Metabolism of Monosaccharides and Disaccharides

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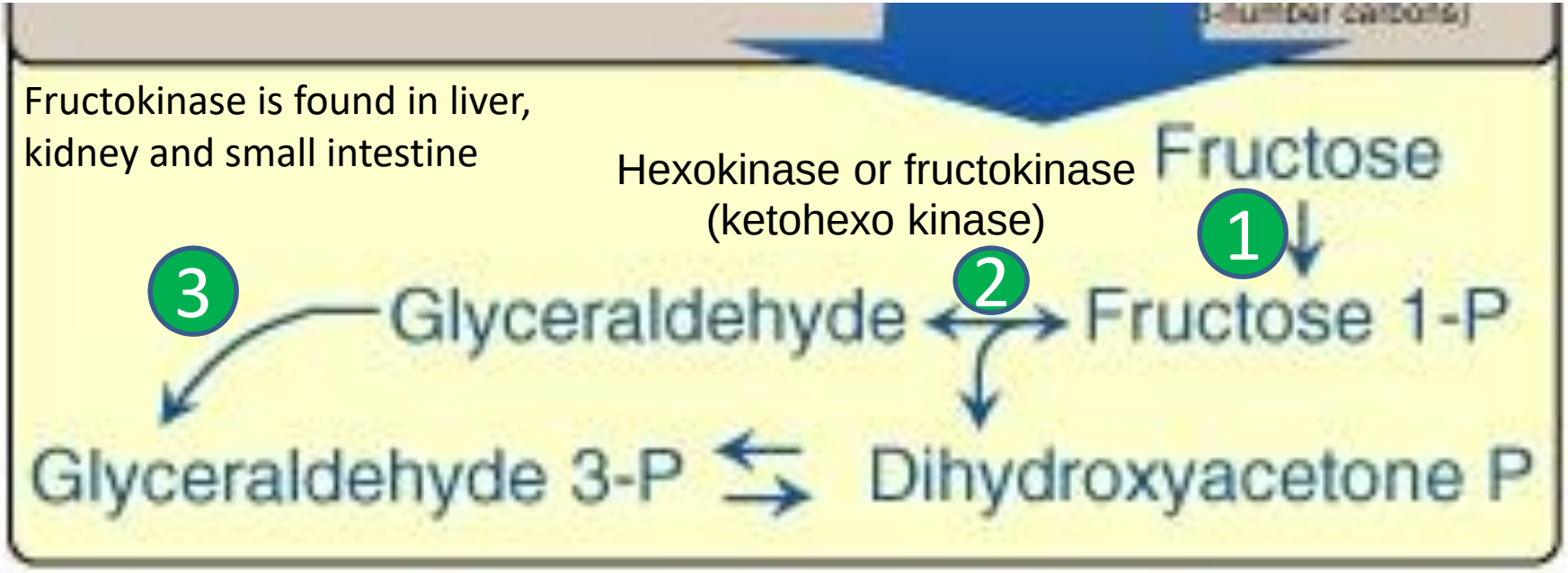
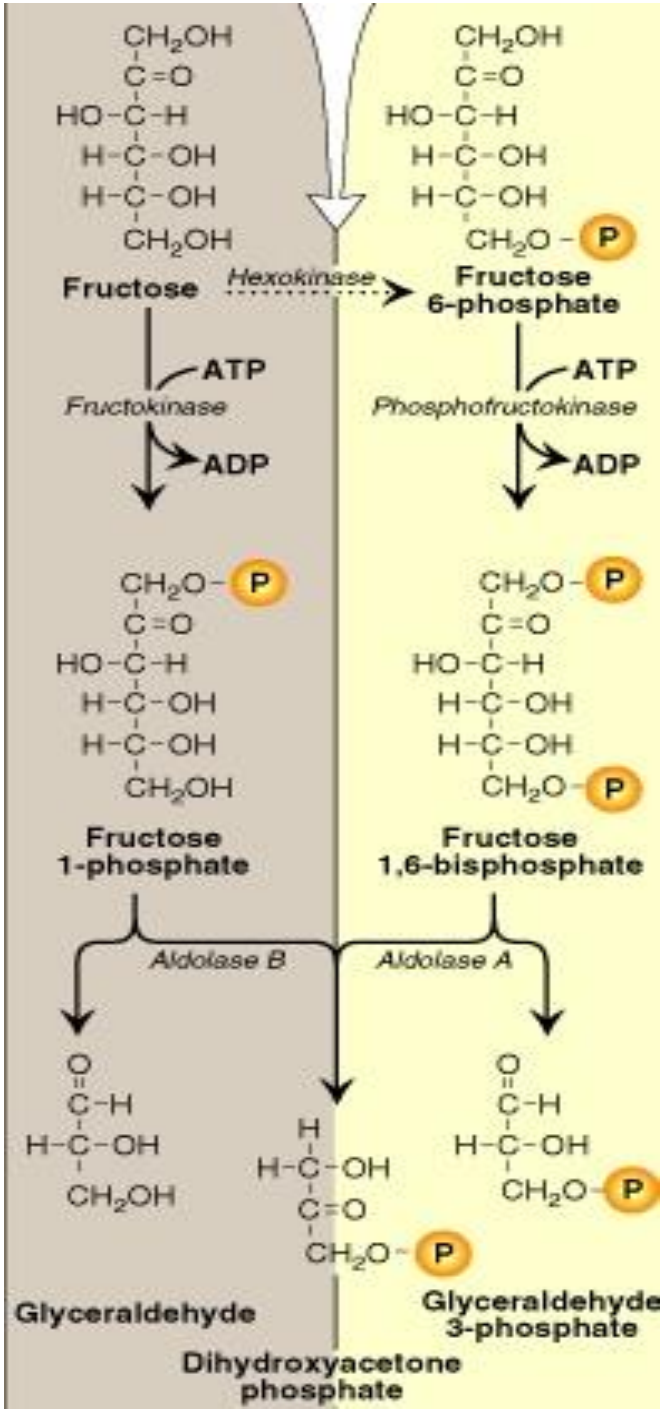
Fructose Metabolism

