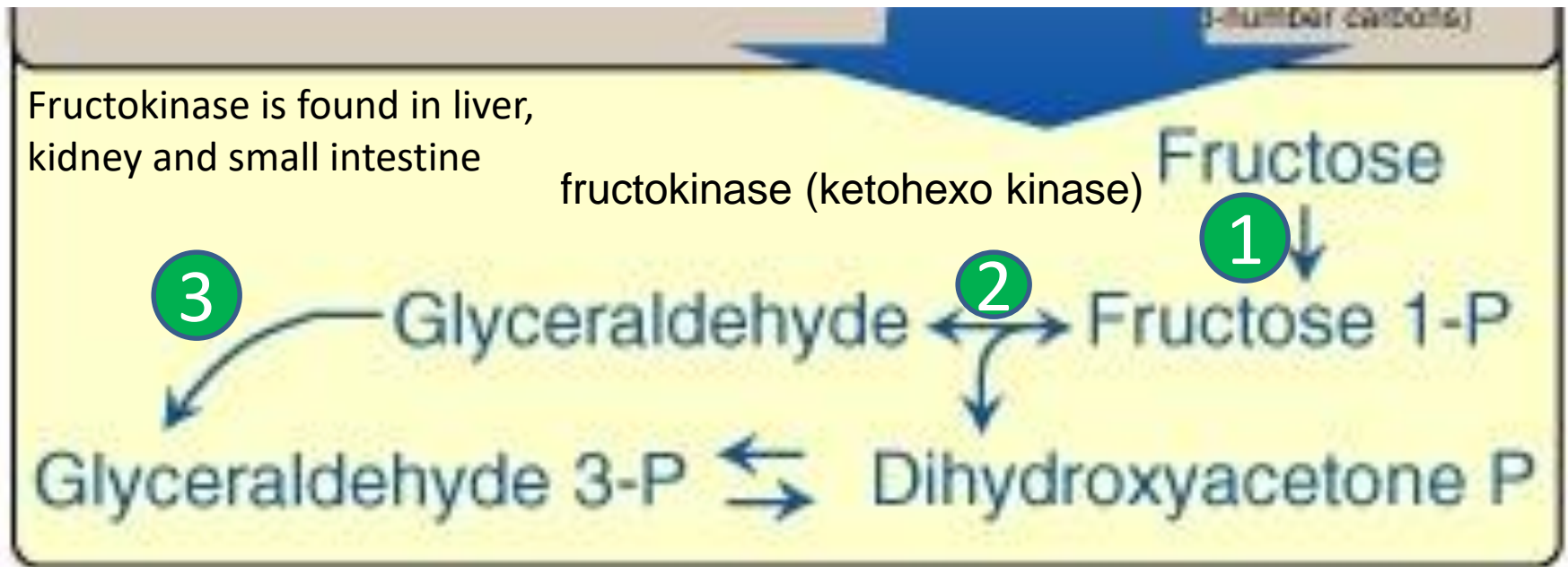


# Metabolism of Monosaccharides and Disaccharides

Dr. Diala Abu-Hassan, DDS, PhD

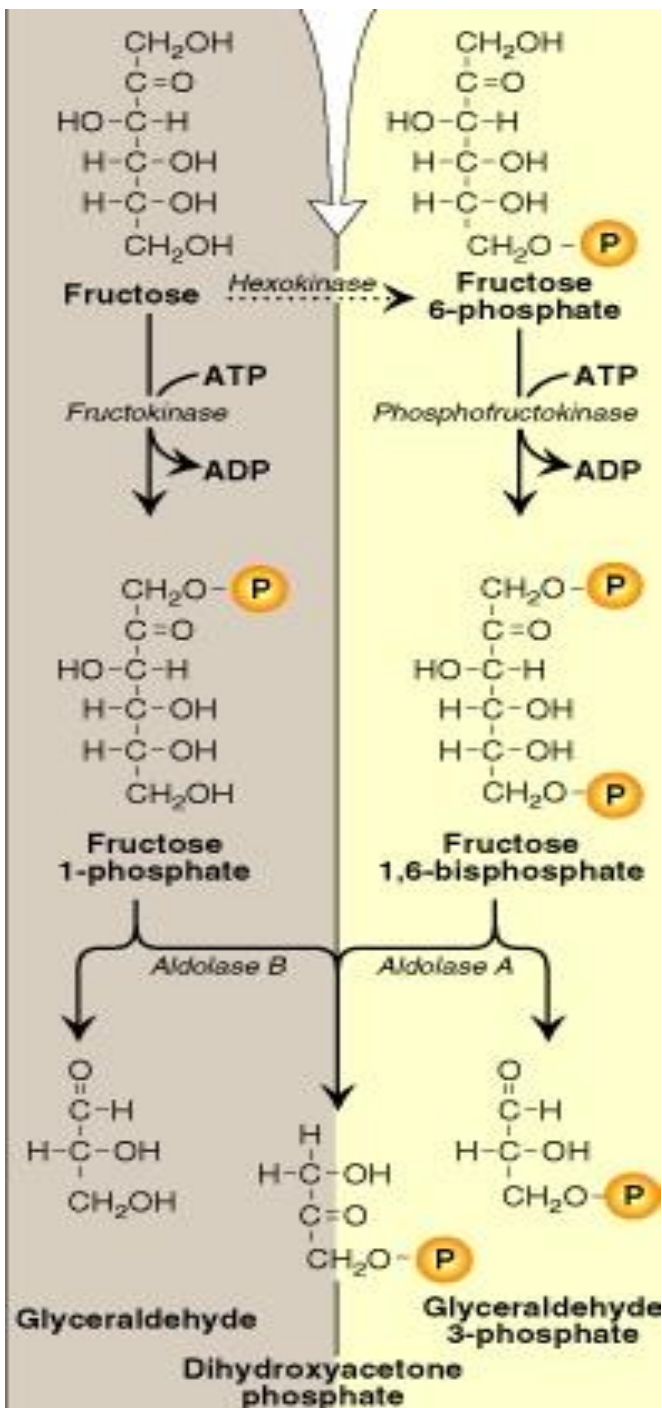
# Fructose Metabolism

- 10% of the daily calorie intake
- Sources: sucrose, Fruits, honey, high-fructose corn syrup
- Entry into cells is not insulin dependent.
- Does NOT promote the secretion of insulin

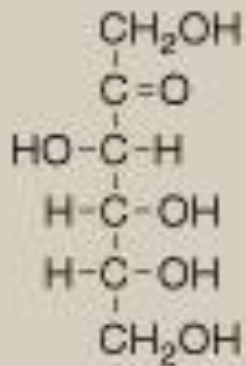


# Fructose Metabolism

Hexokinase affinity to fructose is low

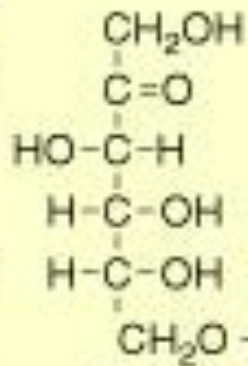


- The rate of fructose metabolism is more rapid than that of glucose because the trioses formed from fructose 1-phosphate bypass *phosphor fructokinase-1-P* the major rate-limiting step in glycolysis



