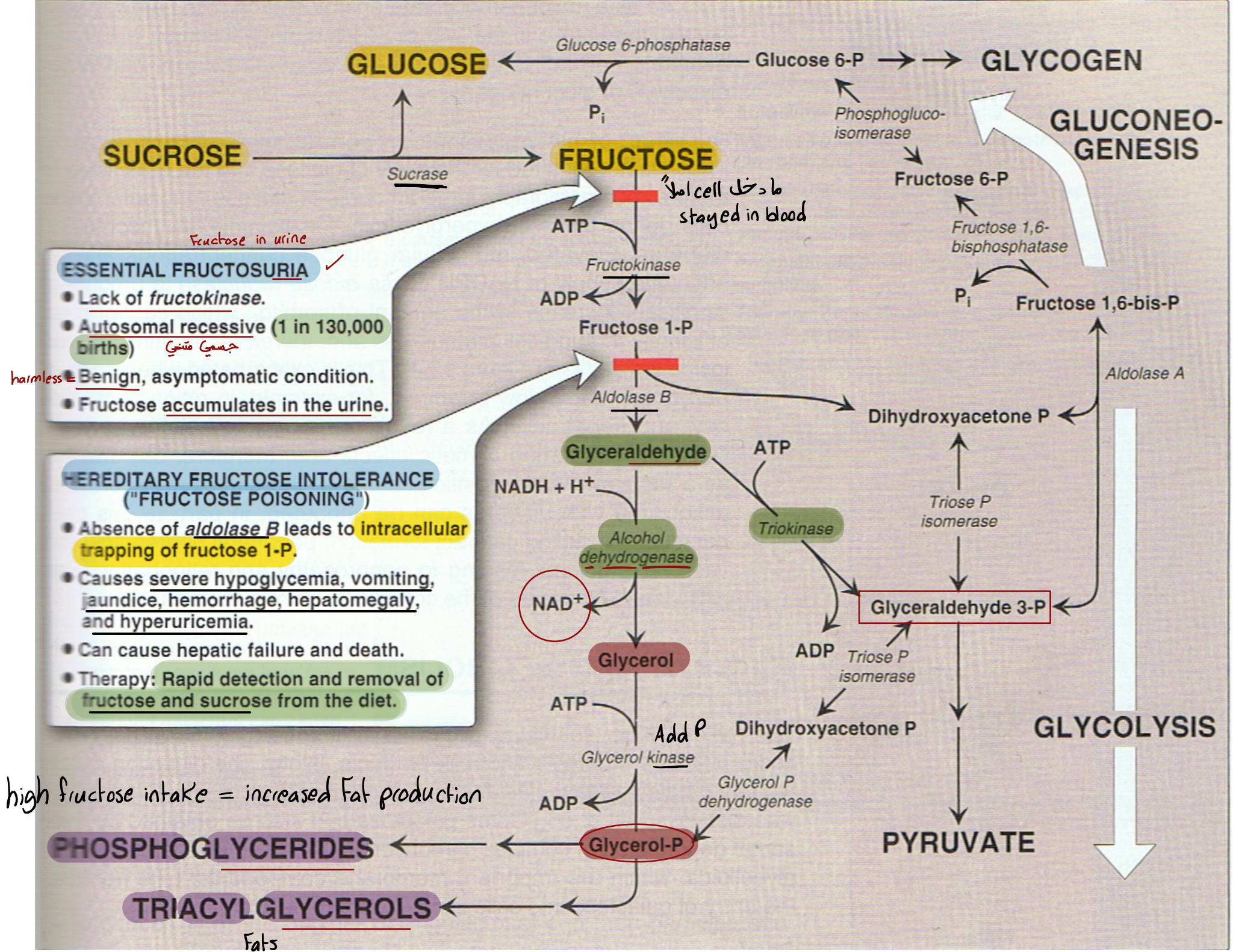
If fructose was not removed from the diet, liver failure and death can occur.

Diagnosis of HFI can be made on the basis of fructose in the urine

Summary Tip: * No **Fructokinase** = Fructose in the urine (No big deal).

- No **Aldolase B** = Fructose "poisoning" (Emergency).