- 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

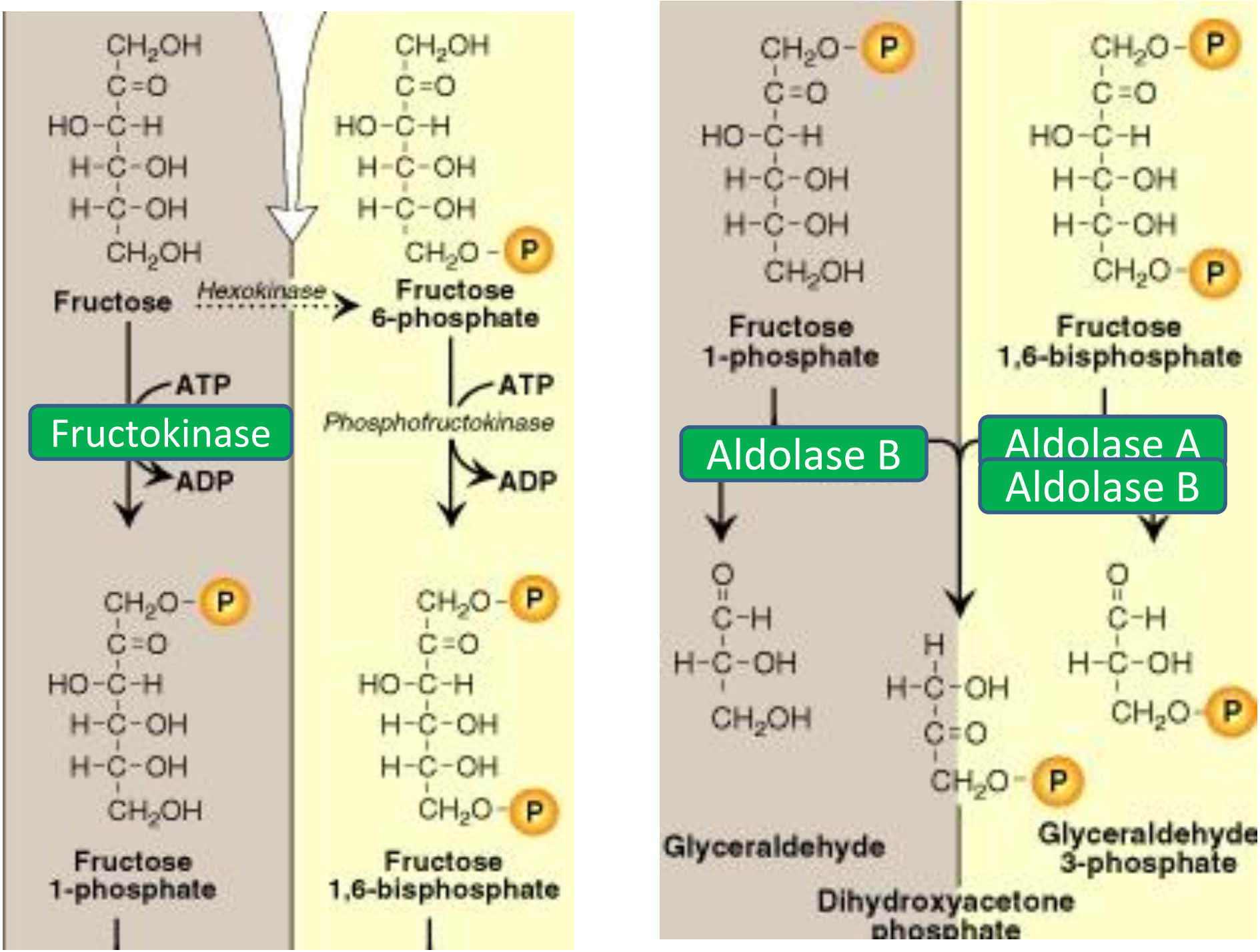




Fructose Metabolism

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
ATP
Fructokinase
ADP
ATP
Phosphofructokinase
ADP
Fructose 1-phosphate
Fructose 1,6-bisphosphate
Fructose 1-phosphate
Fructose 1,6-bisphosphate
Aldolase B
Aldolase A
Aldolase B
Glyceraldehyde
Dihydroxyacetone phosphate
Glyceraldehyde 3-phosphate