Fructose

Hexokinase



Fructose 6-phosphate

Phosphofructokinase

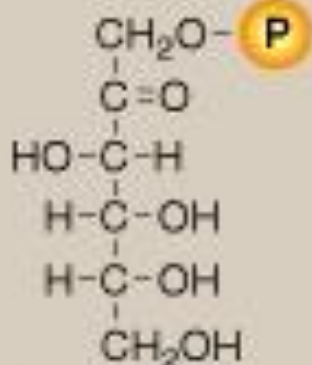
Fructokinase

ATP

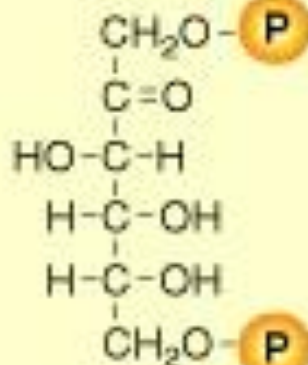
ADP

ATP

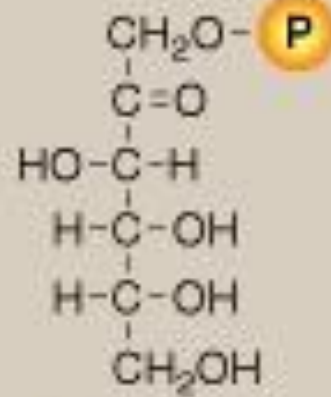
ADP



Fructose 1-phosphate



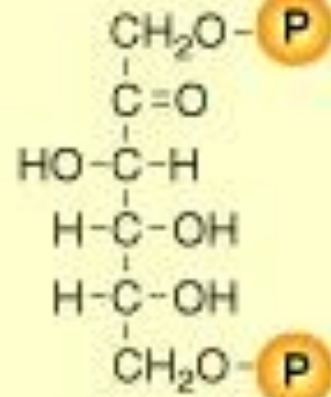
Fructose 1,6-bisphosphate



Fructose 1-phosphate

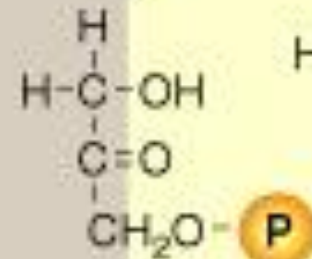
Aldolase B

Glyceraldehyde

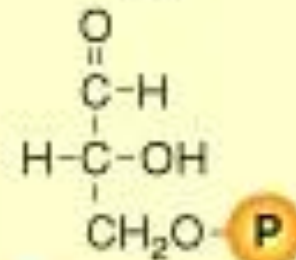


Fructose 1,6-bisphosphate

Aldolase A  
Aldolase B



Dihydroxyacetone phosphate



Glyceraldehyde 3-phosphate

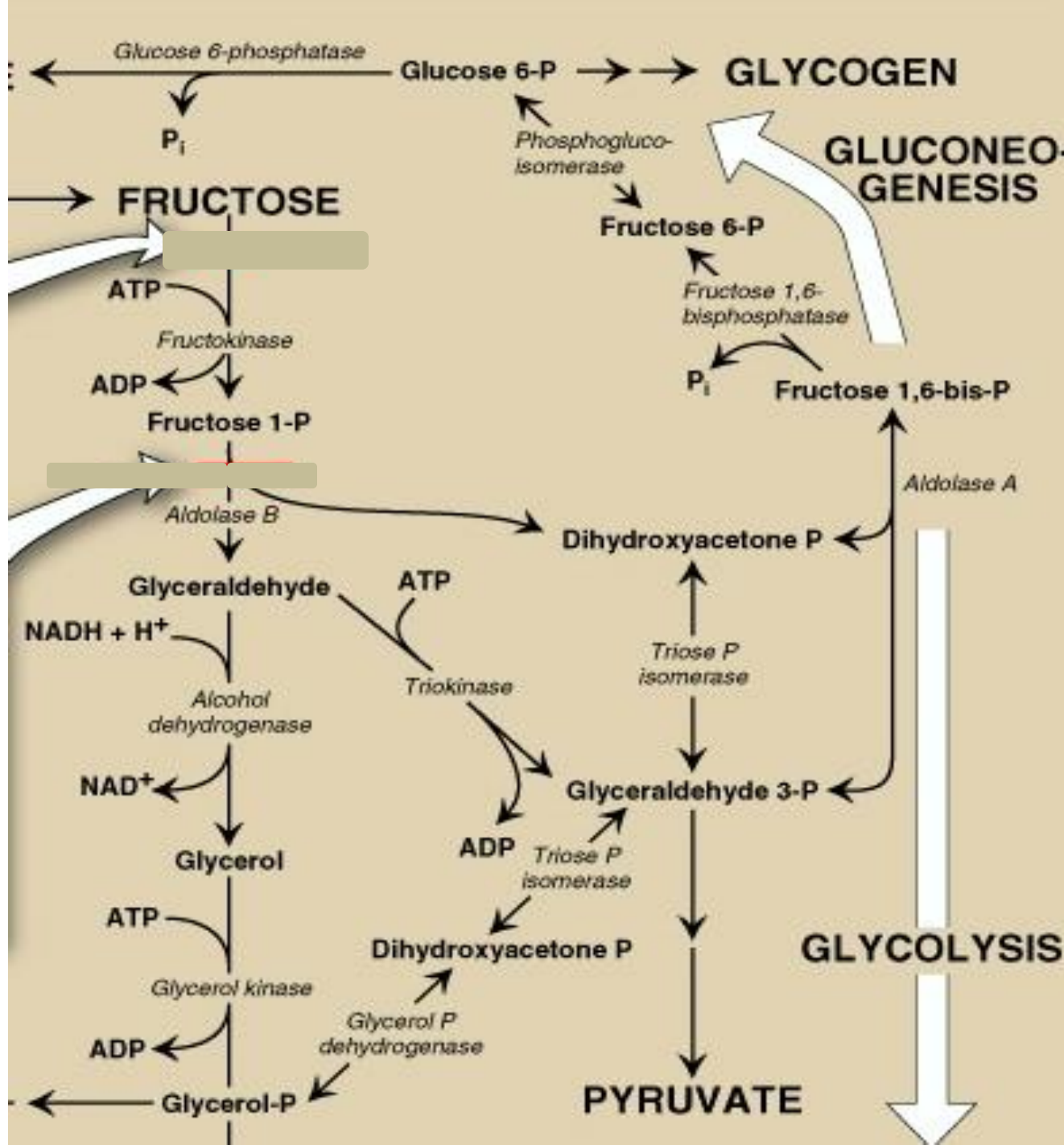
# Human expresses three forms of aldolase

## Aldolase B

- Liver, kidney, small intestine
- Substrate  
Fruc. 1 phosphosphate  
Also  
Fruc. 1,6 bisphosphate
- $\downarrow$  activity  $\rightarrow$  fructose intolerance

