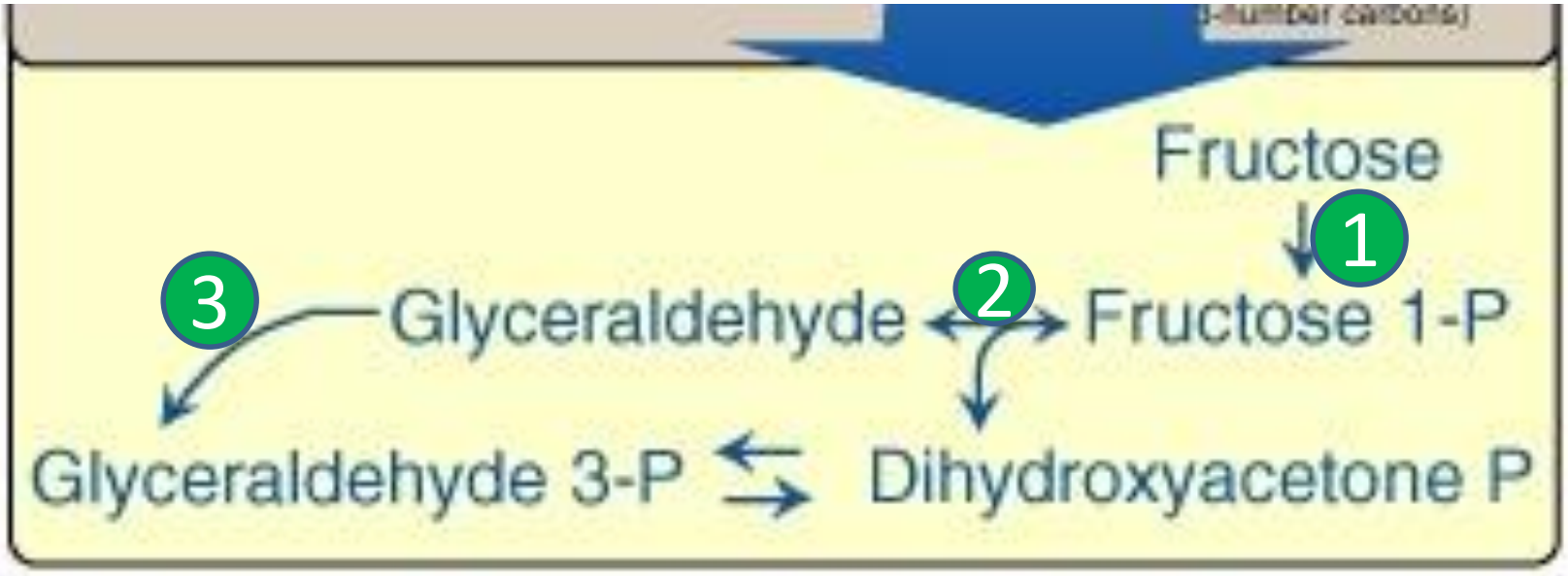
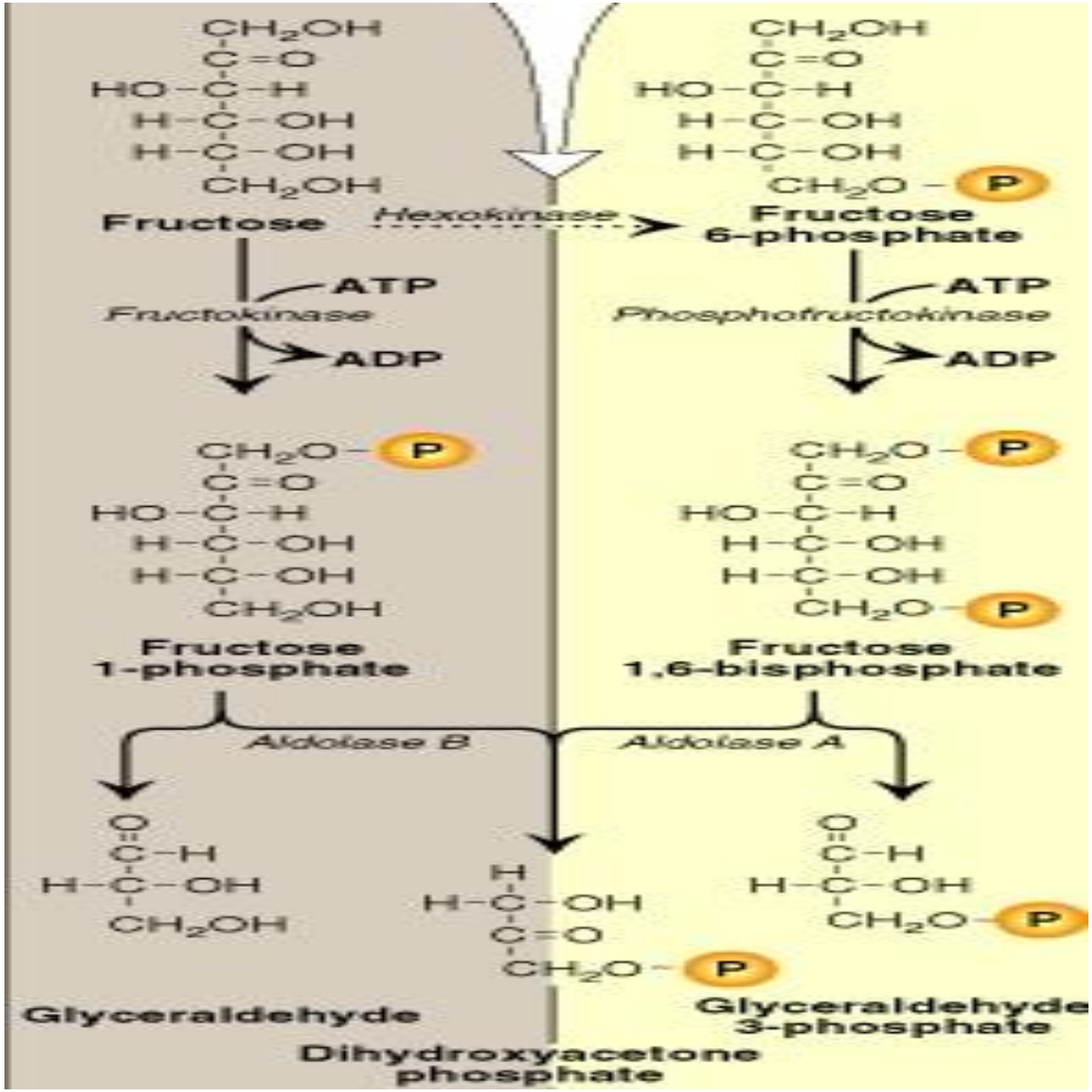
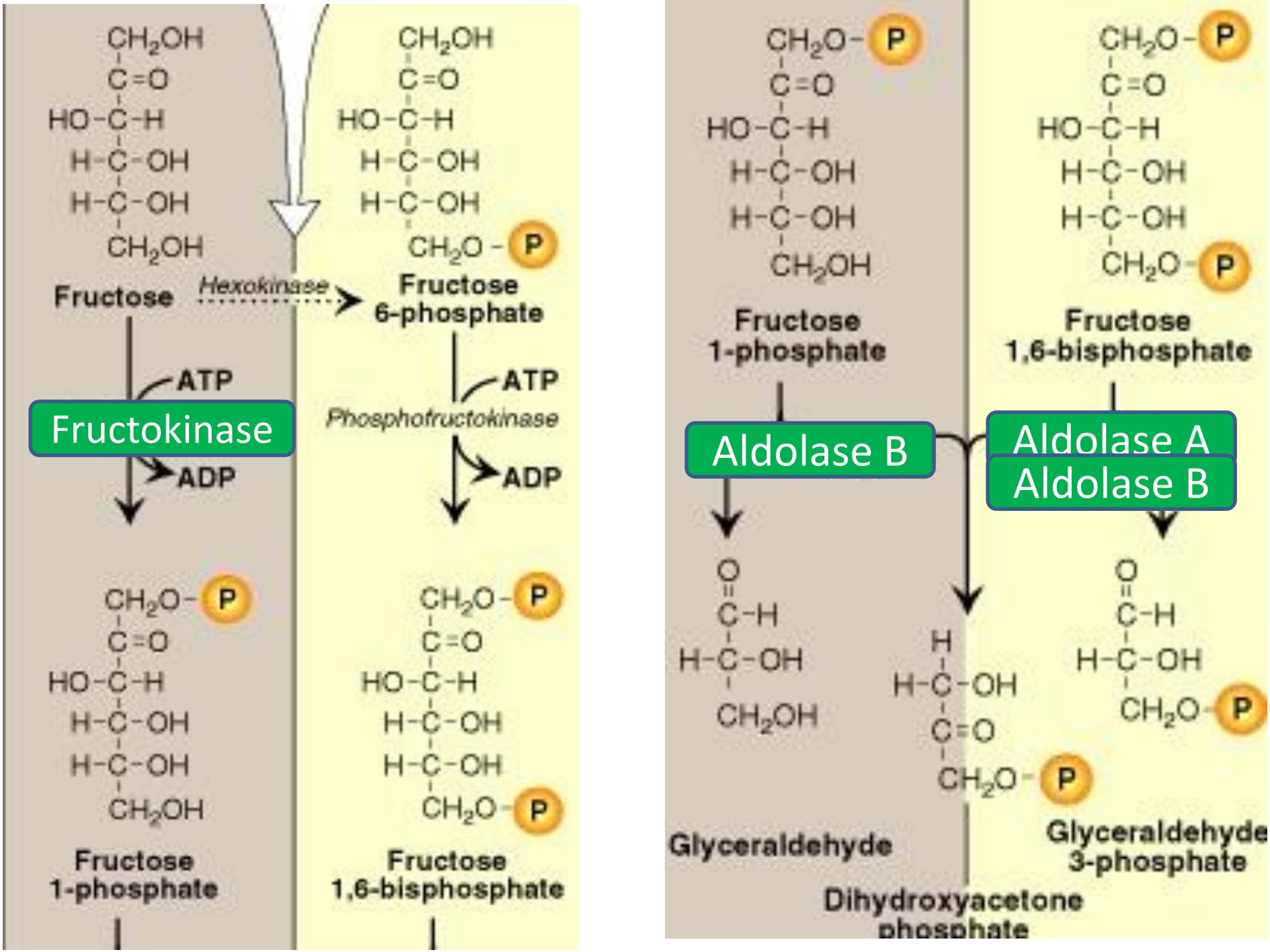
Metabolism of Monosaccharides and Disaccharides