Human expresses three forms of aldolase

Aldolase B

- Liver, kidney, small intestine

- Substrate

  Fruc. 1 phopsphate

  Also

  Fruc. 1,6 bisphospate

  ↓activity➔ fructose intolerance

Aldolase A

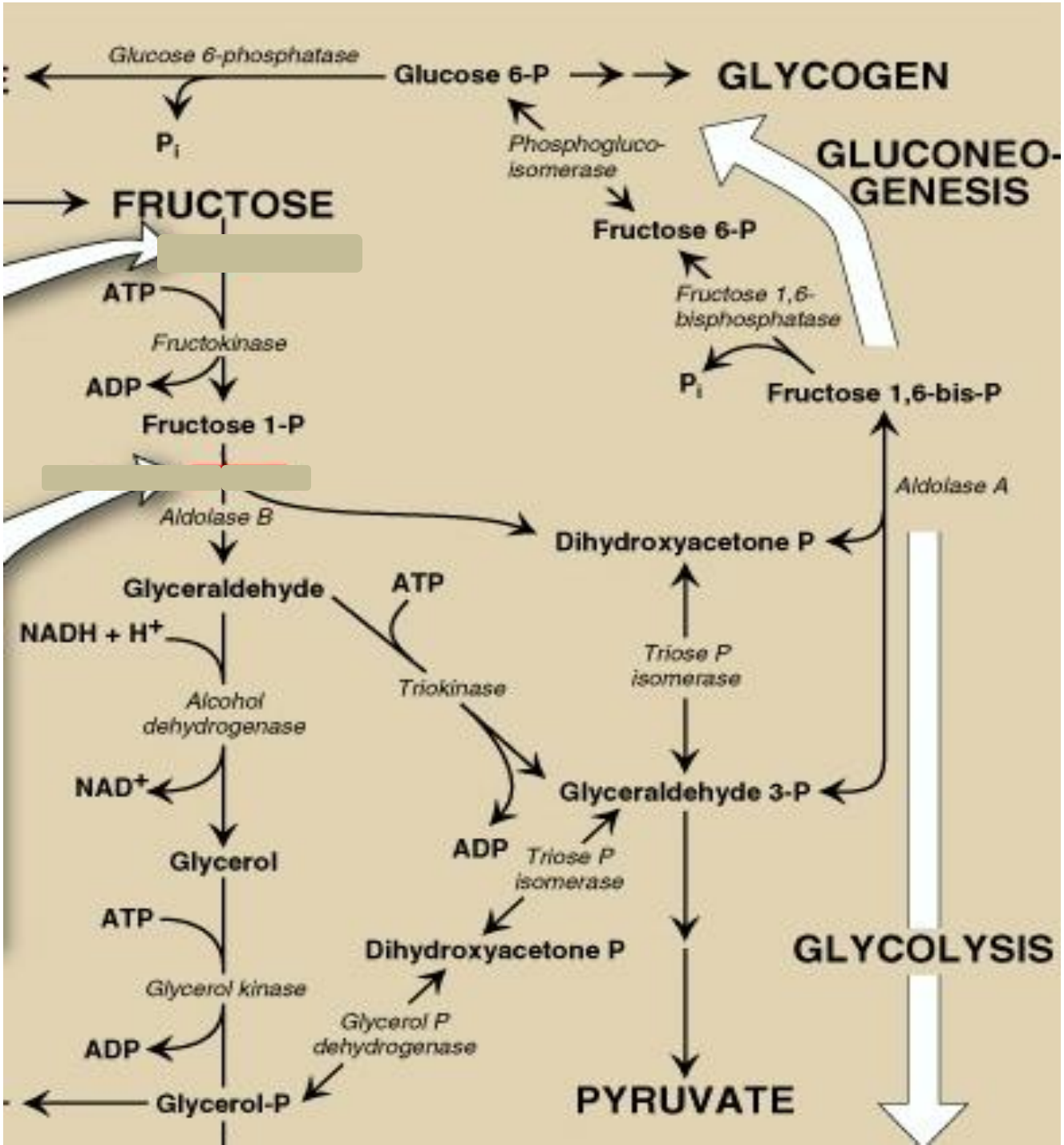
- In most tissues

- Substrate

Fruc. 1,6 bisphospate

Not

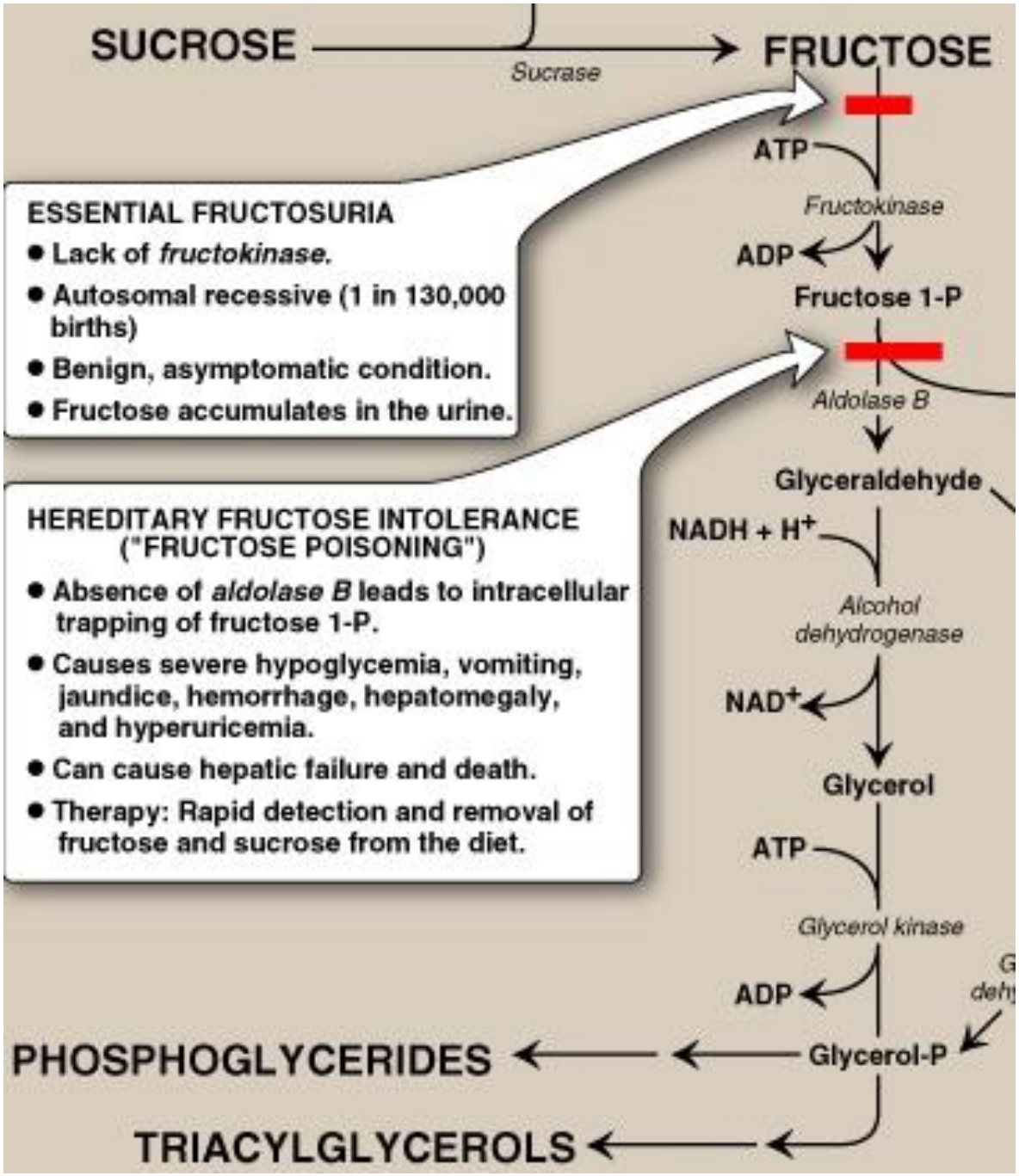
Fruc. 1 phpsphate



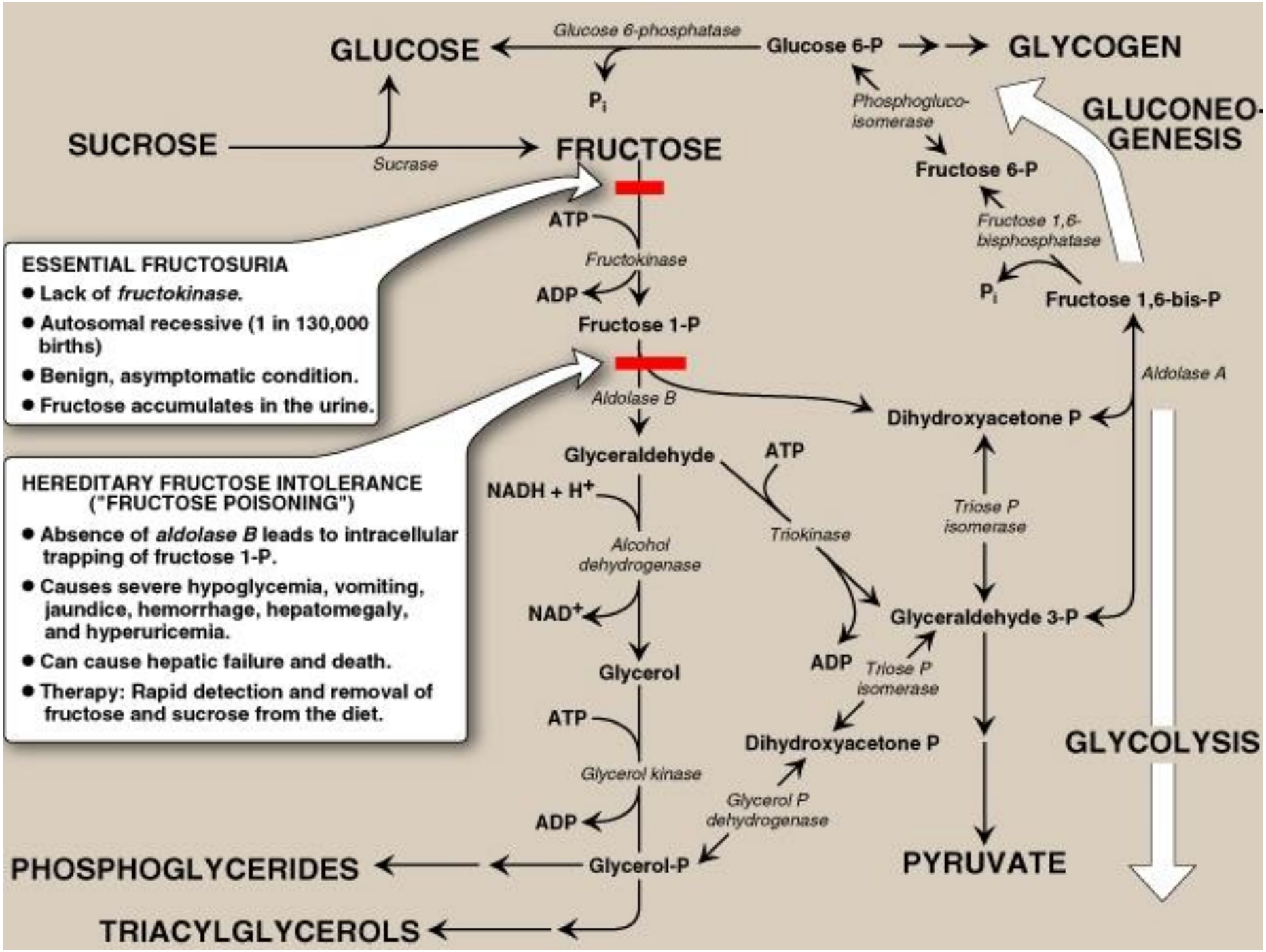
Fructose Metabolism and Interaction with other Pathways

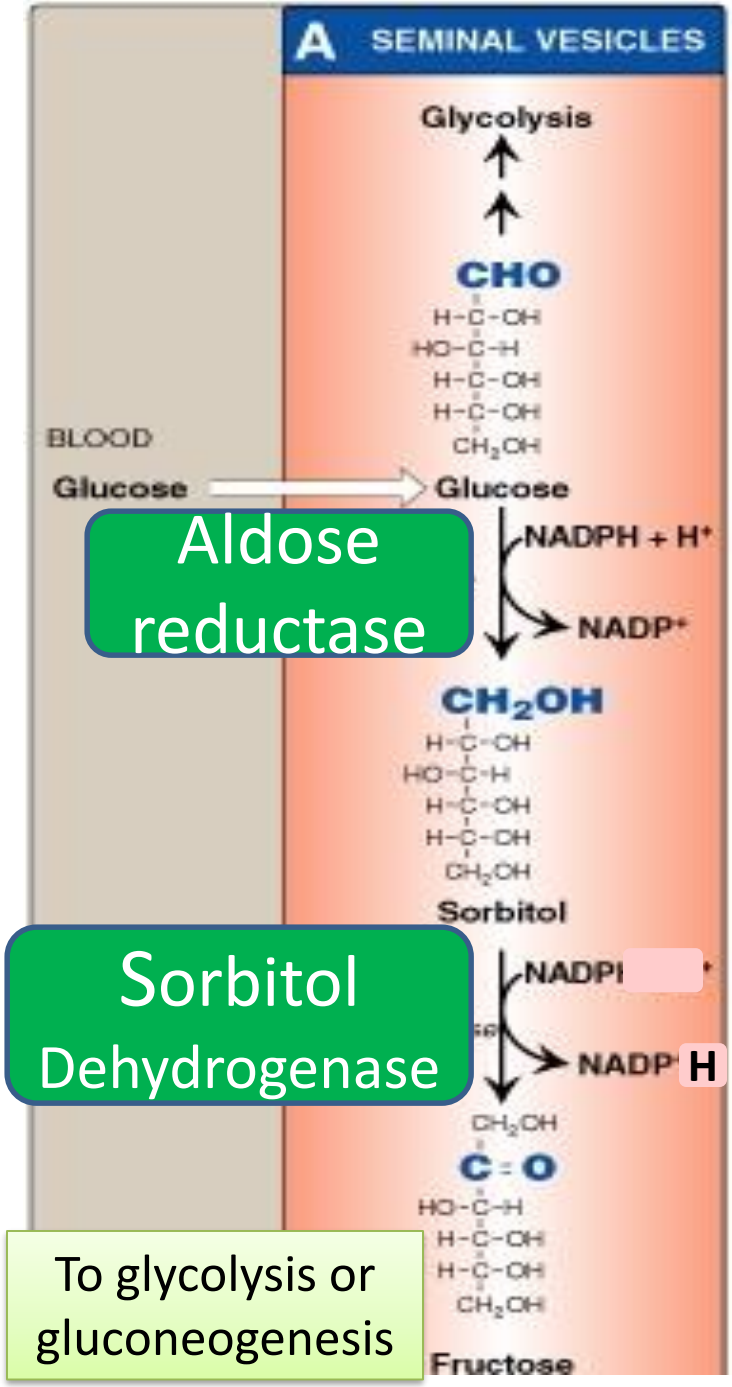
Disorders of Fructose Metabolism

- 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


GLUCOSE
Glucose 6-phosphatase
Glucose 6-P
GLYCOGEN
P_i
SUCROSE
Sucrase
FRUCTOSE
Phosphogluco-isomerase
GLUCONEO-GENESIS
Fructose 6-P
ATP
Fructokinase
Fructose 1,6-bisphosphatase
ADP
P_i
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
Dihydroxyacetone P
GLYCOLYSIS
Glycerol kinase
Glycerol P dehydrogenase
ADP
PHOSPHOGLYCERIDES
Glycerol-P
PYRUVATE
TRIACYLGLYCEROLS
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.