↳ F-1-P accumilation


GLUCOSE
Glucose 6-phosphatase
Glucose 6-P
GLYCOGEN
Pi
Phosphogluco-isomerase
GLUCONEO-GENESIS
SUCROSE
Sucrase
FRUCTOSE
Fructose 6-P
ما دخل cell امثلا stayed in blood
ATP
Fructose 1,6-bisphosphatase
Fructokinase
ADP
Pi
Fructose 1,6-bis-P
Fructose 1-P
Aldolase A
Aldolase B
Dihydroxyacetone P
Glyceraldehyde
ATP
NADH + H+
Triose P isomerase
Triokinase
Alcohol dehydrogenase
NAD+
Glyceraldehyde 3-P
ADP
Triose P isomerase
Glycerol
ATP
Add P
Dihydroxyacetone P
GLYCOLYSIS
Glycerol kinase
Glycerol P dehydrogenase
ADP
PHOSPHOGLYCERIDES
Glycerol-P
PYRUVATE
TRIACYLGLYCEROLS
Fats
Fructose in urine
ESSENTIAL FRUCTOSURIA
Lack of fructokinase.
Autosomal recessive (1 in 130,000 births)
جسمي متنحي
harmless = Benign, asymptomatic condition.
Fructose accumulates in the urine.
HEREDITARY FRUCTOSE INTOLERANCE ("FRUCTOSE POISONING")
Absence of aldolase B leads to intracellular trapping of fructose 1-P.
Causes severe hypoglycemia, vomiting, jaundice, hemorrhage, hepatomegaly, and hyperuricemia.
Can cause hepatic failure and death.
Therapy: Rapid detection and removal of fructose and sucrose from the diet.
high fructose intake = increased fat production

Metabolism of fructose

OH on C_2 to left epimer

monosaccharide

A. Conversion of mannose to fructose 6-phosphate

6 P

Hexokinase phosphorylates mannose, producing mannose 6-phosphate, which is (reversibly) isomerized to fructose 6-phosphate by phosphomannose isomerase.

sugar alcohol

B. Conversion of glucose to fructose via sorbitol

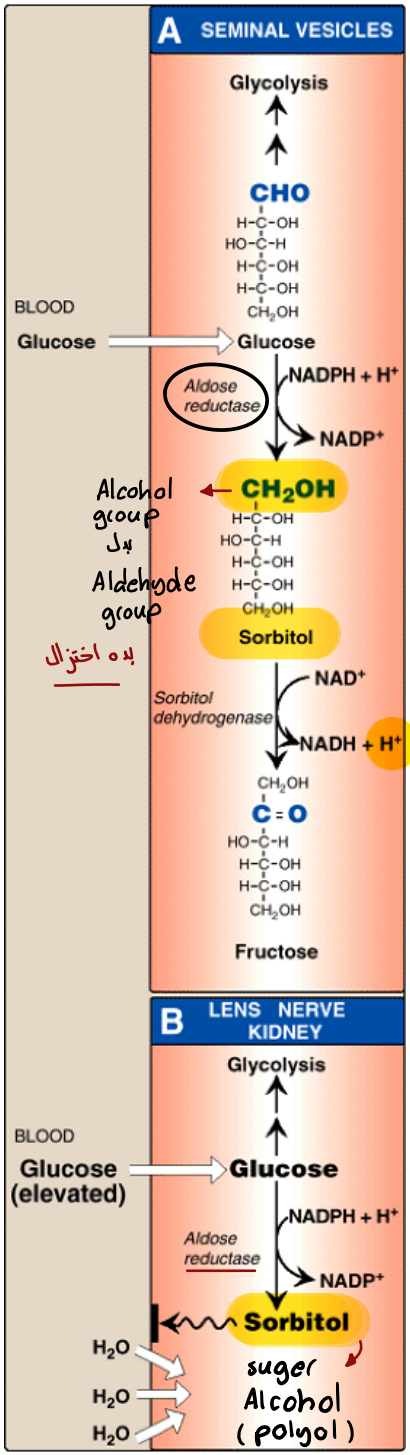
A. In seminal vesicles, glucose converts to sorbitol by aldehyde reductase followed by oxidation of sorbitol by sorbitol dehydrogenase to produce fructose. This is necessary in seminal vesicles as fructose is a major carbohydrate energy source.

use NADPH

produce NADH

B. In hyperglycemia as in uncontrolled diabetes glucose enter these cells (retina, lens, kidney, nerve cells) convert to sorbitol which will be trapped inside the cell, leading to water retention due to osmosis. cataract formation, peripheral neuropathy, and vascular problems leading to nephropathy and retinopathy.

