Metabolism of mono and disaccharide

Metabolism of fructose

sources of fructose ?

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

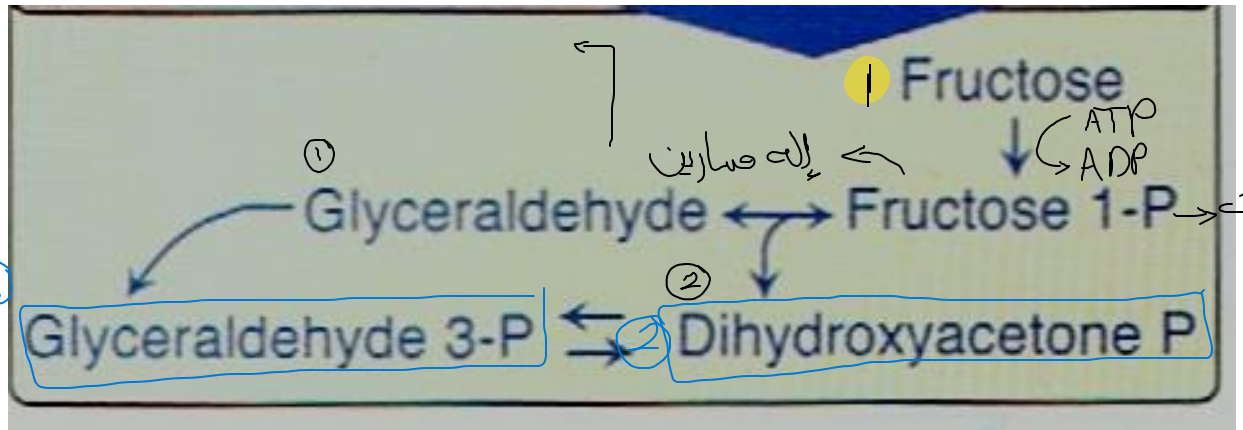
كميات متساوية

- 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.