Conversion of glucose to fructose via sorbitol

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

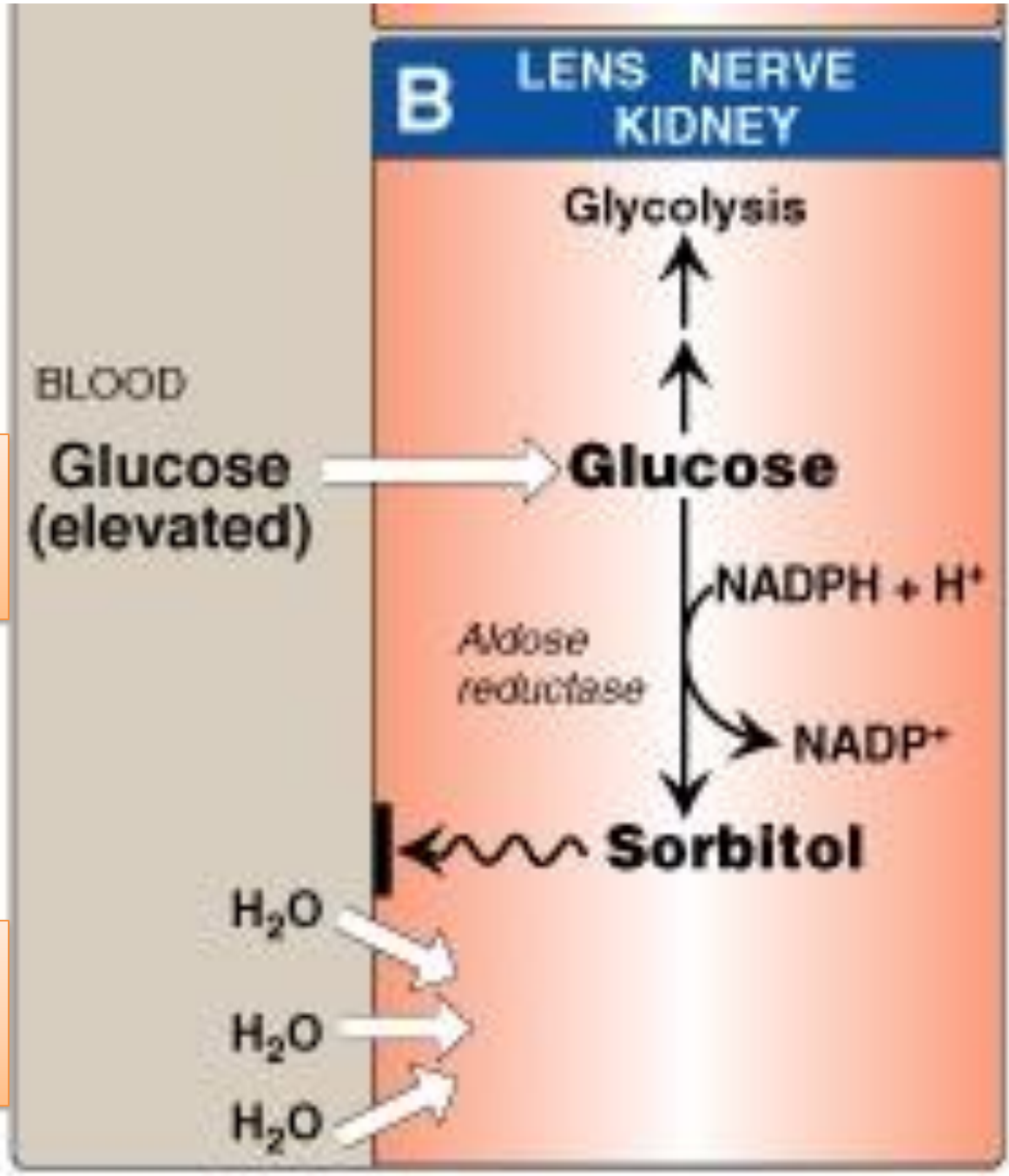
Sorbitol Dehydrogenase:
Liver, ovaries and seminal vesicles