## Aldolase A

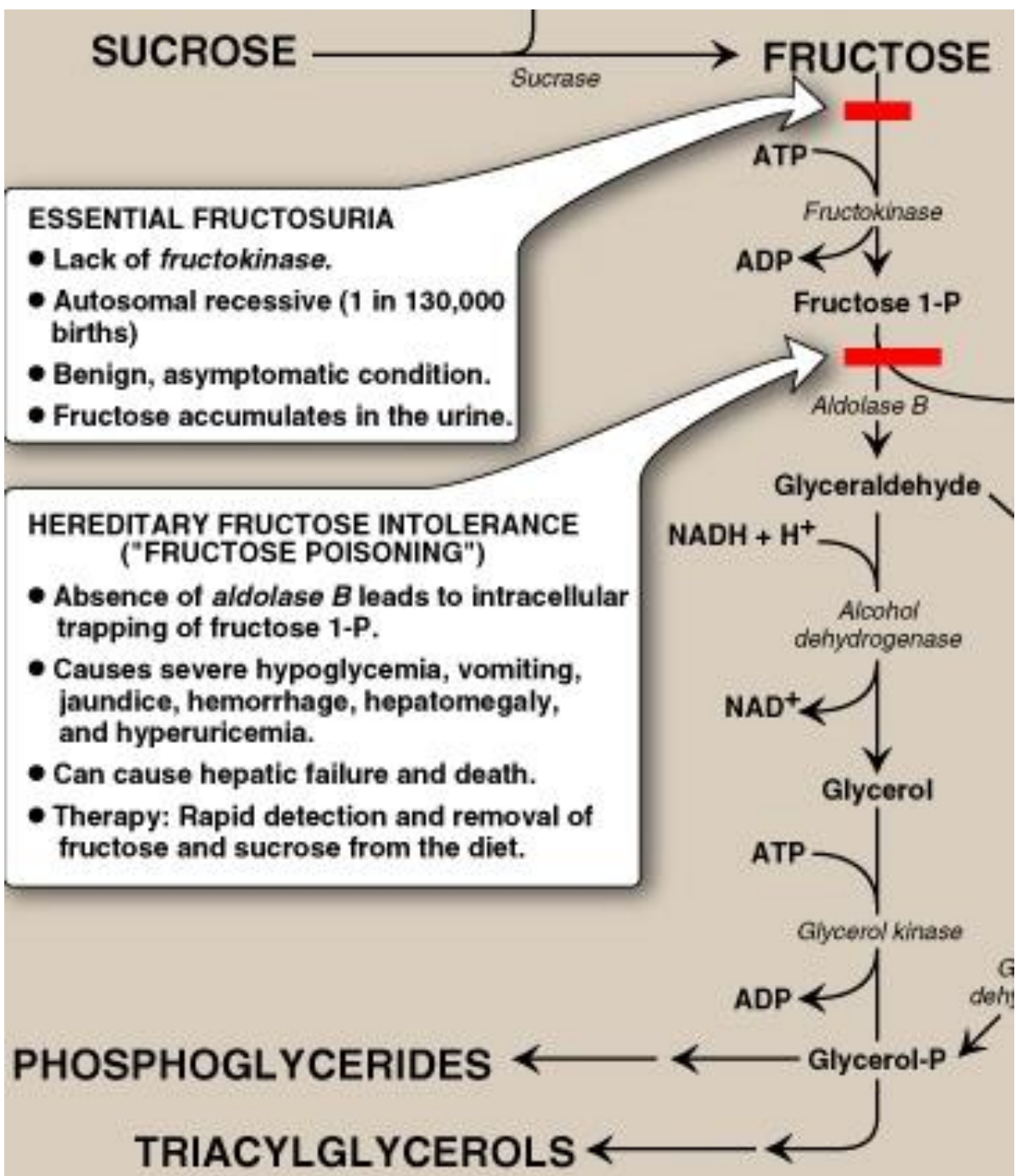
- In most tissues
- Substrate  
Fruc. 1,6 bisphosphate  
**Not**  
Fruc. 1 phosphosphate



# Fructose Metabolism and Interaction with other Pathways

# Disorders of Fructose Metabolism

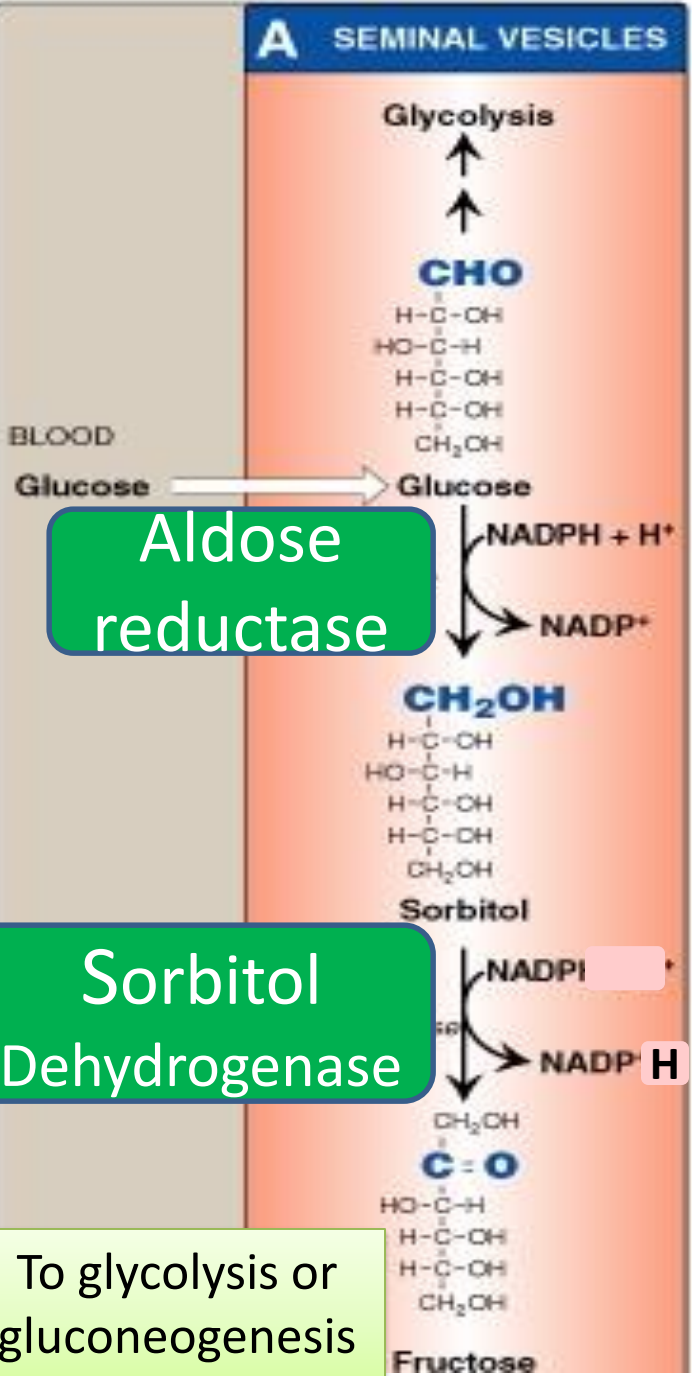
- **Fructokinase Deficiency** → essential fructosuria
  - Accumulation of fructose → fructosuria
  - Benign condition
- **Aldolase Deficiency** → hereditary fructose intolerance, (Fructose Poisoning)
  - Severe disturbance in liver and kidney metabolism
  - ↑↑↑ Fruc. 1-Phosph. → drop in  $P_i$  → drop in ATP →  
↑↑ AMP → ↑ degradation of AMP
  - Hypoglycemia and lacticacidemia (lactic acidosis)
  - Hyperuricemia
  - Hepatic failure due to reduced hepatic ATP
  - Avoid fructose, sucrose and sorbitol