تحلية

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

الغلوكوز يحفز إفراز الانسولين بينما الفركتوز لا يحفز إفرازه



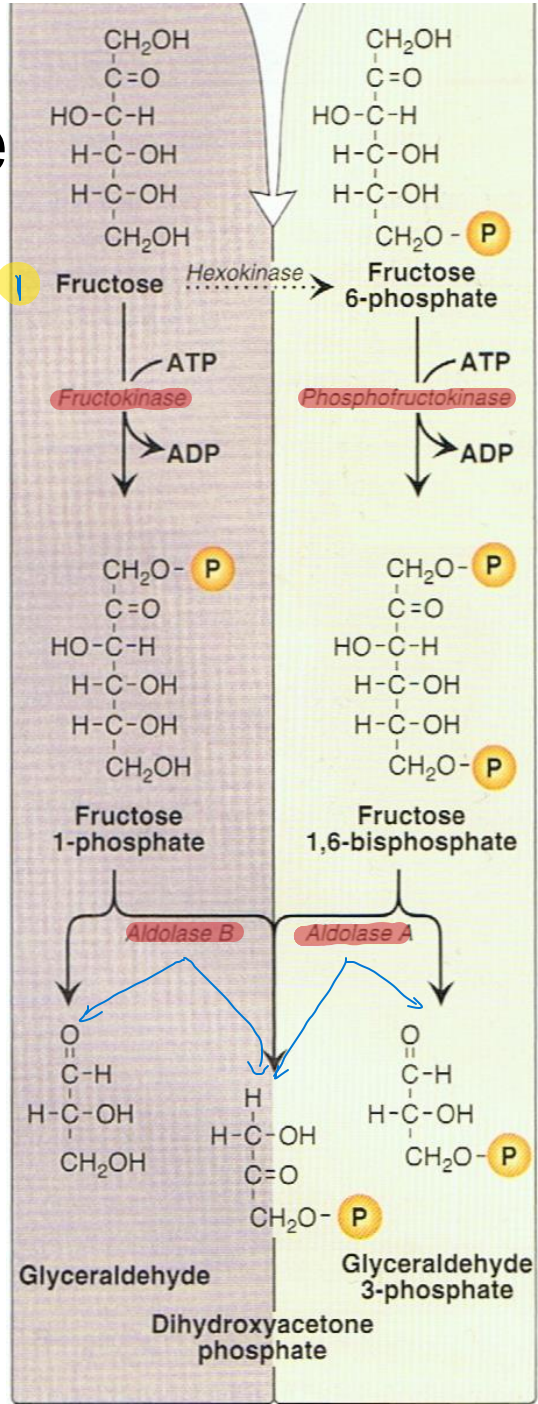
الناتج النهائي

يرتبط فقري فوسفات عند كاربون رقم 1

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

C. 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.

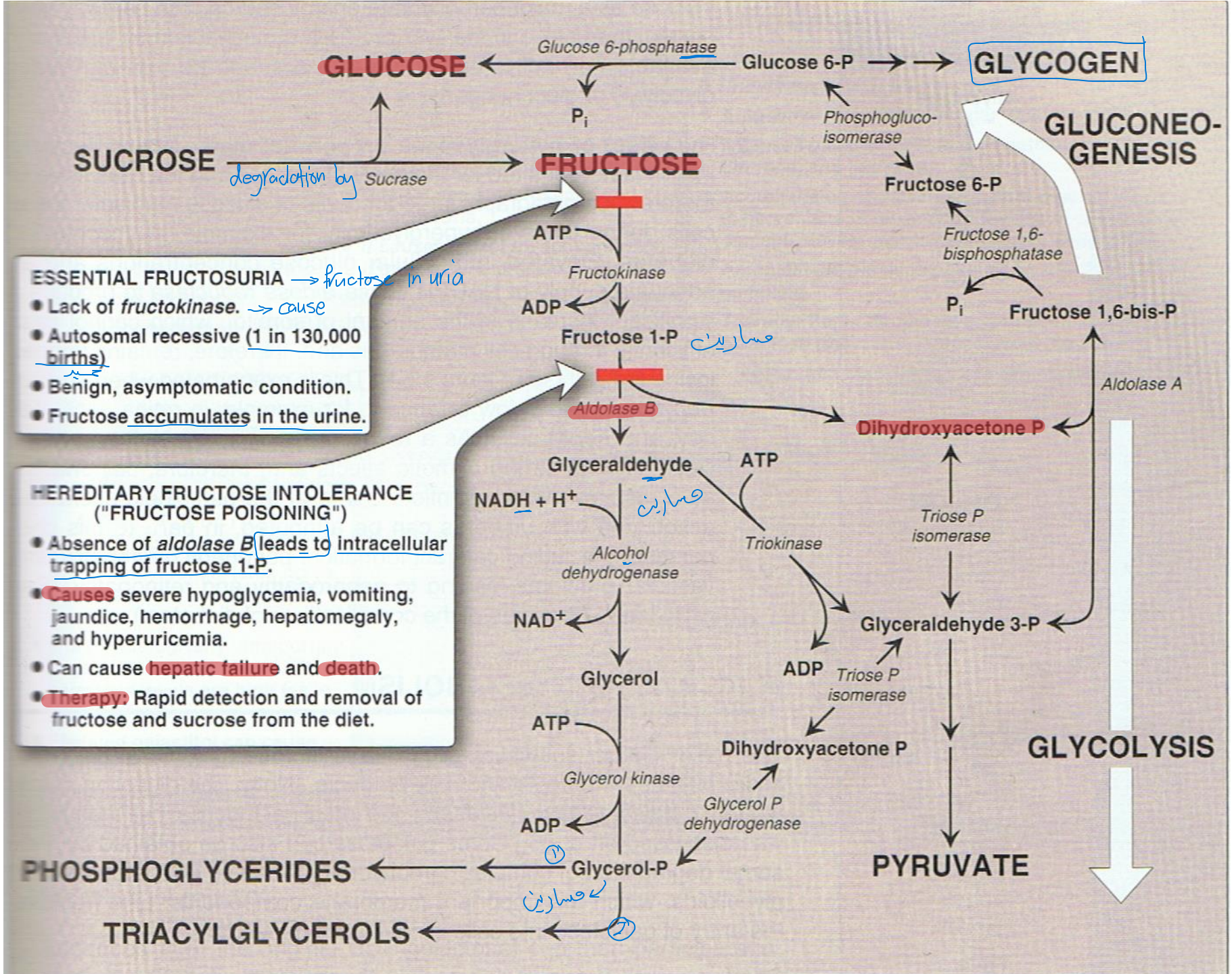
D. Disorders of fructose metabolism

A. 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.

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



ESSENTIAL FRUCTOSURIA

- Lack of *fructokinase*.
- Autosomal recessive (1 in 130,000 births)
- 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.