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

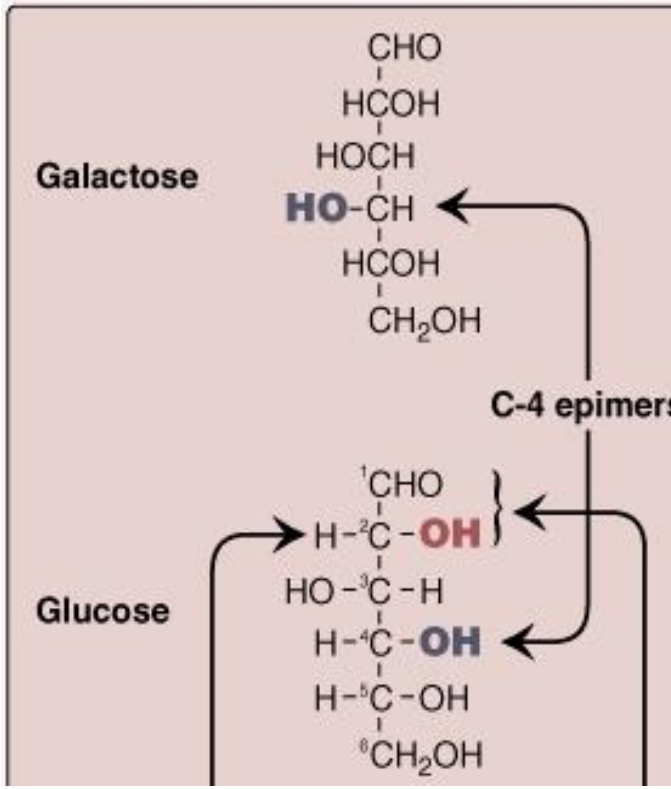


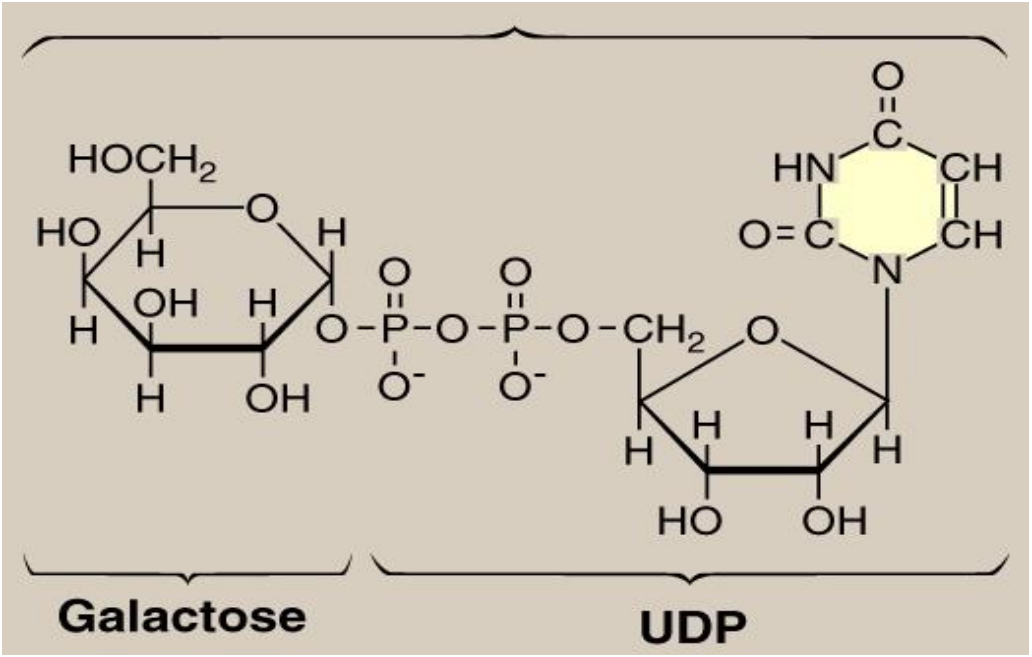
Galactose Metabolism

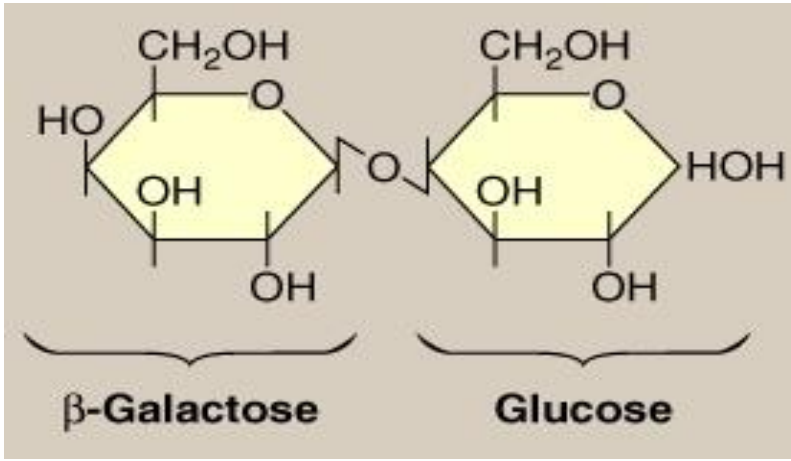
- An epimer of glucose
- Sources: component of lactose,