# Disorders of Fructose Metabolism



# Conversion of glucose to fructose via sorbitol



**Aldose Reductase:**  
Found in many tissues;  
Lens, retina, schwan cells, liver,  
kidney, ovaries, and seminal  
vesicle

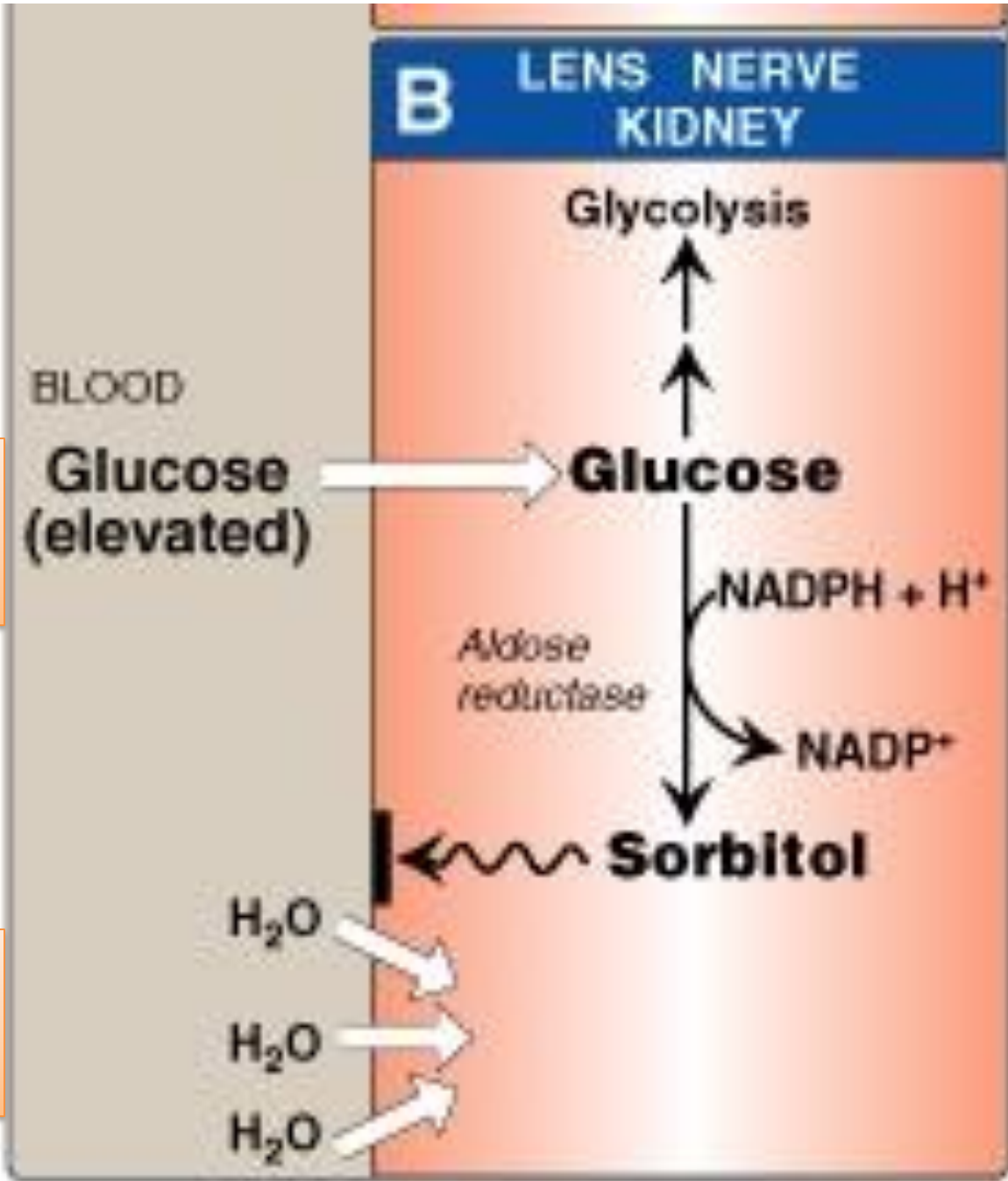
**Sorbitol Dehydrogenase:**  
Liver, ovaries and seminal  
vesicles