Metabolism of fructose

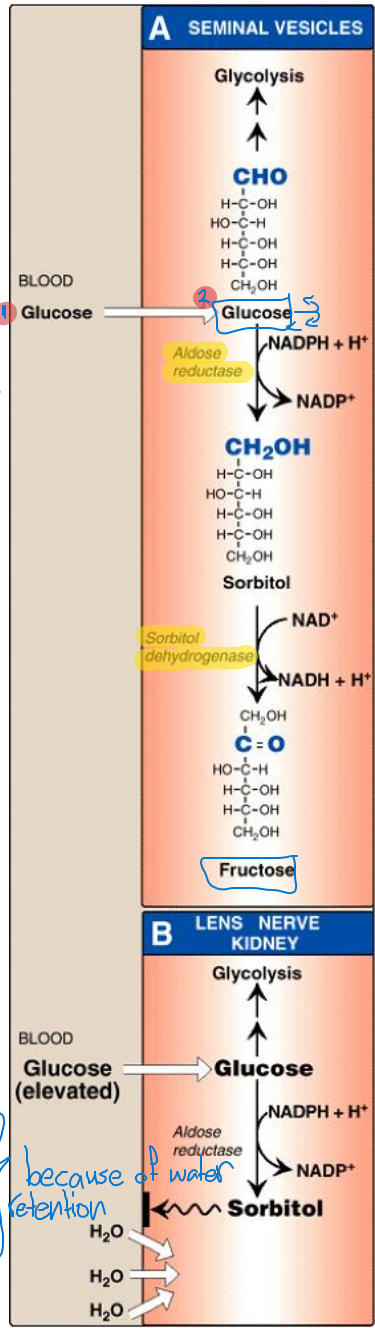
E. Conversion of mannose to fructose 6-phosphate

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

F. Conversion of glucose to fructose via sorbitol

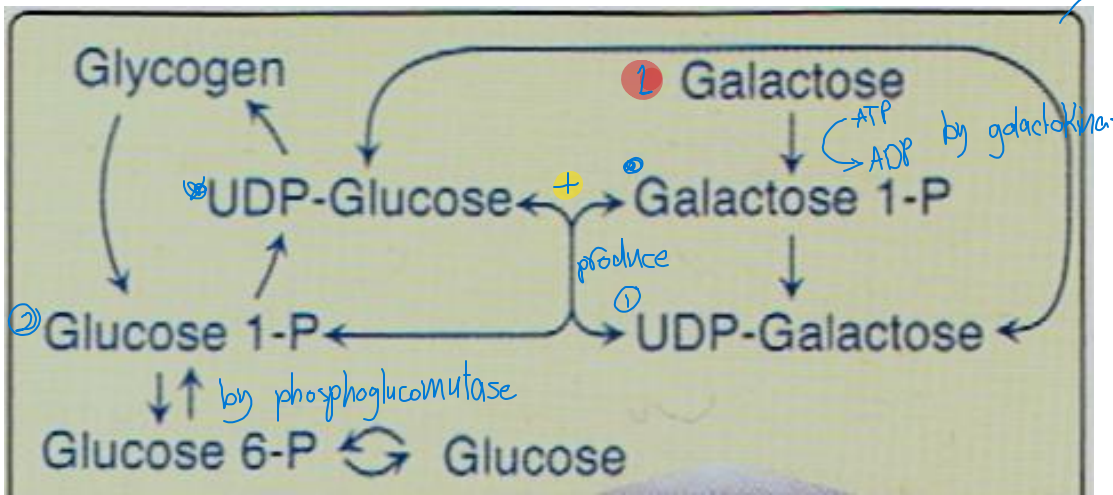
A. In seminal vesicles, glucose converts to sorbitol by aldehyde reductase followed by oxidation of sorbitol by sorbitol dehydrogenase to produce fructose. This is necessary in seminal vesicles as fructose is a major carbohydrate energy source.