lysosomal degradation glycolipids and glycoproteins

- Entry to cells is insulin independent



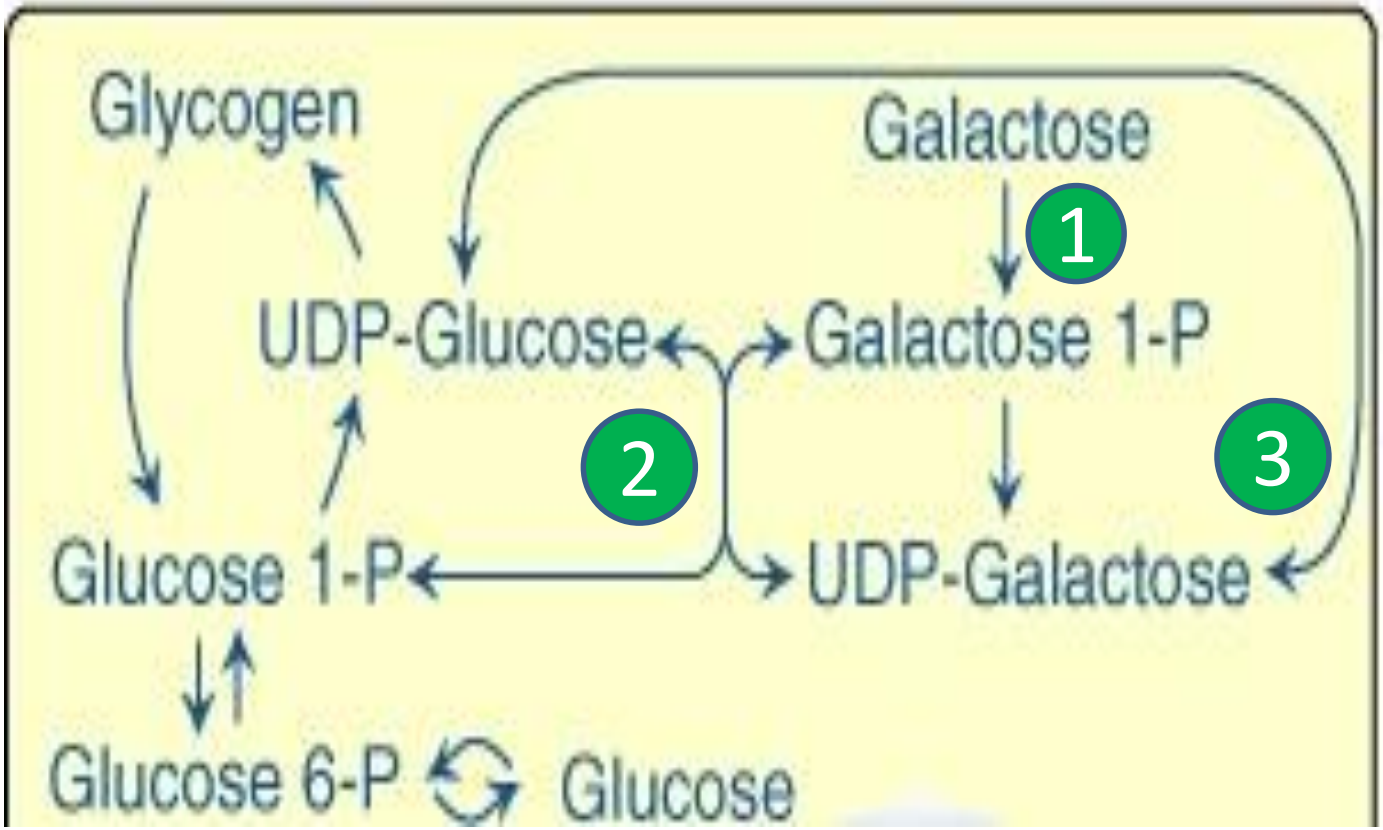




Lactose

UDP Galactose; an Intermediate in Galactose Metabolism

Galactose Metabolism

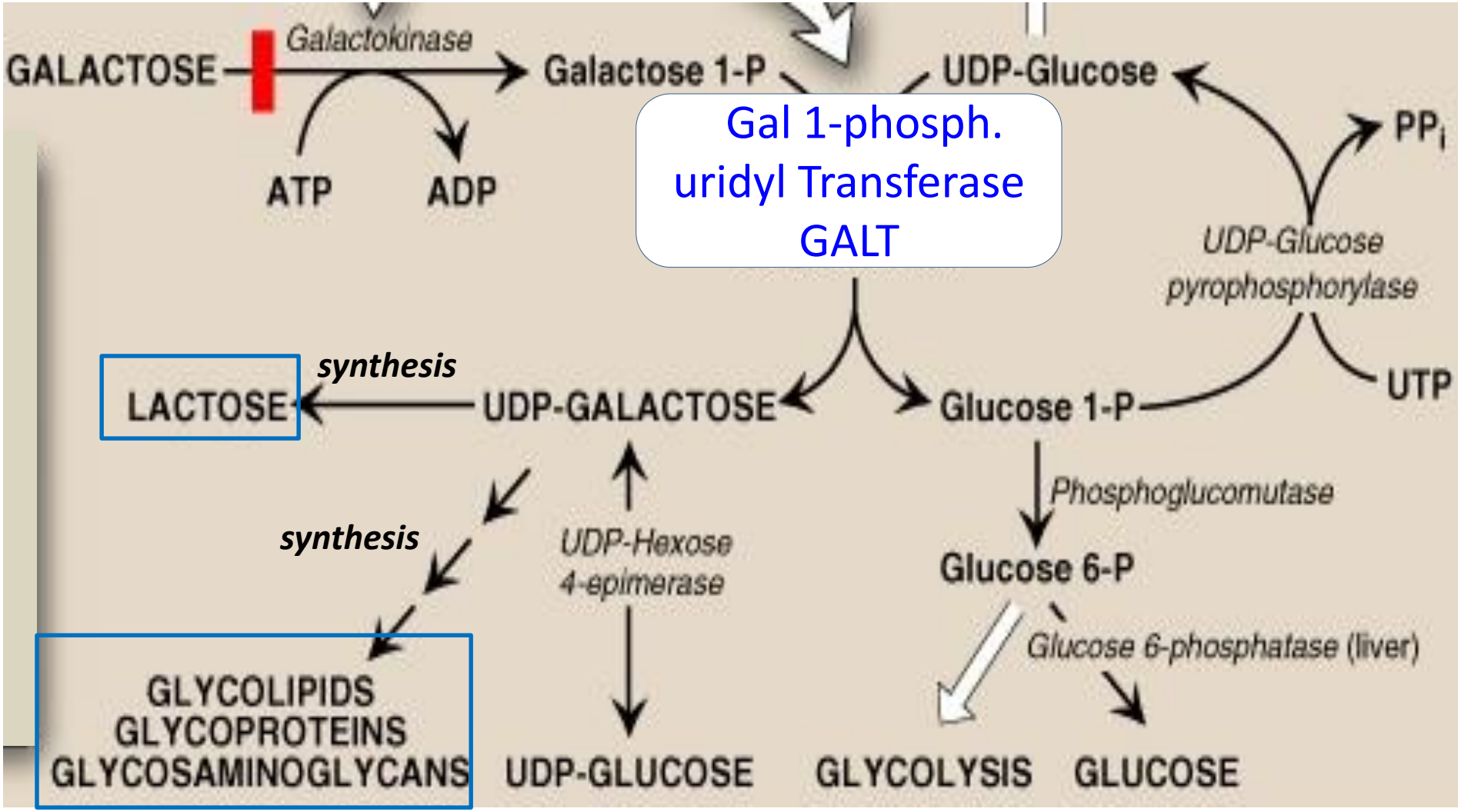


Galactose + ATP —(Galactokinase)→ Gal. 1-Phosph ADP

Gal 1-Phosph + UDP Glc. —(Transferase (GALT))⇌ UDP- Galactose + Glc1-Phosph

UDP Galactose —(Epimerase)⇌ UDP Glucose

Galactose metabolism and fates



Disorders of Galactose Metabolism

1. Deficiency of GALT → classic Galactosemia

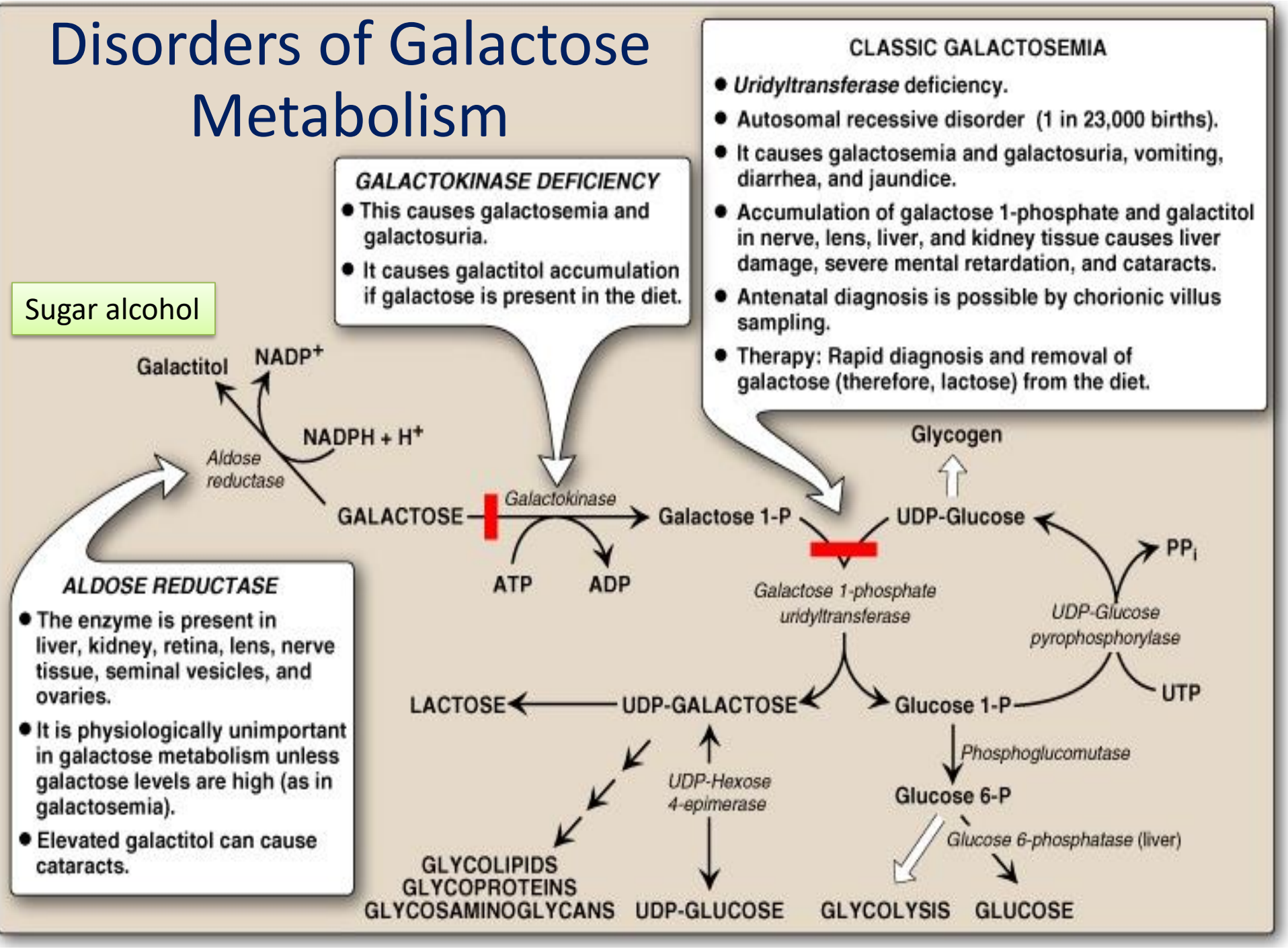
- Accumulation of Galactose 1-Phosphate and galactose
- Similar consequences to those in fructose intolerance