**Fructose :** the major energy  
source for sperm cells

# Conversion of glucose to sorbitol and Diabetic Complications

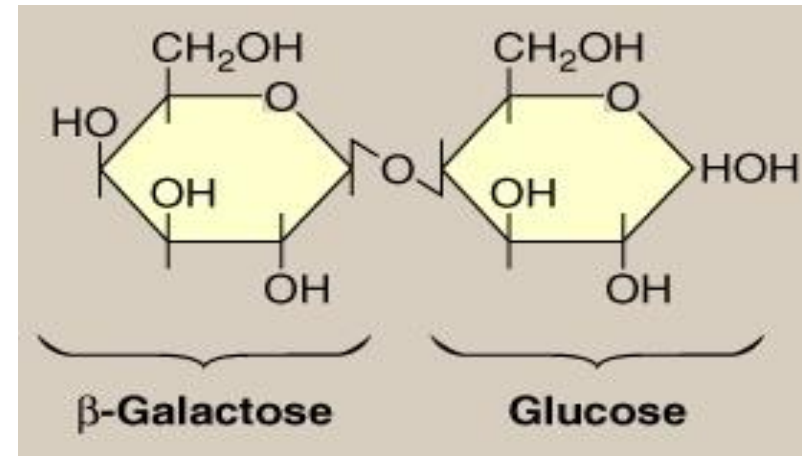
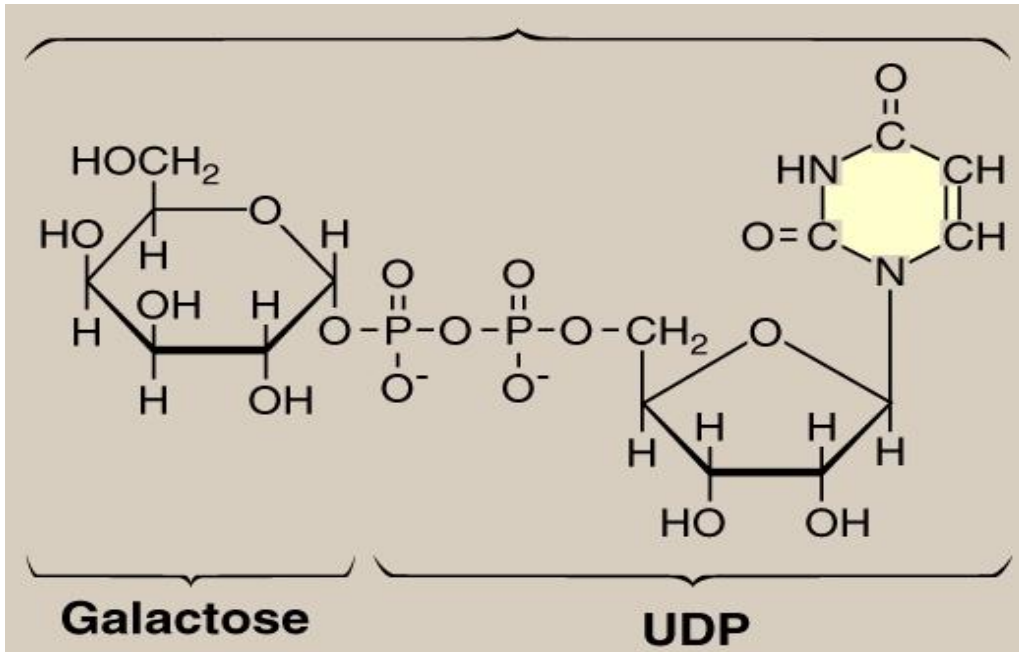
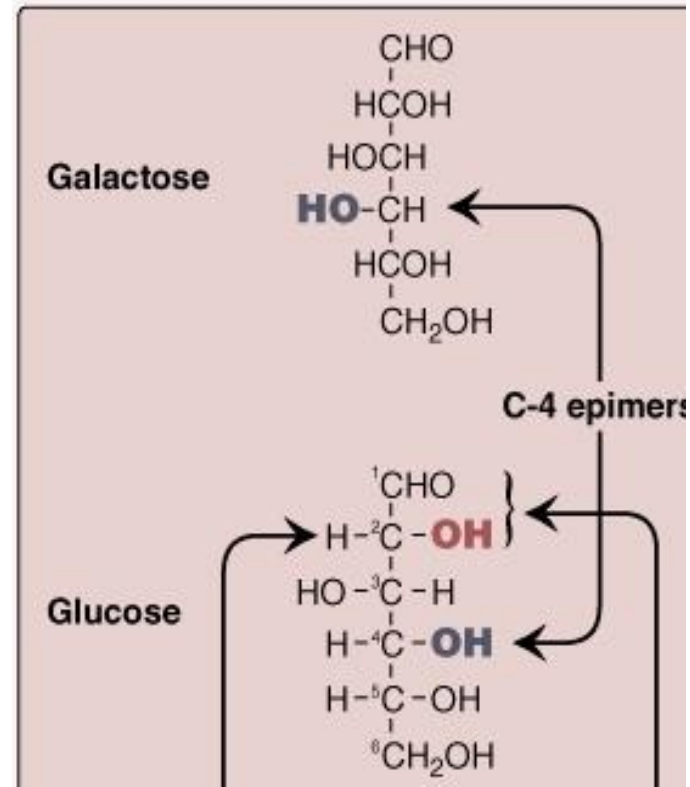
Glucose entry is insulin independent in these tissues