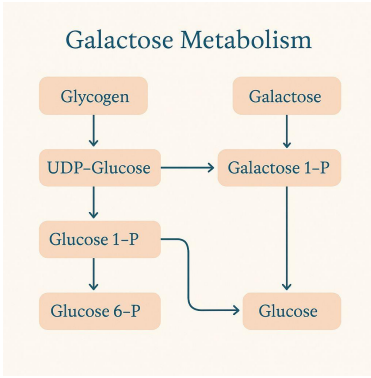
B. In hyperglycemia as in uncontrolled diabetes glucose enter these cells (retina, lens, kidney, nerve cells) convert to sorbitol which will be trapped inside the cell, leading to water retention due to osmosis. cataract formation, peripheral neuropathy, and vascular problems leading to nephropathy and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



Galactose metabolism

- The major dietery source is lactose (in milk)
- Phosphorylation of galactose by **galactokinase** to galactose 1P using ATP as phosphate donor
- Formation of UDP-galactose by exchange with UDP-glucose. The enzyme that catalyzes this reaction is **galactose 1-phosphate uridyl-transferase.**





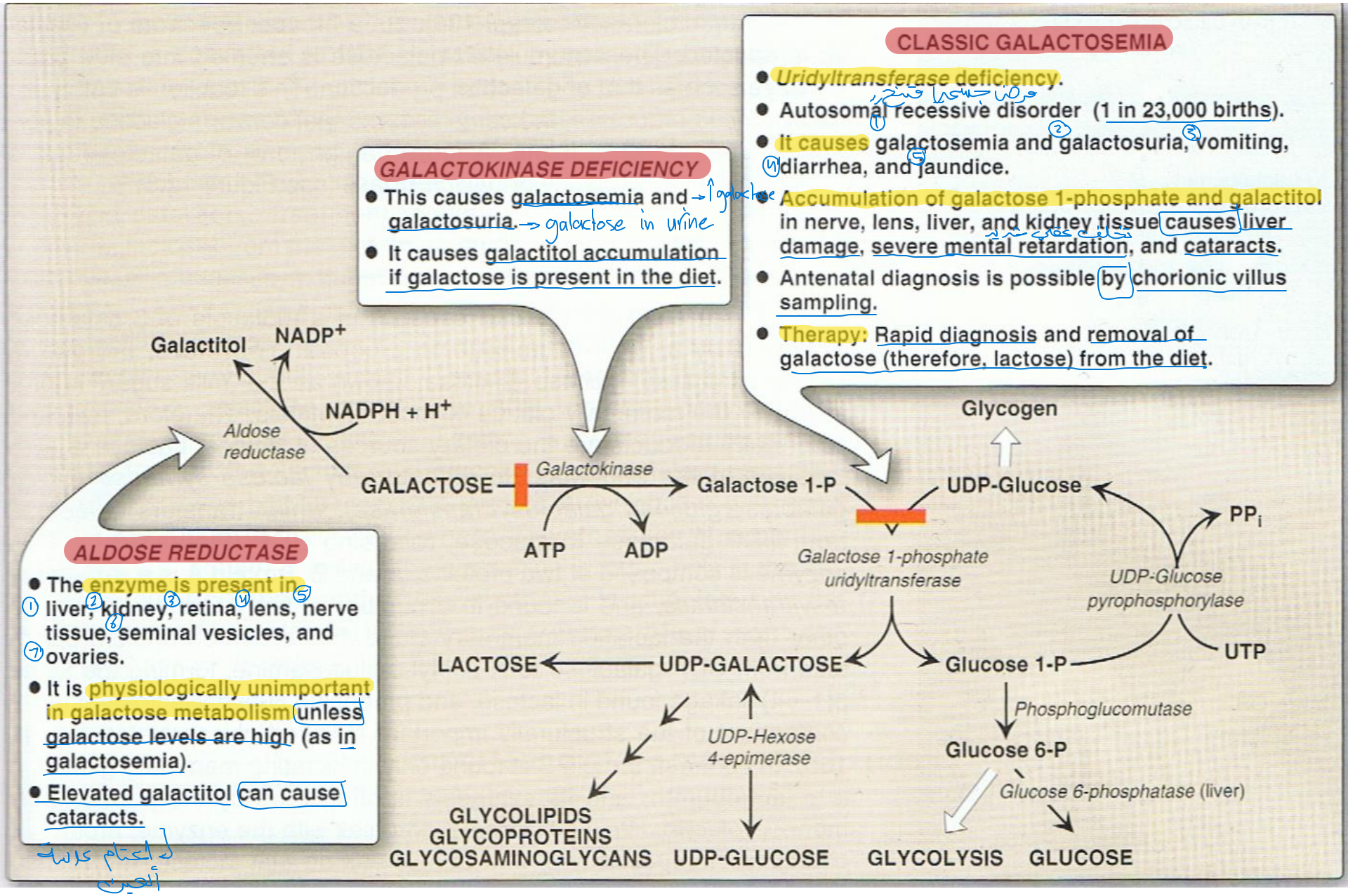
Galactose metabolism

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.