Fructose Metabolism

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




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

  Also

  Fruc. 1,6 bisphospate

  ↓activity➔ fructose intolerance

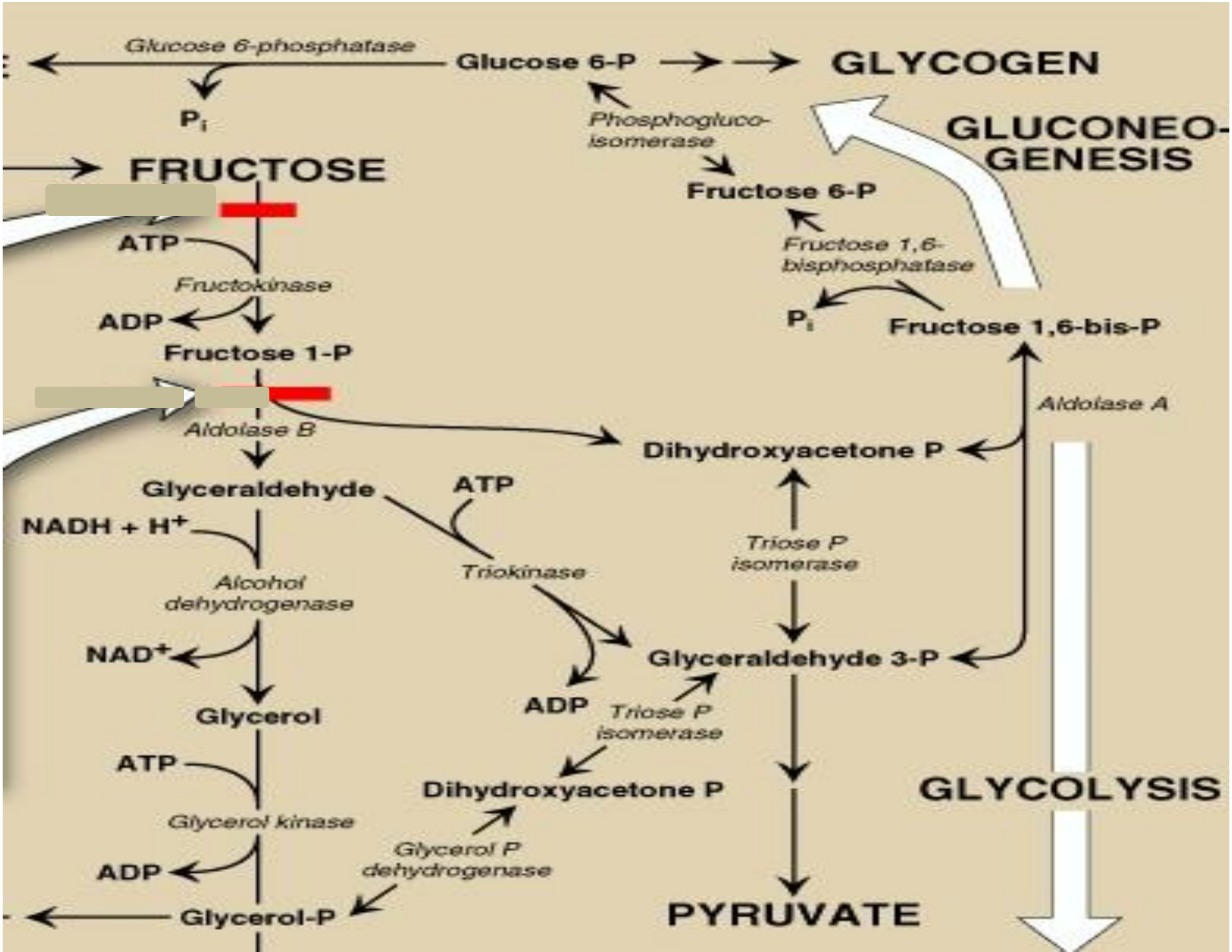
Aldolase A

- In most tissues
- Substrate

Fruc. 1,6 bisphospate

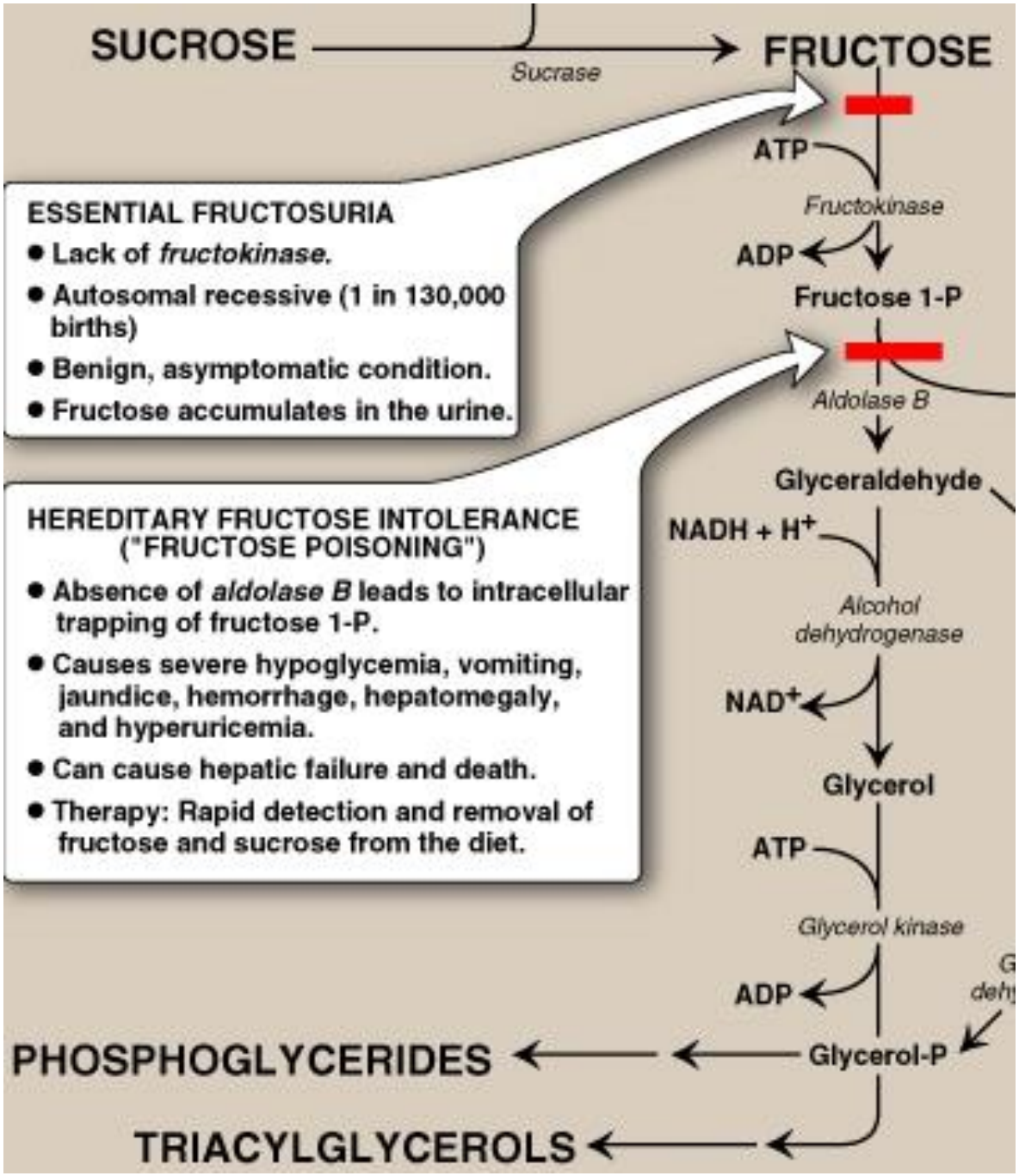
Not

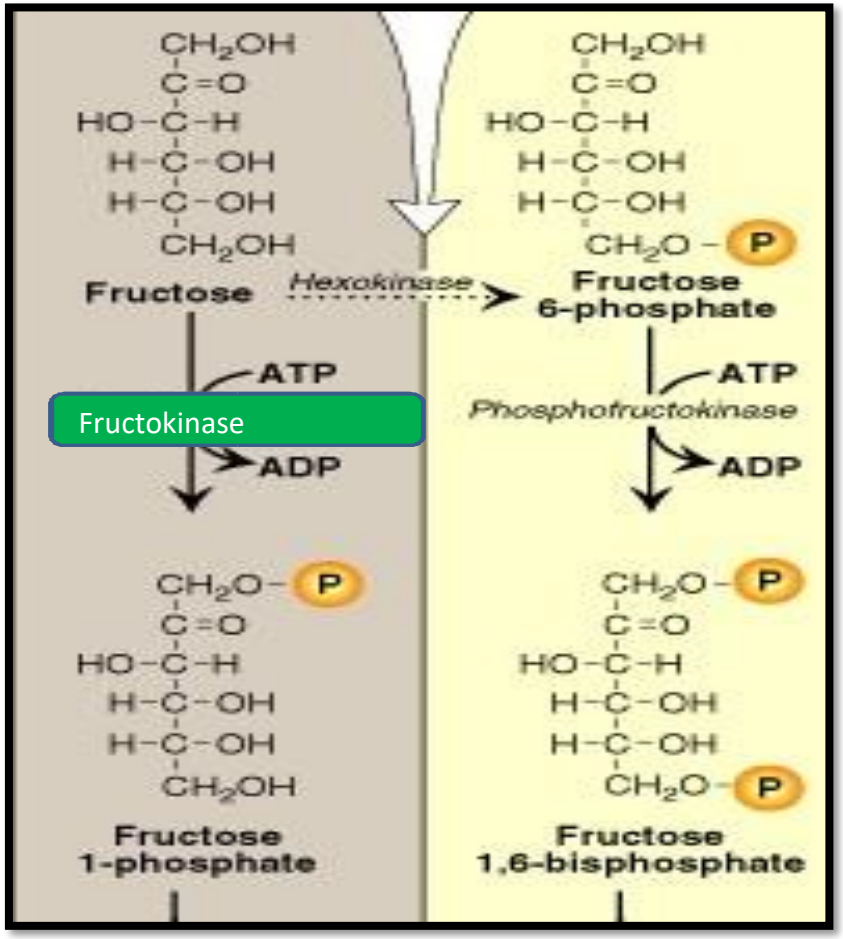
Fruc. 1 phpsphate

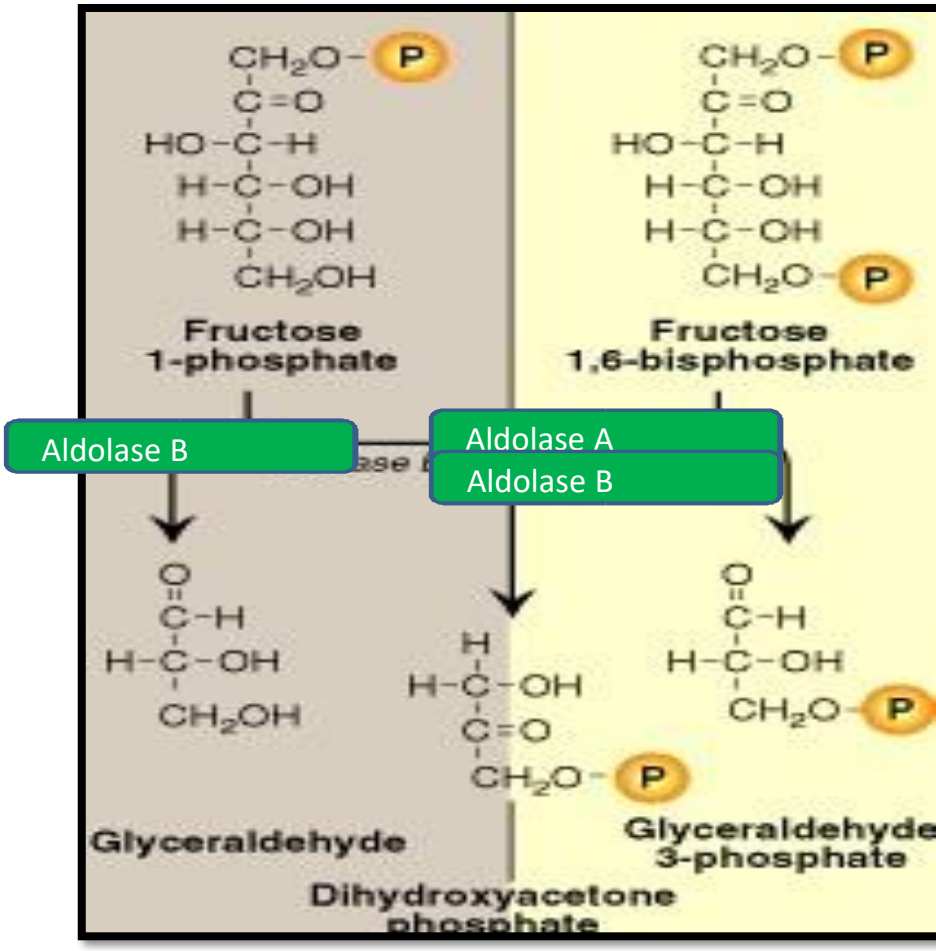

Glucose 6-phosphatase
Glucose 6-P
GLYCOGEN
P_i
Phosphogluco-isomerase
GLUCONEO-GENESIS
FRUCTOSE
Fructose 6-P
ATP
Fructose 1,6-bisphosphatase
Fructokinase
ADP
P_i
Fructose 1,6-bis-P
Fructose 1-P
Aldolase A
Aldolase B
Dihydroxyacetone P
Glyceraldehyde
ATP
$NADH + H^+$
Triose P isomerase
Triokinase
Alcohol dehydrogenase
NAD^+
Glyceraldehyde 3-P
ADP
Triose P isomerase
Glycerol
ATP
Dihydroxyacetone P
GLYCOLYSIS
Glycerol kinase
Glycerol P dehydrogenase
ADP
Glycerol-P
PYRUVATE