4. **The Osmotic Effect:** Sorbitol is osmotically active; it pulls **water** into the cell, causing swelling. This leads to cataracts and nerve damage .



Feature	A. Seminal Vesicles	B. Lens, Nerve, Kidney
Purpose	To produce Fructose as the main energy source for sperm.	Usually, this pathway is inactive or very slow.
Enzyme Status	Has both Aldose Reductase & Sorbitol Dehydrogenase. (use NADPH; produce NADH)	Has Aldose Reductase, but lacks or has very low Sorbitol Dehydrogenase. (عشان هيك بصير عنا Sorbitol accumilation)
Outcome	Glucose (reduction) → Sorbitol (oxidation) → Fructose.	Glucose → Sorbitol (Trapped).
Clinical Effect	Healthy, normal function.	Cataracts, peripheral Neuropathy, and Nephropathy in Diabetes. Water retention due to osmosis

1. A patient with a rare deficiency in Triokinase would most likely struggle with which specific conversion in the liver?

A) Fructose $\rightarrow$ Fructose 1-P

B) Fructose 1-P $\rightarrow$ DHAP + Glyceraldehyde

C) Glyceraldehyde $\rightarrow$ Glyceraldehyde 3-P

D) Glucose $\rightarrow$ Sorbitol

C

2. Why does Hereditary Fructose Intolerance (Aldolase B deficiency) cause severe hypoglycemia?

A) Fructose 1-P directly inhibits the secretion of insulin.

B) Accumulation of Fructose 1-P "traps" Pi, inhibiting glycogenolysis and gluconeogenesis.

C) Fructose is converted too quickly into fat, leaving no sugar for the blood.

D) The lack of Fructokinase prevents glucose from entering the cell.

B

3. In the lens of a patient with uncontrolled diabetes, the "Sorbitol Trap" occurs because:

A) The V_{max} of Sorbitol Dehydrogenase is much higher than Aldose Reductase.

B) NADPH is depleted, preventing the conversion of Sorbitol to Fructose.

C) Glucose levels exceed the capacity of the glycolytic pathway, shunting glucose into the polyol pathway where Sorbitol cannot be efficiently cleared.

D) Insulin is required to transport Sorbitol out of the cell.

C

Galactose metabolism

- The major dietery source is lactose (in milk)

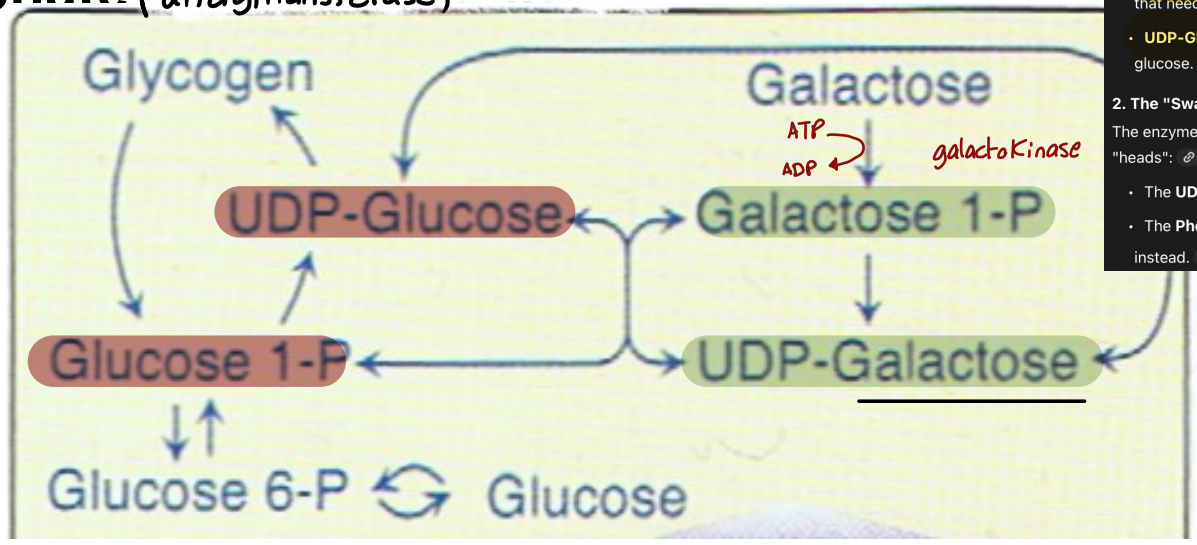
  β-glucose + galactose
  β(1-4) linkage