Water retention and cell swelling leading to diabetic complications



# Galactose Metabolism

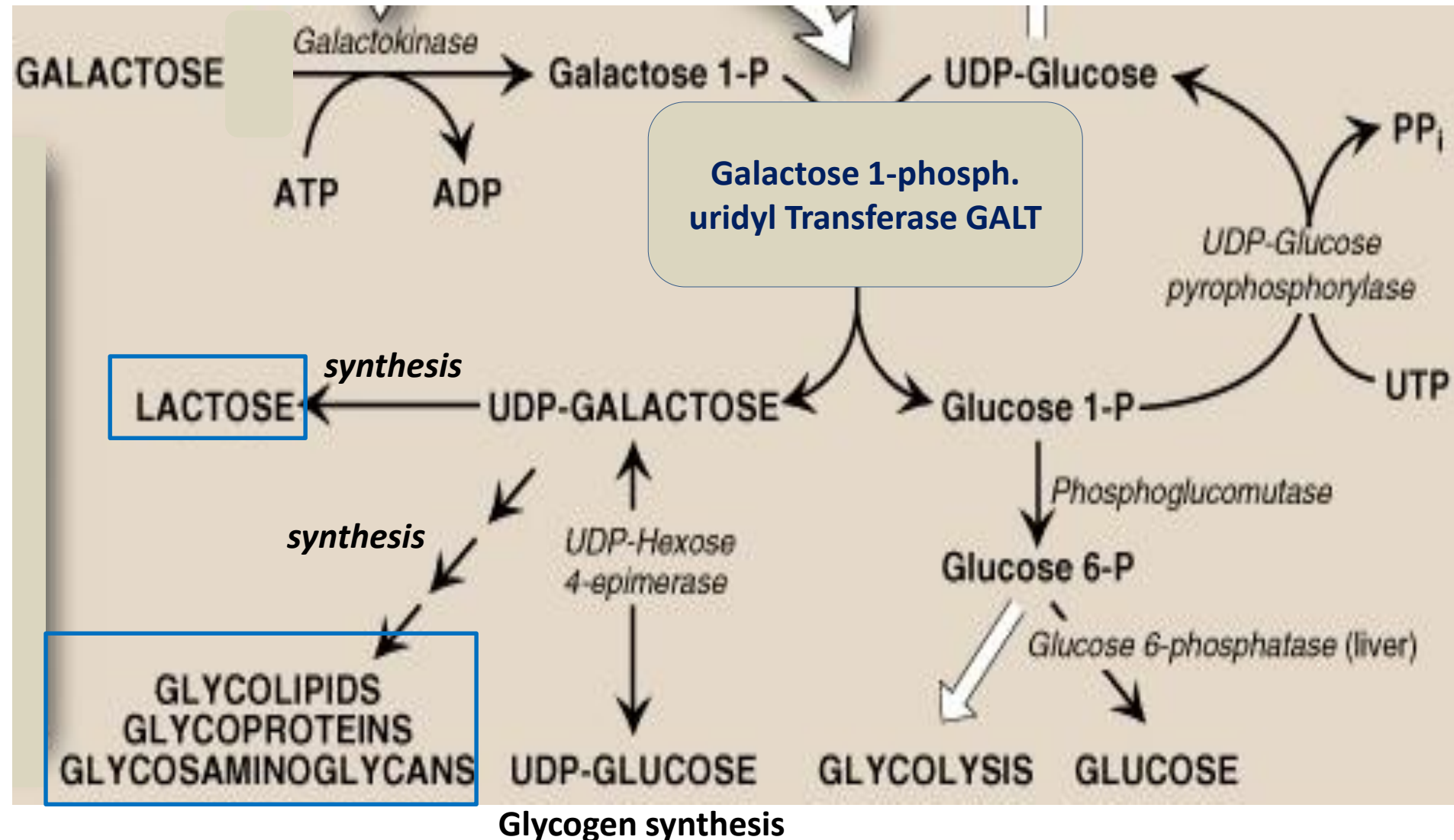
- An epimer of glucose
- Sources: component of lactose, lysosomal degradation glycolipids and glycoproteins
- Entry to cells is insulin independent



UDP Galactose; an Intermediate in Galactose Metabolism

Lactose

# Galactose metabolism and fates



# Disorders of Galactose Metabolism

Sugar alcohol

## GALACTOKINASE DEFICIENCY

- This causes galactosemia and galactosuria.
- It causes galactitol accumulation if galactose is present in the diet.