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
  - Hepatic failure

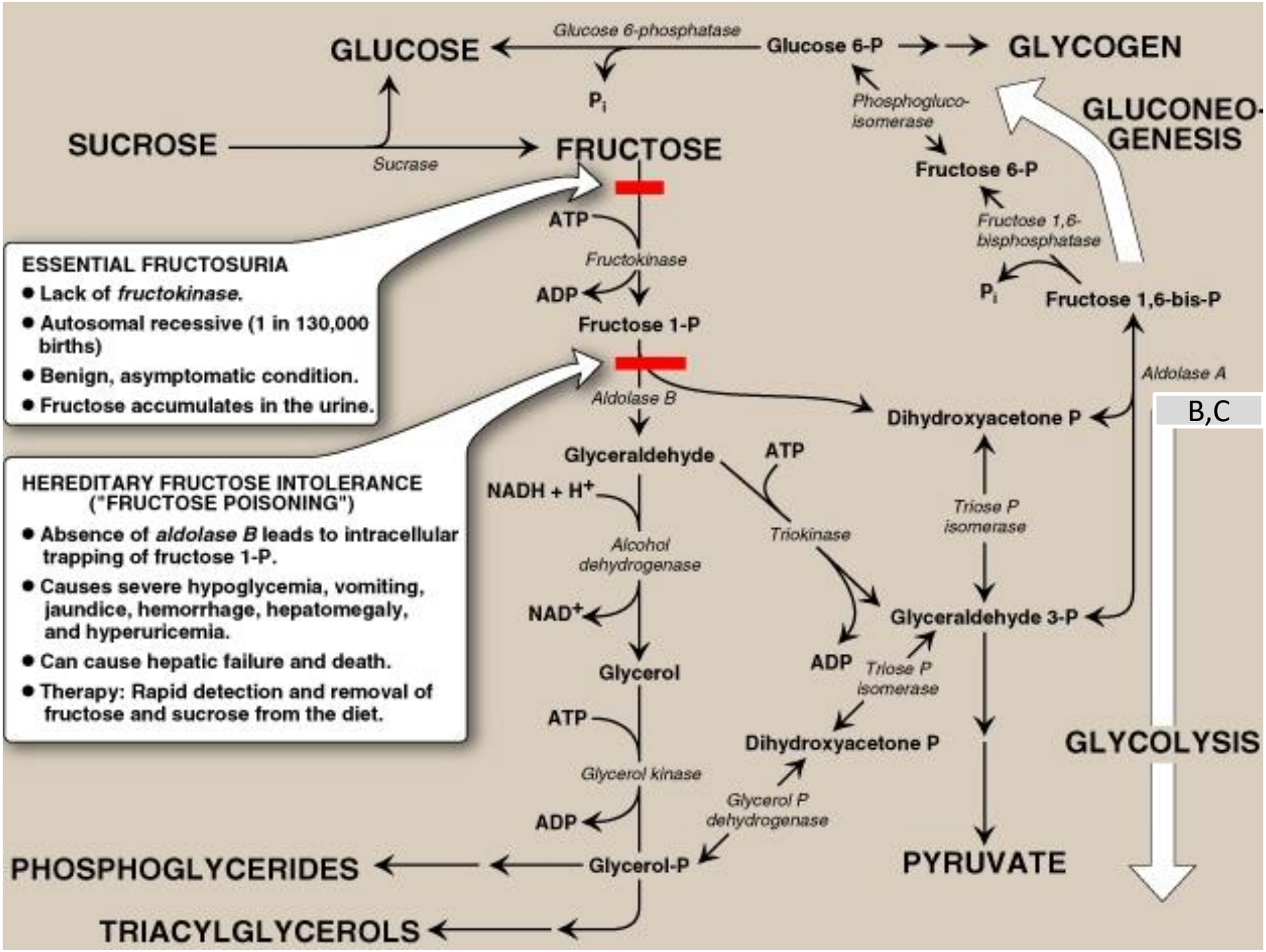

SUCROSE
Sucrase
FRUCTOSE
ATP
Fructokinase
ADP
Fructose 1-P
Aldolase B
Glyceraldehyde
NADH + H+
Alcohol dehydrogenase
NAD+
Glycerol
ATP
Glycerol kinase
ADP
Glycerol-P
PHOSPHOGLYCERIDES
TRIACYLGLYCEROLS
ESSENTIAL FRUCTOSURIA
• Lack of fructokinase.
• Autosomal recessive (1 in 130,000 births)
• Benign, 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.





Human expresses three forms of aldolase

Aldolase B	Aldolases : A and C
Found in liver , kidney , small intestine	C : found in the brain Aldolase A found in most tissues.
Act on fructose -1-phosphate , and fructose 1 ,6 –bisphosphate	Act on fructose 1 ,6 –bisphosphate only