- Phosphorylation of galactose by **galactokinase** to galactose 1P using ATP as phosphate donor

  = phosphorylation
  add (P)

- Formation of UDP-galactose by exchange with UDP-glucose. The enzyme that catalyzes this reaction is **galactose 1-phosphate** (uridyltransferase)

  shifter
  يبدل



To work, this enzyme needs two things sitting next to each other:

- **Galactose 1-P:** The "new" sugar you just got from your milk (lactose) that needs to be processed.
- **UDP-Glucose:** A "carrier" molecule that is already holding a piece of glucose.

2. The "Swap" (The Mechanism)

The enzyme grabs both molecules and makes them trade their sugar "heads":

- The **UDP** lets go of the **Glucose** and grabs the **Galactose** instead.
- The **Phosphate** (P) lets go of the **Galactose** and grabs the **Glucose** instead.

Galactose metabolism

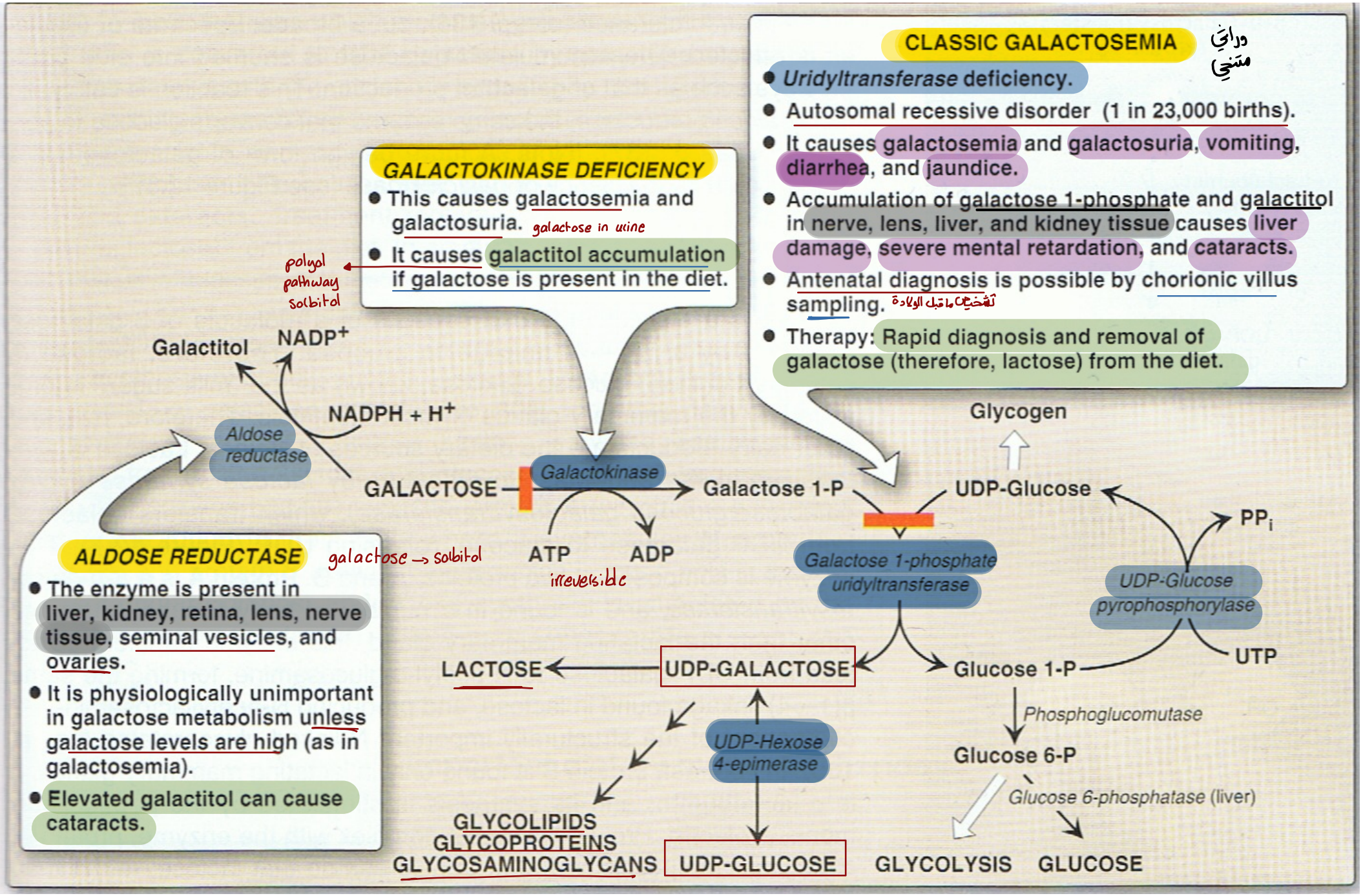
C. Use of UDP-galactose as a carbon source for glycolysis or gluconeogenesis. UDP-galactose is then converted to UDP-glucose by **UDP-hexose 4-epimerase**.