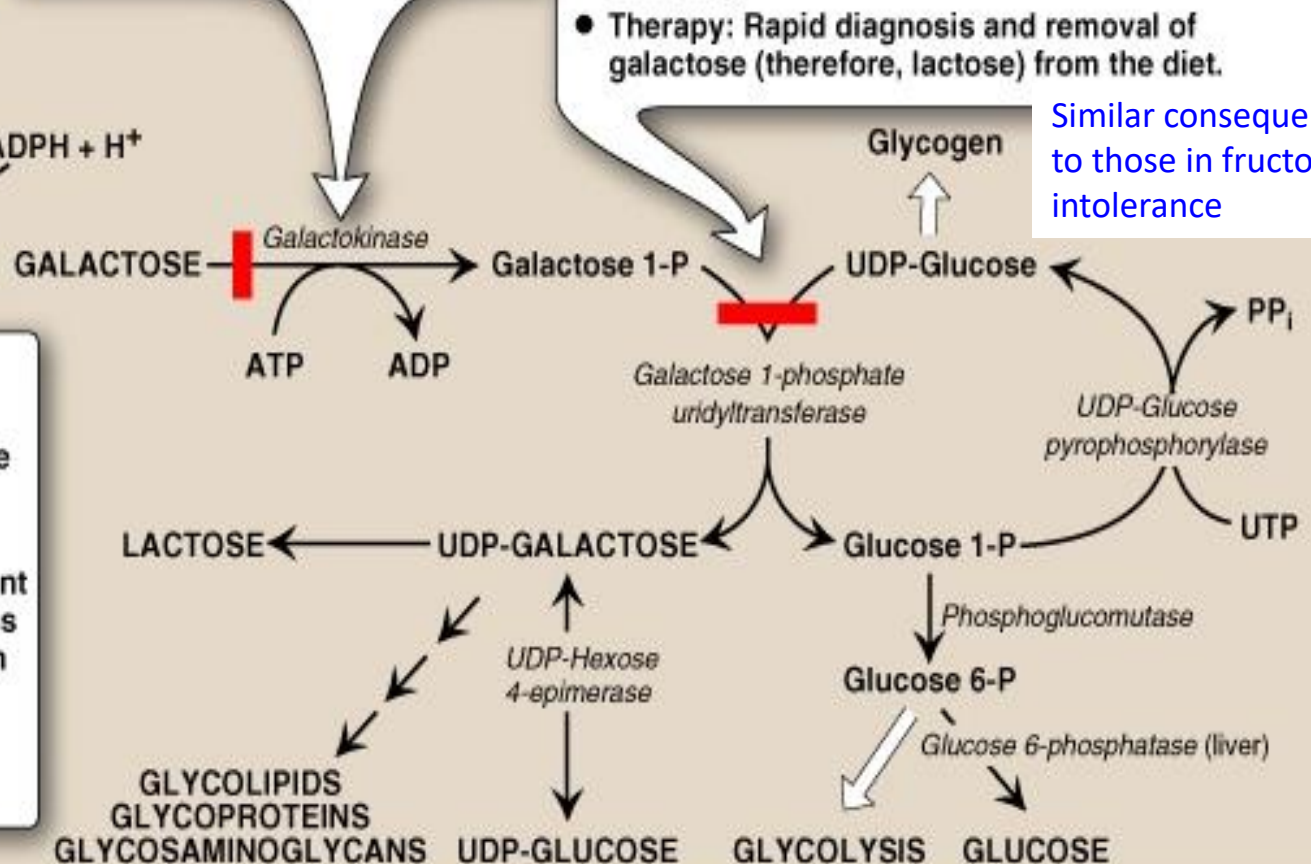
## CLASSIC GALACTOSEMIA

- **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.

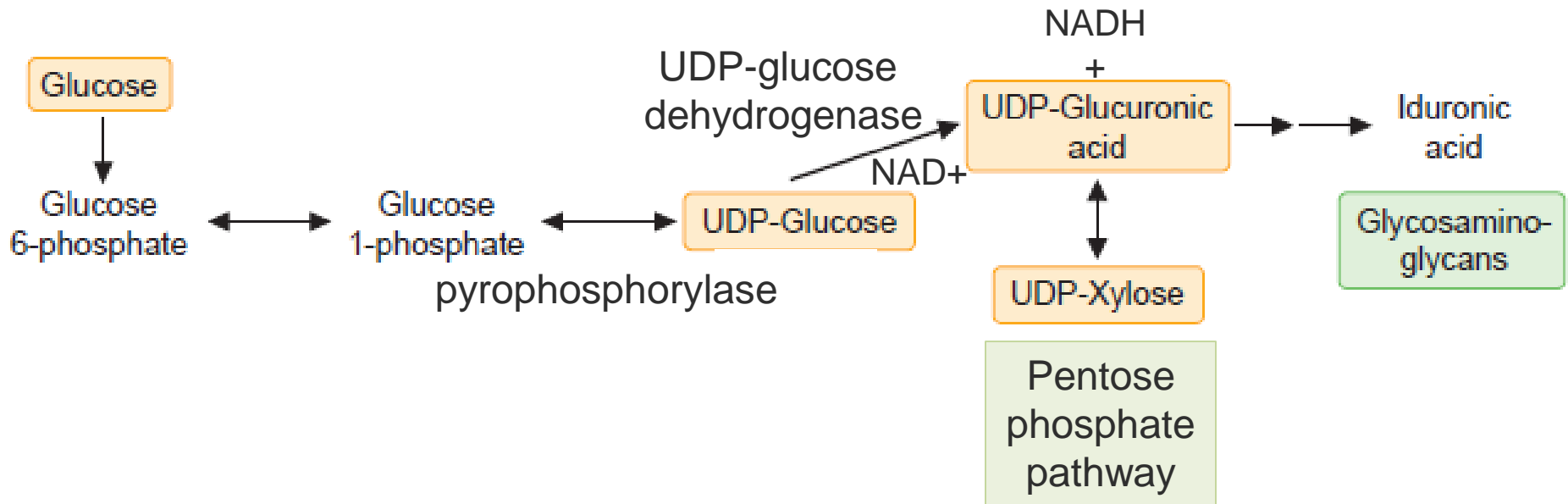
Similar consequences to those in fructose intolerance

## 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.



# Metabolism of Glucuronic acid



- Is a quantitatively minor route of glucose metabolism
- It provides biosynthetic precursors and interconverts some less common sugars to ones that can be metabolized.

# Lactose Synthesis

- Lactose is Galactosyl  $\beta$  (1 $\rightarrow$ 4) glucose
- Produced by mammary glands
- Galactosyl  $\beta$  (1 $\rightarrow$ 4) glucose is found in glycolipids and glycoproteins

## Lactose Synthase



- Lactose Synthase: complex of 2 proteins

Galactosyl transferase (Protein A) 

$\alpha$ -lactalbumin (Protein B)

Only in mammary glands, its synthesis is stimulated by prolactin

- In glycolipids and N-linked glycoprotein synthesis