- Galactose ••••••→ Galactitol production

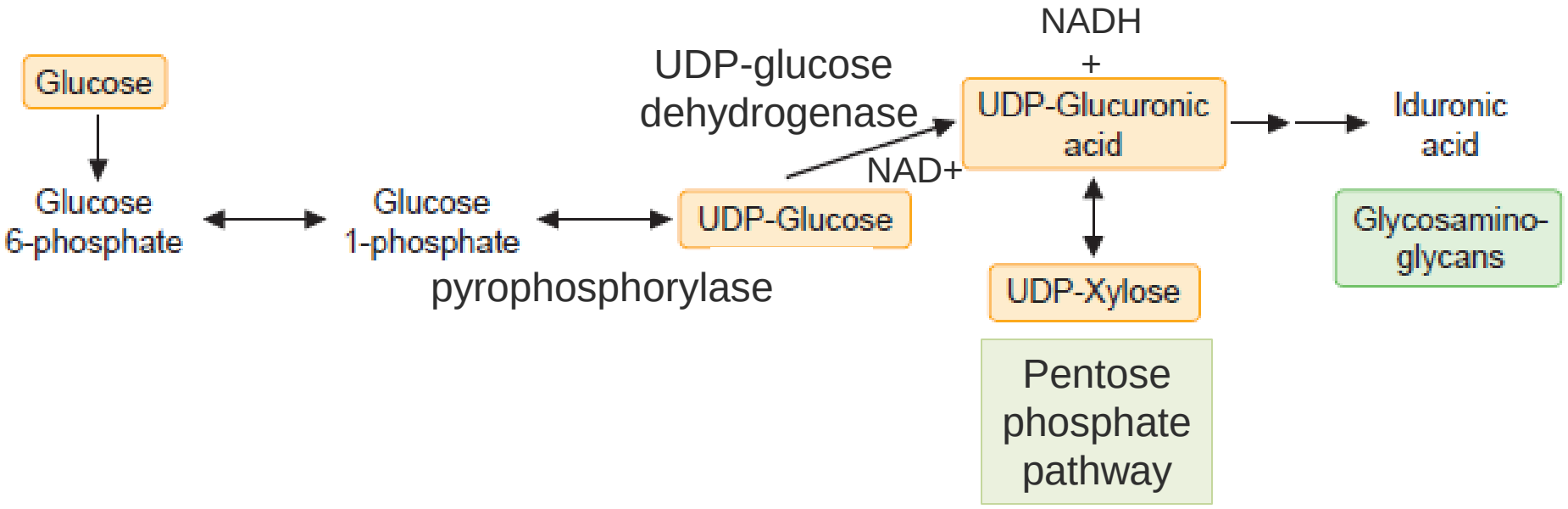
2. Deficiency of Galactokinase

- Accumulation of Galactose ••••••→ Galactitol

Disorders of Galactose Metabolism



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.

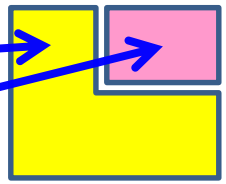
Lactose Synthesis

- Lactose is Galactosyl β (1→4) glucose
- Produced by mammary glands
- Galactosyl β (1→4) glucose is found in glycolipids and glycoproteins

Lactose Synthase

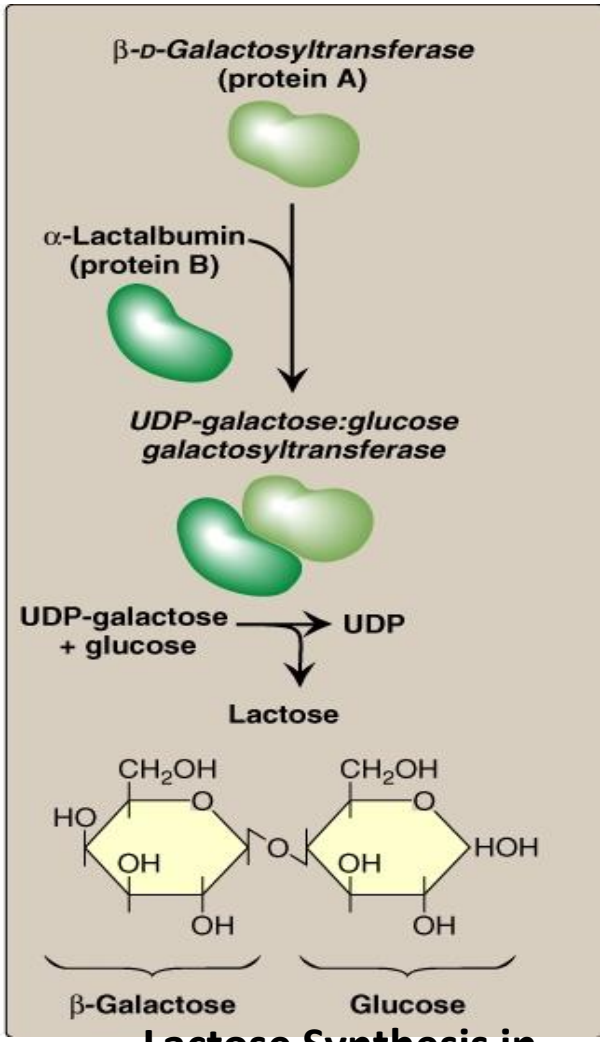
UDP Gal. + Glucose → Lactose + UDP

- Lactose Synthase: complex of 2 proteins
  - Galactosyl transferase (Protein A)
  - α-lactalbumin (Protein B)
  - Only in mammary glands, its synthesis is stimulated by prolactin



- In glycolipids and N-linked glycoprotein synthesis

UDP-Gal + N acetyl glucosamine —Protein A→ N-acetyllactosamine



Lactose Synthesis in Mammary Glands