D. Role of UDP-galactose in biosynthetic reactions: can be utilized in many metabolic pathways as in biosynthesis of lactose, glycoproteins, glycolipids, and glycosaminoglycans.

milk synthesis in mammary glands

A. Disorders of galactose metabolism

A. classic galactosemia: **Galactose 1-phosphate uridyltransferase** is missing and so galactose 1P and galactose accumulate in cell causing a problem similar to that in fructose intolerance


CLASSIC GALACTOSEMIA
دراني متنحي
Uridyltransferase deficiency.
Autosomal recessive disorder (1 in 23,000 births).
It causes galactosemia and galactosuria, vomiting, diarrhea, and jaundice.
Accumulation of galactose 1-phosphate and galactitol in nerve, lens, liver, and kidney tissue causes liver damage, severe mental retardation, and cataracts.
Antenatal diagnosis is possible by chorionic villus sampling. تشخيص ماقبل الولادة
Therapy: Rapid diagnosis and removal of galactose (therefore, lactose) from the diet.
GALACTOKINASE DEFICIENCY
This causes galactosemia and galactosuria. galactose in urine
It causes galactitol accumulation if galactose is present in the diet.
polyol pathway sorbitol
Galactitol
NADP+
NADPH + H+
Aldose reductase
GALACTOSE
Galactokinase
ATP
ADP
irreversible
Galactose 1-P
Glycogen
UDP-Glucose
PPi
Galactose 1-phosphate uridyltransferase
UDP-Glucose pyrophosphorylase
UTP
ALDOSE REDUCTASE
galactose → sorbitol
The enzyme is present in liver, kidney, retina, lens, nerve tissue, seminal vesicles, and ovaries.
It is physiologically unimportant in galactose metabolism unless galactose levels are high (as in galactosemia).
Elevated galactitol can cause cataracts.
LACTOSE
UDP-GALACTOSE
Glucose 1-P
Phosphoglucomutase
Glucose 6-P
UDP-Hexose 4-epimerase
Glucose 6-phosphatase (liver)
GLYCOLIPIDS
GLYCOPROTEINS
GLYCOSAMINOGLYCANS
UDP-GLUCOSE
GLYCOLYSIS
GLUCOSE