GLUCOSE
Glucose 6-phosphatase
Glucose 6-P
GLYCOGEN
P_i
Phosphogluco-isomerase
GLUCONEO-GENESIS
SUCROSE
Sucrase
FRUCTOSE
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ATP
Fructose 1,6-bisphosphatase
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ADP
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
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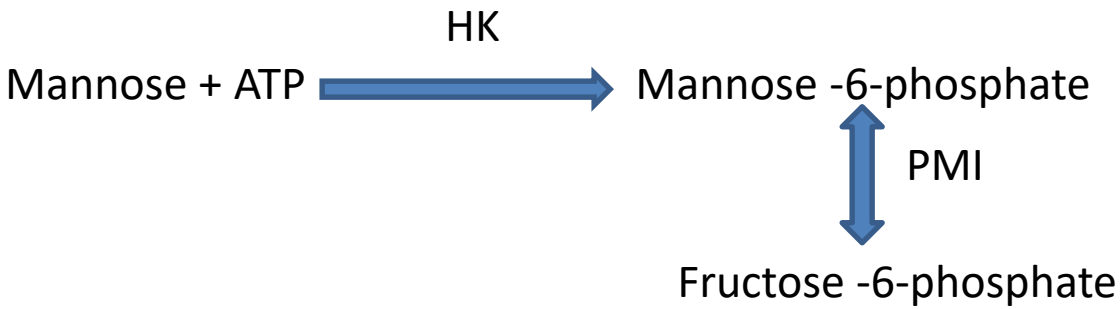
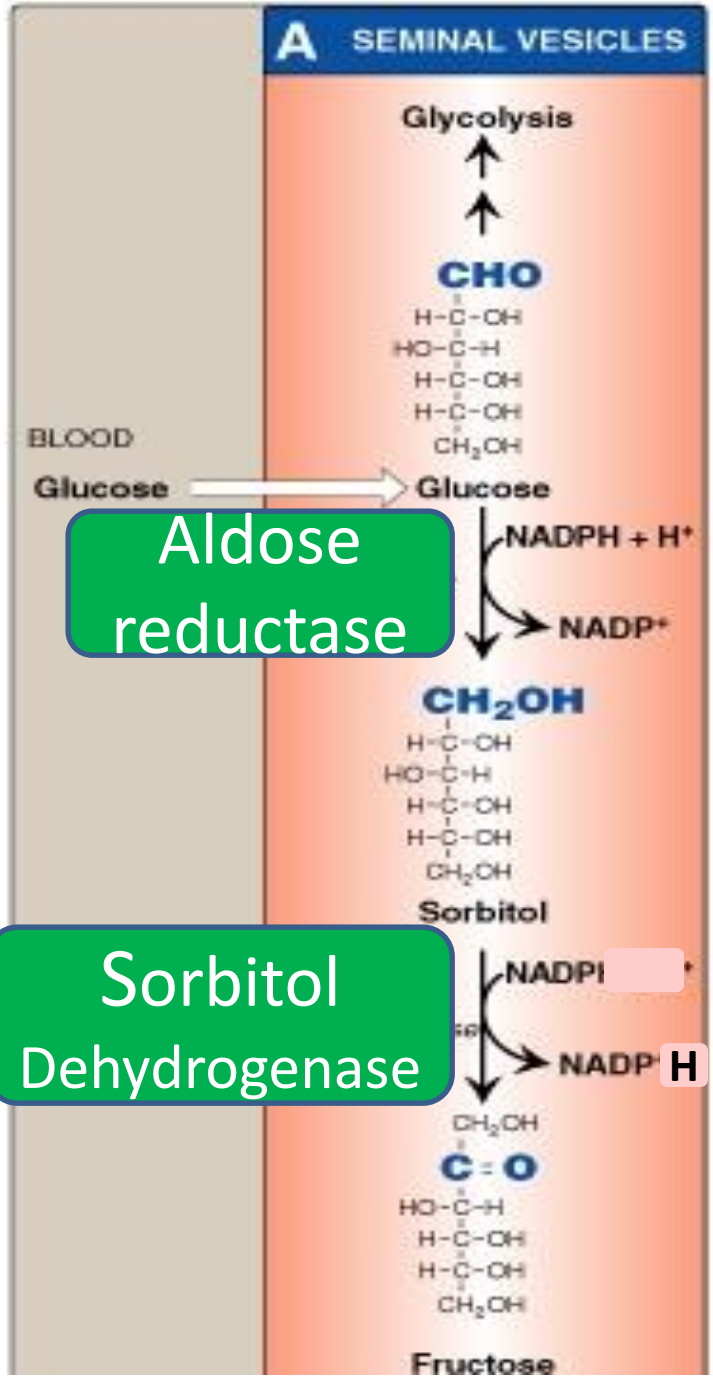
B,C

Metabolism of Mannose (C-2 epimer)



Most of intracellular need of mannose is from fructose

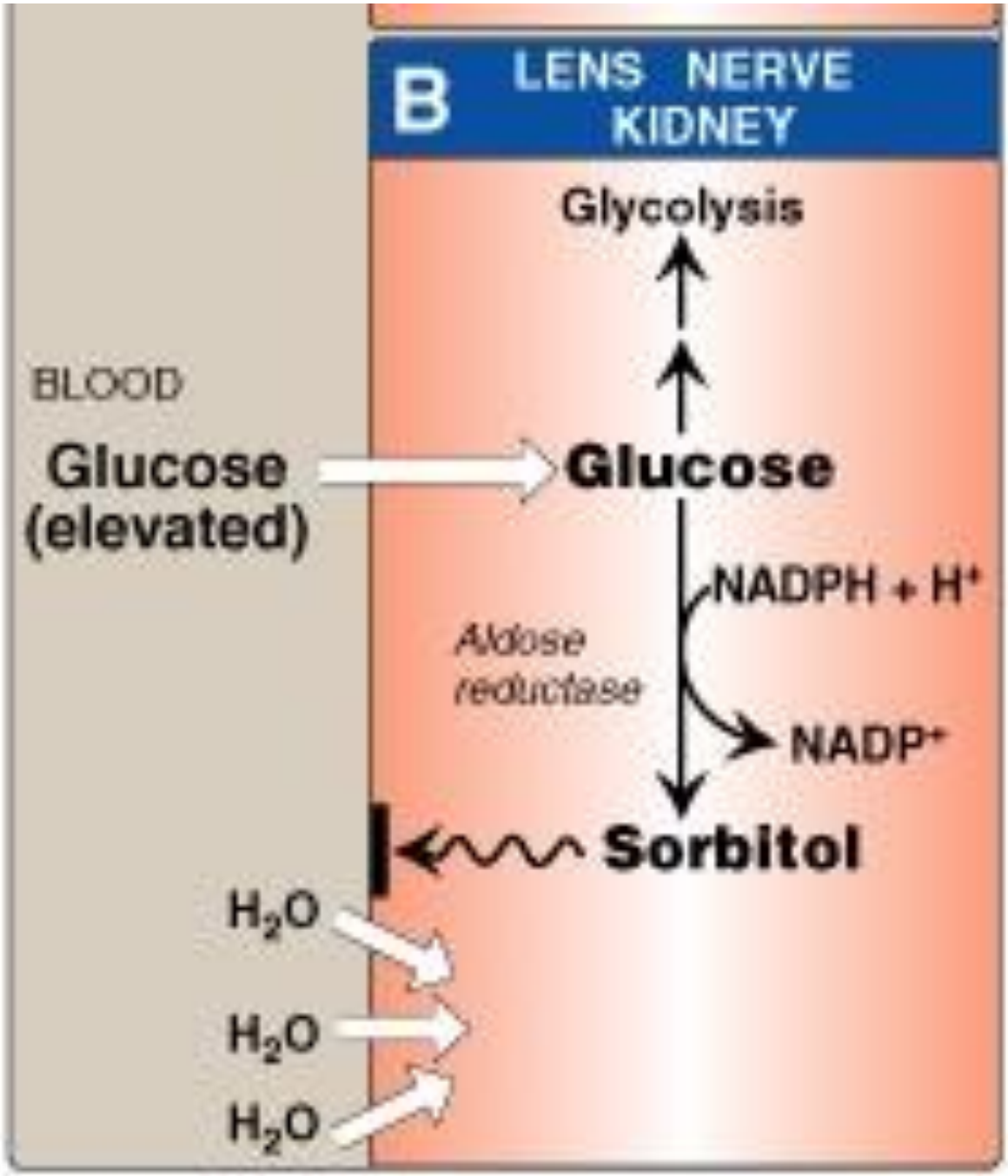


Conversion of glucose to fructose via sorbitol

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

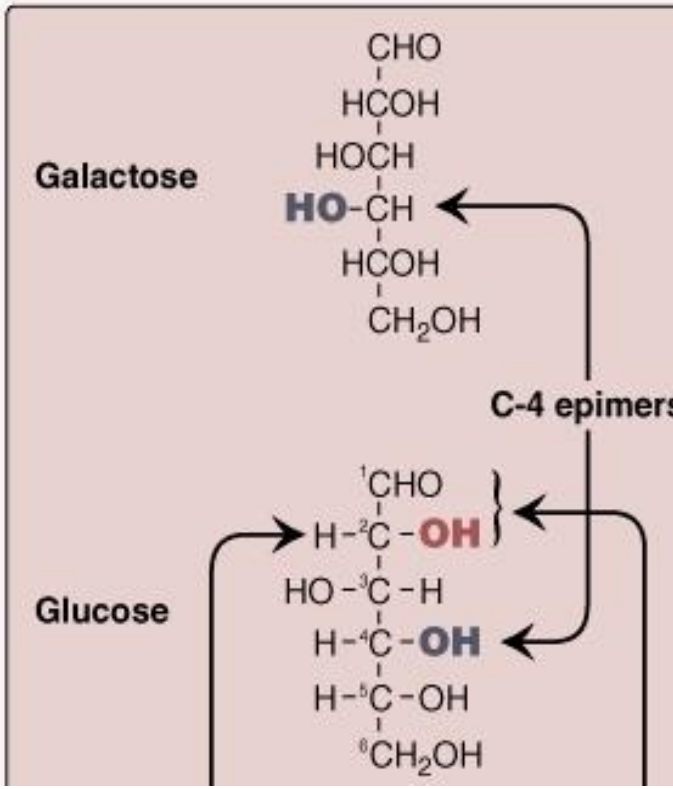
Sorbitol Dehydrogenase:
Liver, ovaries and seminal vesicles