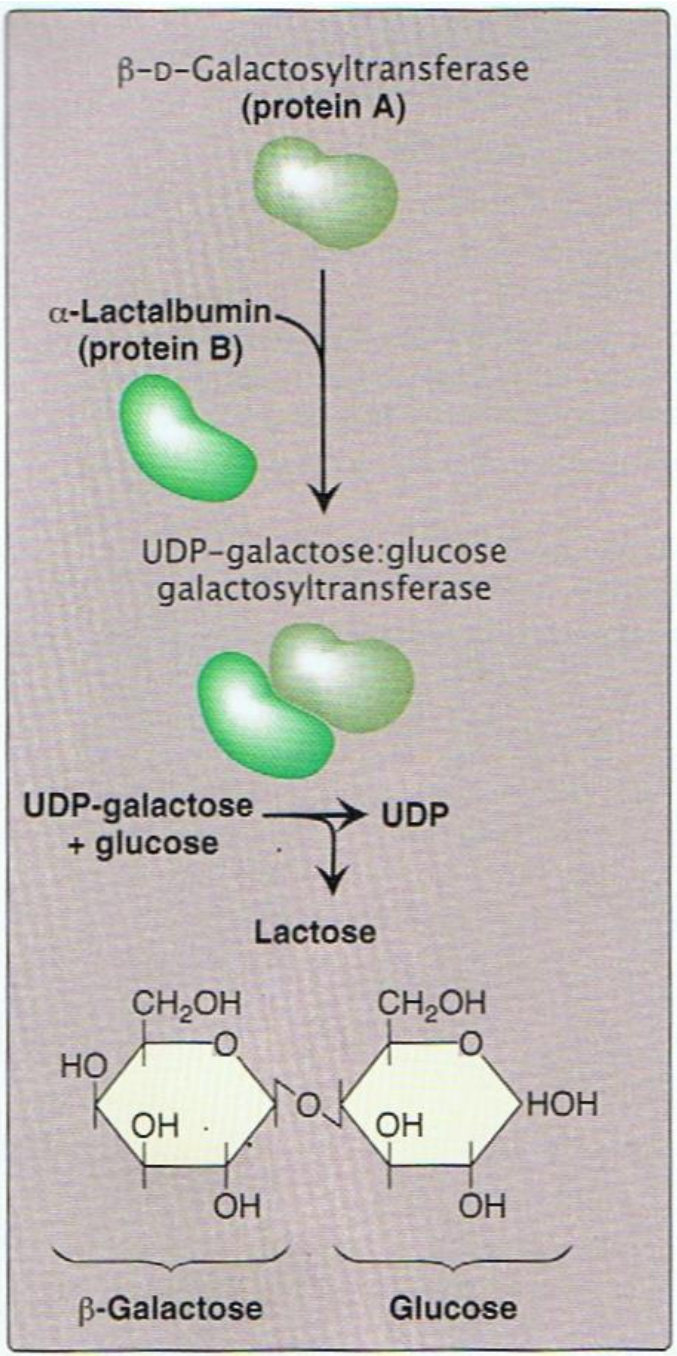
E. Disorders of galactose metabolism

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
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.
Therapy: Rapid diagnosis and removal of galactose (therefore, lactose) from the diet.
GALACTOKINASE DEFICIENCY
This causes galactosemia and galactosuria.
It causes galactitol accumulation if galactose is present in the diet.
ALDOSE REDUCTASE
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.
Galactitol
NADP+
NADPH + H+
Aldose reductase
GALACTOSE
Galactokinase
ATP
ADP
Galactose 1-P
Glycogen
UDP-Glucose
PPi
Galactose 1-phosphate uridyltransferase
UDP-Glucose pyrophosphorylase
UTP
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

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.


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