Feature	Galactokinase Deficiency	Classic Galactosemia
Enzyme Missing	Galactokinase	Uridyltransferase
Accumulated Molecule	Galactose / Galactitol	Galactose 1-P / Galactitol
Severity	Generally milder	Very severe; life-threatening
Key Symptoms	Cataracts	Liver failure, mental retardation, cataracts

β (1 → 4)
galactose glucose

Lactose synthesis

- Produced in mammary glands of mammals
- Lactose is synthesized by lactose transferase which transfers galactose from UDP-galactose to glucose, releasing UDP.
- This enzyme is composed of two proteins, A and B. Protein A is a **β-o-galactosyltransferase**, and is found in a number of body tissues.
- In tissues other than the lactating mammary gland, this enzyme transfers galactose from UDP-galactose to N-acetyl-D-glucosamine, forming the same (1-4) linkage found in lactose, and producing N-acetyllactosamine a component of the structurally important N-linked **glycoproteins**.
- In contrast, protein B is found only in lactating mammary glands. It is **α-lactalbumin**, and its synthesis is stimulated by the peptide hormone, prolactin. Protein B forms a complex with the enzyme, protein A, changing the specificity of that transferase so that lactose, rather than N-acetyllactosamine, is produced.

UDP- galactose → glucos

lactose transferase ← وظيفته

protein A

β-D-galactosyltransferase

body tissues other than mammary glands

protein B

α-lactalbumin

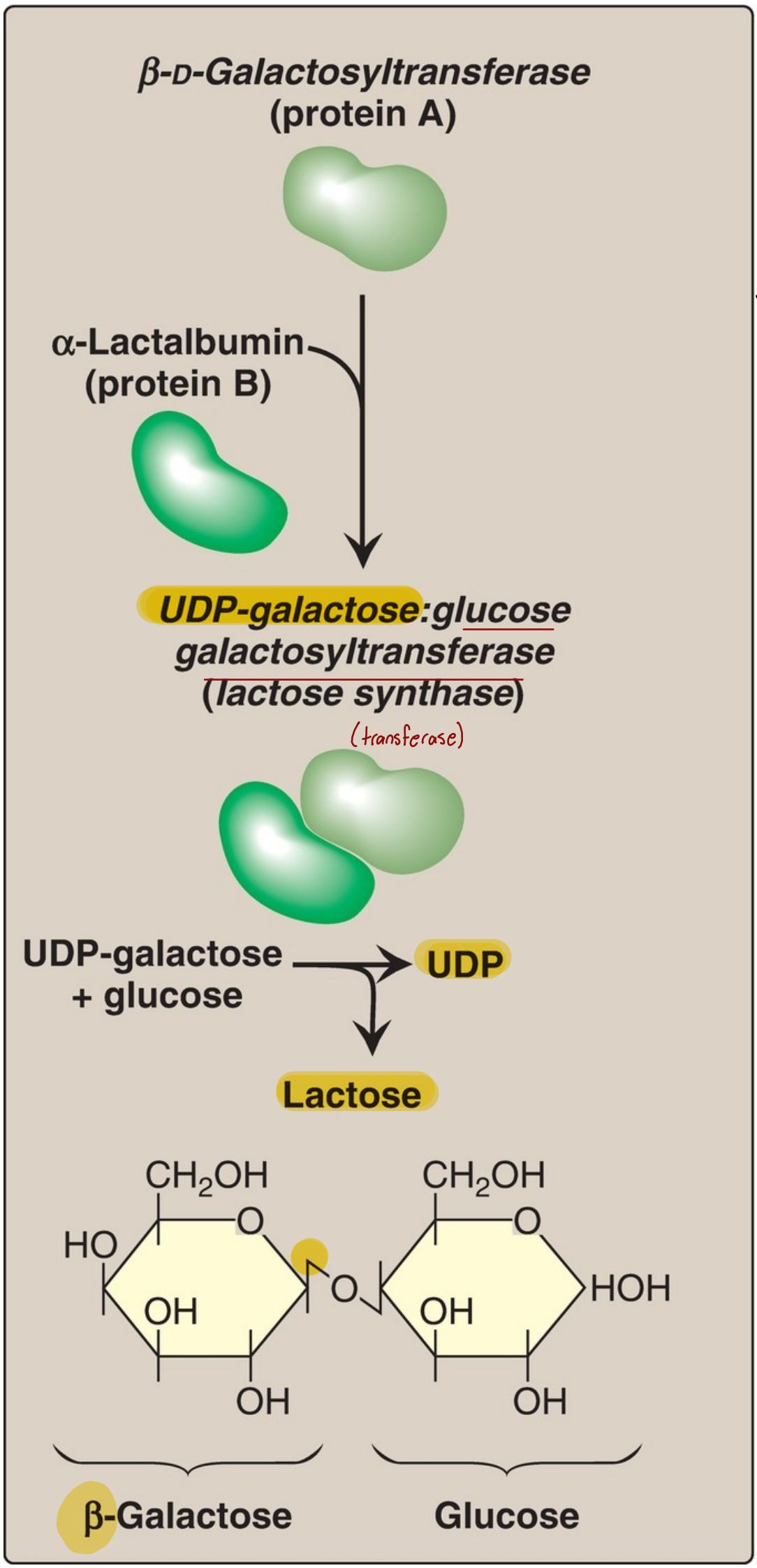
only in lactating mammary glands

trigger: prolactin

UDP-galactose

N-acetyl-D-glucosamine

β(1-4) linkage



ملخص الـ enzymes لشابتر 8

Enzyme (9 enzymes)	Pathway	Function (The Action)	Key Notes
Fructokinase	Fructose	Fructose ⟶ Fructose 1-P (ATP → ADP)	Primary "trapper" in liver. Deficiency: Essential Fructosuria (Benign). (in urine; harmless)
Aldolase B	Fructose	Fructose 1-P ⟶ DHAP + Glyceraldehyde	Cleaves Fructose 1-P. Deficiency: Hereditary Fructose Intolerance (Severe).