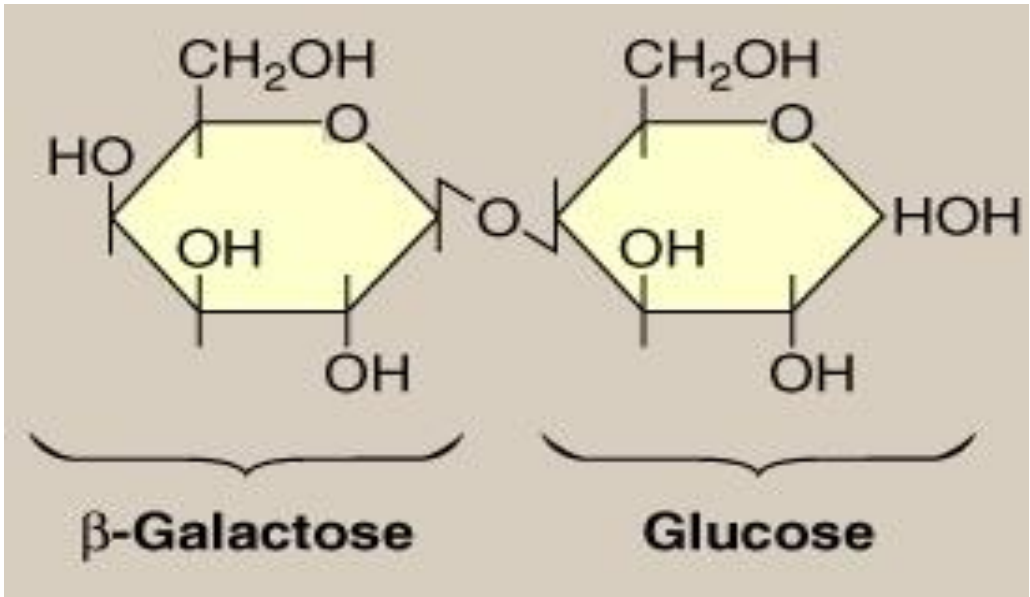
Fructose : the major energy source for sperm cells


B
LENS NERVE
KIDNEY
Glycolysis
BLOOD
Glucose
(elevated)
Glucose
NADPH + H+
Aldose
reductase
NADP+
Sorbitol
H2O
H2O
H2O

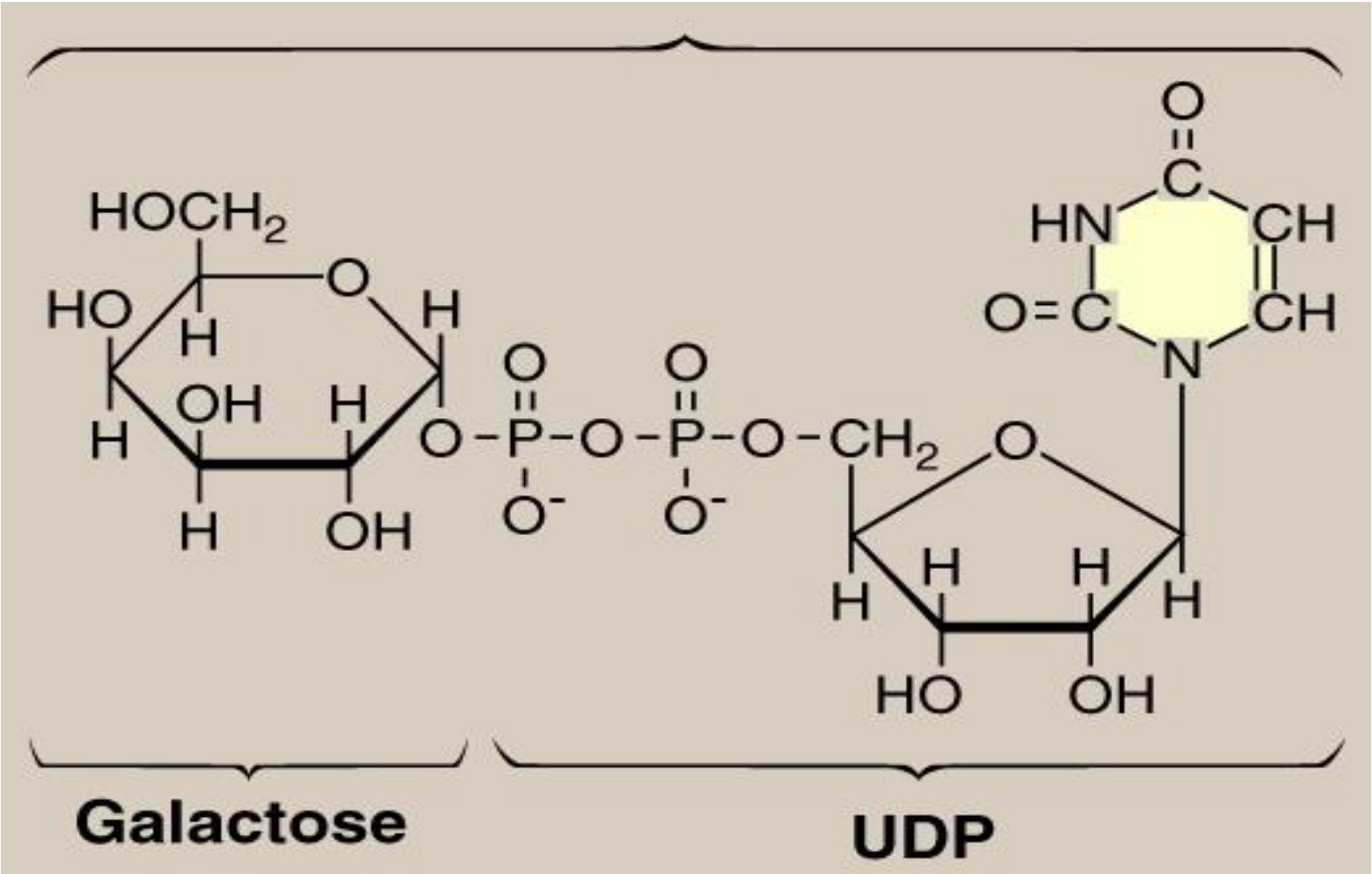
Galactose Metabolism

- Epimer of glucose
- Sources: component of lactose, glycolipids and glycoproteins
- UDP Galactose; an Intermediate in Galactose Metabolism