Triokinase	Fructose	Glyceraldehyde ⟶ Glyceraldehyde 3-P	Allows fructose products to enter Glycolysis highway.
Aldose Reductase (use $NADPH + H^+ \rightarrow NADP^+$)	Polyol	Glucose ⟶ Sorbitol OR Galactose ⟶ Galactitol	Uses NADPH. Causes cataracts/nerve damage in high-sugar states.
Sorbitol Dehydrogenase	Polyol	Sorbitol ⟶ Fructose	Missing in lens/nerves (the "Sorbitol Trap"). High in seminal vesicles.
Galactokinase	Galactose	Galactose ⟶ Galactose 1-P	Primary "trapper" for milk sugar. Deficiency: Causes cataracts.
Galactose 1-P Uridyltransferase (GALT)	Galactose	Trades Galactose 1-P for Glucose 1-P	The "Molecular Trader." Deficiency: Classic Galactosemia (Very Severe).

UDP-hexose 4-epimerase	Galactose	UDP-Galactose ↔ UDP-Glucose	The "Flipper." Makes the cycle reversible for biosynthesis.
Lactose Synthase (Protein A + B)	Synthesis	UDP-Galactose + Glucose → Lactose	Protein B (α-lactalbumin) is the "switch" found only in milk production.

BIOCHEMISTRY QUESTION BANK

Fructose & Galactose Metabolism

Question 1

Which enzyme is the primary “trapper” of fructose in the liver, and what is the product of this reaction?

- A) Hexokinase; Fructose 6-phosphate
- B) Fructokinase; Fructose 1-phosphate
- C) Aldolase B; DHAP
- D) Triokinase; Glyceraldehyde

Answer: B

> *Key Fact: Fructokinase traps fructose in the liver by converting it into Fructose 1-phosphate.*

Question 2

A 6-month-old infant is switched from breast milk to a formula containing sucrose. Shortly after, the infant develops vomiting and hypoglycemia. Which enzyme is likely deficient?

- A) Fructokinase
- B) Galactokinase
- C) Aldolase B
- D) Glucokinase

Answer: C

> *Key Fact: Hereditary Fructose Intolerance results from Aldolase B deficiency, causing toxic buildup of Fructose 1-phosphate.*

Question 3

Why does high fructose consumption often lead to increased fat synthesis (lipogenesis) in the liver?

- A) Fructose stimulates massive insulin release.
- B) Fructose bypasses the PFK-1 rate-limiting step of glycolysis.
- C) Fructose cannot be used for energy and must be stored.
- D) Fructose inhibits the breakdown of fatty acids.

Answer: B

> *Key Fact: Fructose bypasses PFK-1, flooding glycolysis with intermediates that fuel lipogenesis.*

Question 4

In “Essential Fructosuria,” why is the condition considered benign (harmless)?

- A) The body uses an alternative pathway to process all the fructose.
- B) Fructose 1-phosphate is safely stored in the muscles.
- C) Fructose is not trapped in the cells and can be excreted in the urine.
- D) The kidneys convert all fructose into glucose.

Answer: C

> *Key Fact: Without Fructokinase, fructose isn’t phosphorylated and simply leaves via urine.*

Question 5

Which enzyme is responsible for creating Galactitol from Galactose in the lens of the eye?

- A) Galactokinase
- B) Aldose Reductase
- C) Sorbitol Dehydrogenase
- D) GALT

Answer: B

> *Key Fact: Aldose Reductase converts Galactose into Galactitol, causing osmotic cataracts.*

Question 6

What is the “Molecular Trade” catalyzed by Galactose 1-phosphate uridyltransferase (GALT)?

- A) Galactose + ATP → Galactose 1-P
- B) UDP-Galactose ↔ UDP-Glucose
- C) Galactose 1-P + UDP-Glucose → UDP-Galactose + Glucose 1-P
- D) Lactose → Glucose + Galactose

Answer: C

> *Key Fact: GALT swaps UDP from glucose to galactose, enabling galactose metabolism.*

Question 7

A patient with “Classic Galactosemia” must strictly avoid which of the following?

- A) Table sugar (Sucrose)
- B) Milk and dairy (Lactose)
- C) Honey
- D) High-fructose corn syrup

Answer: B

> *Key Fact: Lactose contains galactose, which cannot be metabolized in Classic Galactosemia.*

Question 8

In the mammary gland, what specifically allows the enzyme “Protein A” to start making Lactose instead of Glycoproteins?

- A) High levels of insulin
- B) The binding of Protein B (α-lactalbumin)
- C) A decrease in glucose levels
- D) The presence of Fructose 6-phosphate

Answer: B

> *Key Fact: α-lactalbumin, induced by prolactin, switches the enzyme to lactose synthesis.*

Question 9

What is the fate of Sorbitol in the seminal vesicles?

- A) It is trapped and causes cell swelling.
- B) It is converted into Fructose to provide energy for sperm.
- C) It is converted into Galactose for milk production.
- D) It is excreted as a waste product.

Answer: B

> *Key Fact: Sorbitol Dehydrogenase converts Sorbitol into Fructose, the preferred sperm fuel.*

Question 10

Which enzyme “recycles” the UDP-carrier so that galactose metabolism can continue?

- A) UDP-hexose 4-epimerase
- B) Galactokinase
- C) Phosphoglucomutase
- D) Triokinase

Answer: A

> *Key Fact: Epimerase flips UDP-Galactose back into UDP-Glucose for reuse.*

3. Which enzyme is responsible for the 'Sorbitol Trap' in the lens of a diabetic patient, and what is the underlying mechanism of damage?

A. Aldose reductase; it produces osmotically active sorbitol that pulls water into the cell.

B. Sorbitol dehydrogenase; it creates toxic levels of fructose.

C. Glucokinase; it causes ATP depletion in the retina.

D. Hexokinase; it over-phosphorylates glucose to glucose 6-P.

A

Question: Which of the following describes a shared biochemical mechanism between Hereditary Fructose Intolerance (Aldolase B deficiency) and Classic Galactosemia (GALT deficiency)?

- **A) Both involve a deficiency in the initial kinase step, preventing sugar entry into cells.**
- **B) Both lead to the intracellular accumulation of phosphorylated sugars, sequestering inorganic phosphate and depleting ATP.**
- **C) Both are characterized by the overproduction of galactitol via the polyol pathway, causing liver failure.**
- **D) Both conditions are clinically benign and managed by monitoring sugar levels in the urine.**

Answer: B