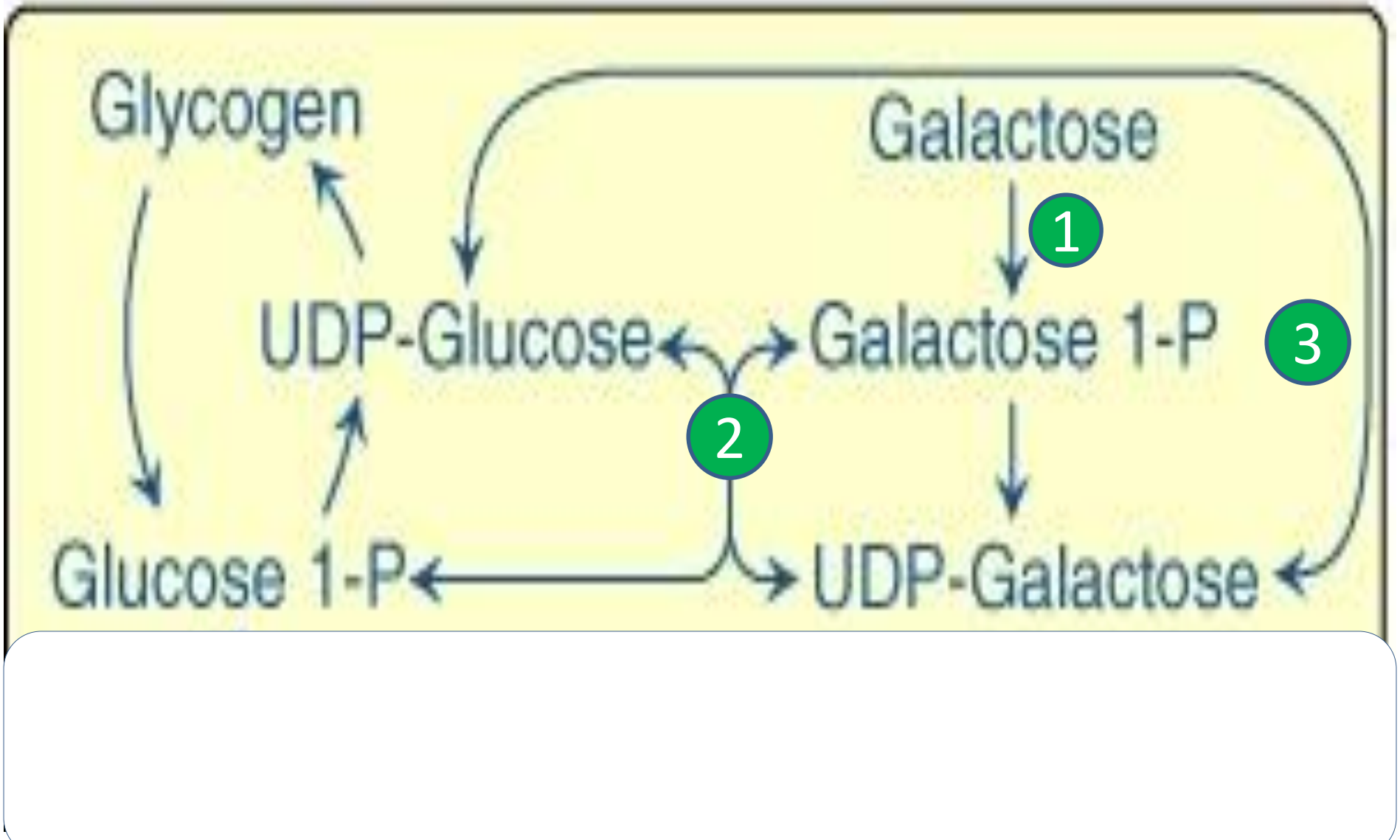


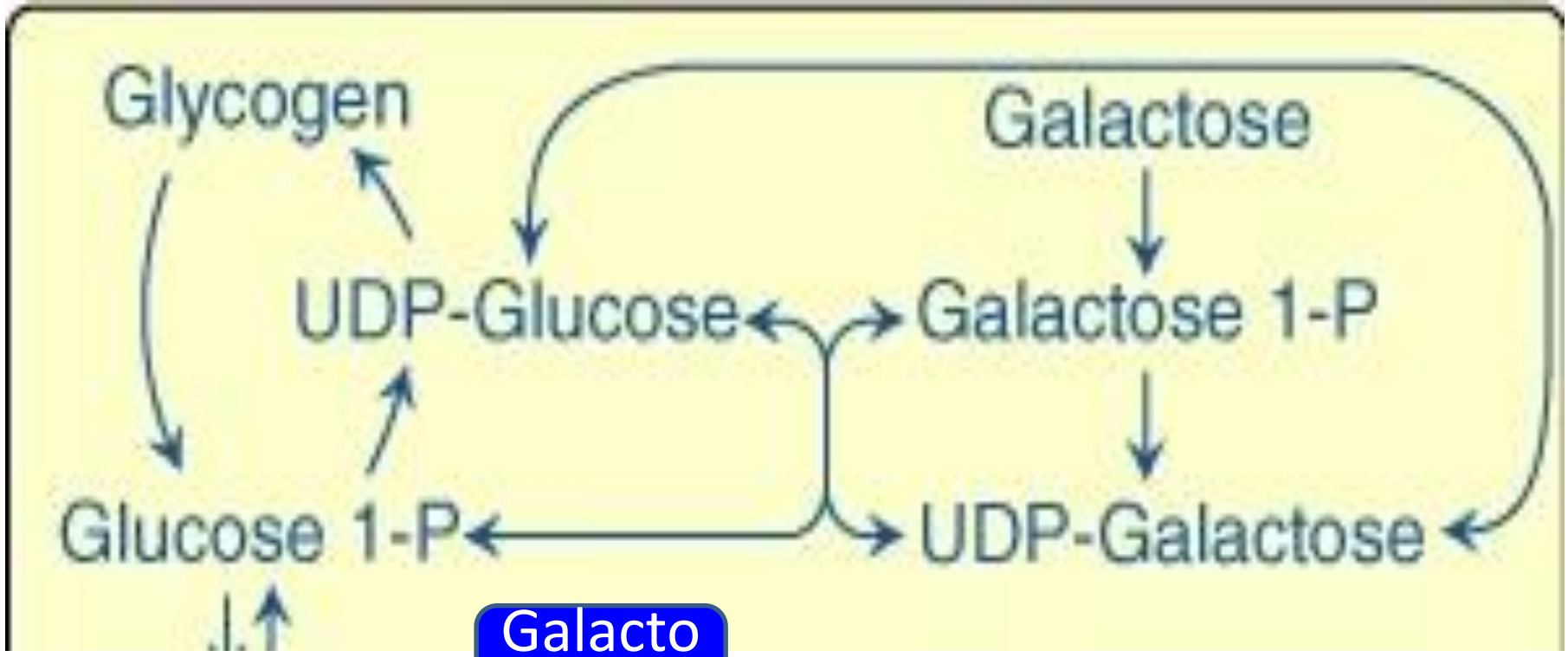


UDP Galactose; an Intermediate in Galactose Metabolism



Galactose Metabolism





Galacto kinase

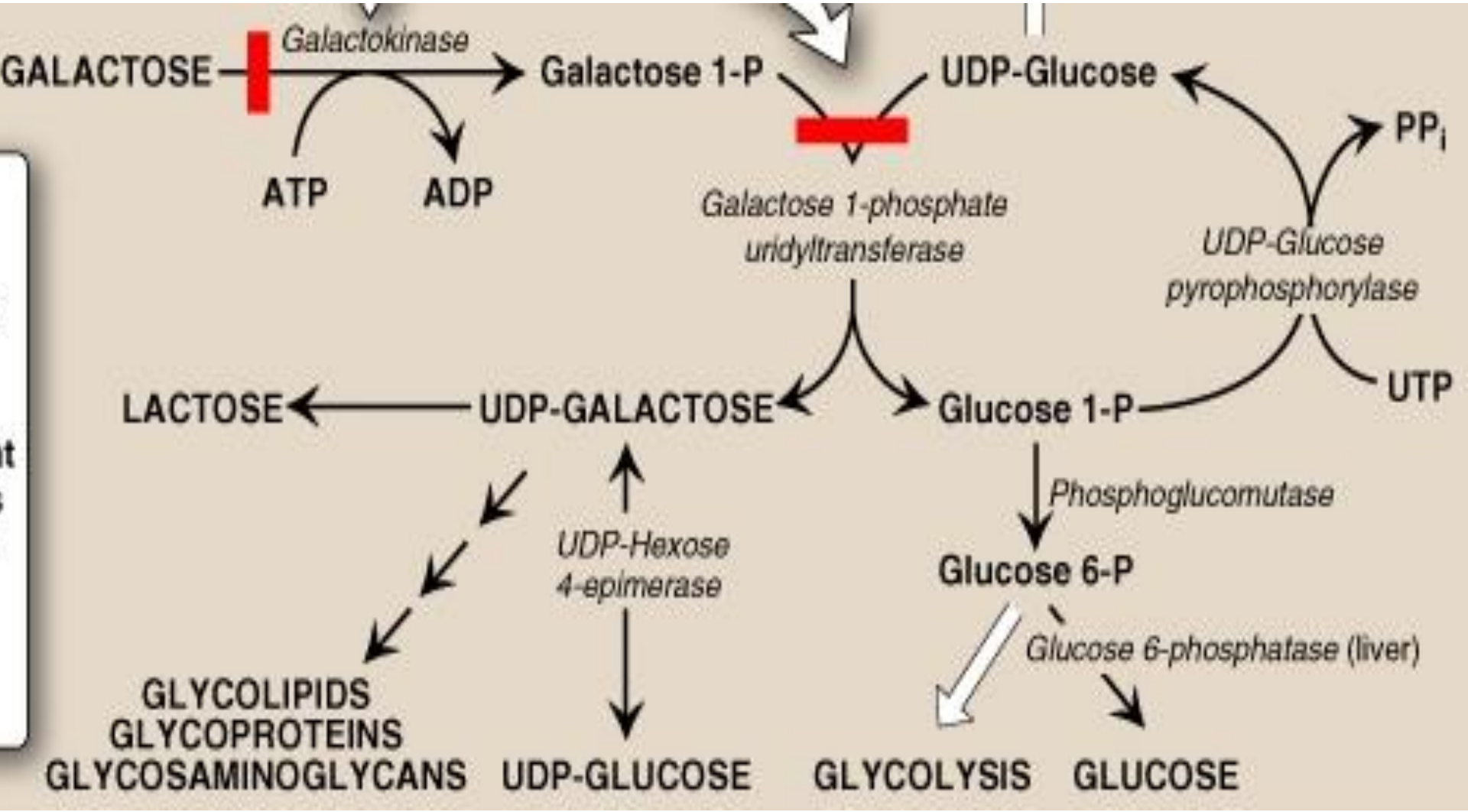
Galactose + ATP → Gal. 1-Phosph ADP

transferase

Gal 1-Phosph + UDP Glc. ⇌ UDP- Galactose + Glc1-Phosph

epimerase

UDP Galactose ⇌ UDP Glucose

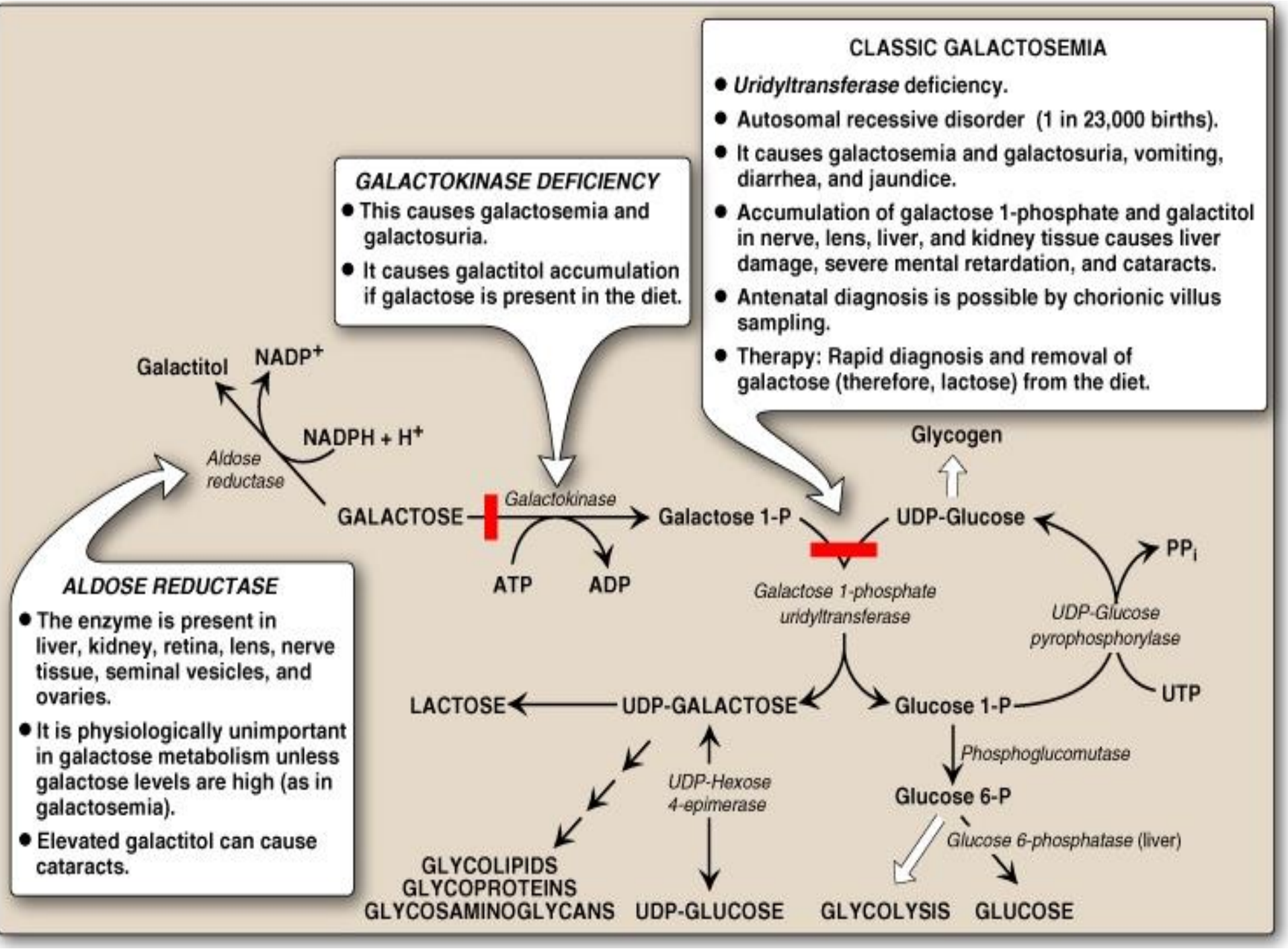

GALACTOSE
Galactokinase
ATP
ADP
Galactose 1-P
UDP-Glucose
PPi
Galactose 1-phosphate uridyltransferase
UDP-Glucose pyrophosphorylase
UTP
LACTOSE
UDP-GALACTOSE
Glucose 1-P
Phosphoglucomutase
UDP-Hexose 4-epimerase
Glucose 6-P
Glucose 6-phosphatase (liver)
GLYCOLIPIDS
GLYCOPROTEINS
GLYCOSAMINOGLYCANS
UDP-GLUCOSE
GLYCOLYSIS
GLUCOSE

Disorders of Galactose Metabolism

- Deficiency of GALT → classic Galactosemia
- Accumulation of Galactose 1-Phosphate and galactose
- Similar consequences to those in fructose intolerance

- Galactose ••••••→ Galactitol
- Deficiency of Galactokinase

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


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.
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
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.

Lactose Synthesis

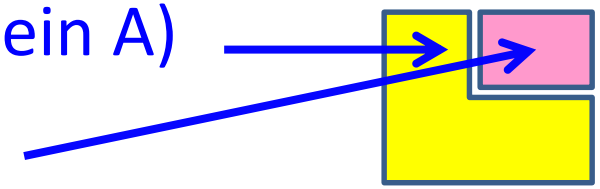
- Lactose is Galactosyl β (1→4) glucose
- Galactosyl β (1→4) glucose is found in glycolipids and glycoproteins

UDP Gal. + Glucose —(Lactose Synthase)→ Lactose + UDP

- Lactose Synthase: complex of 2 proteins

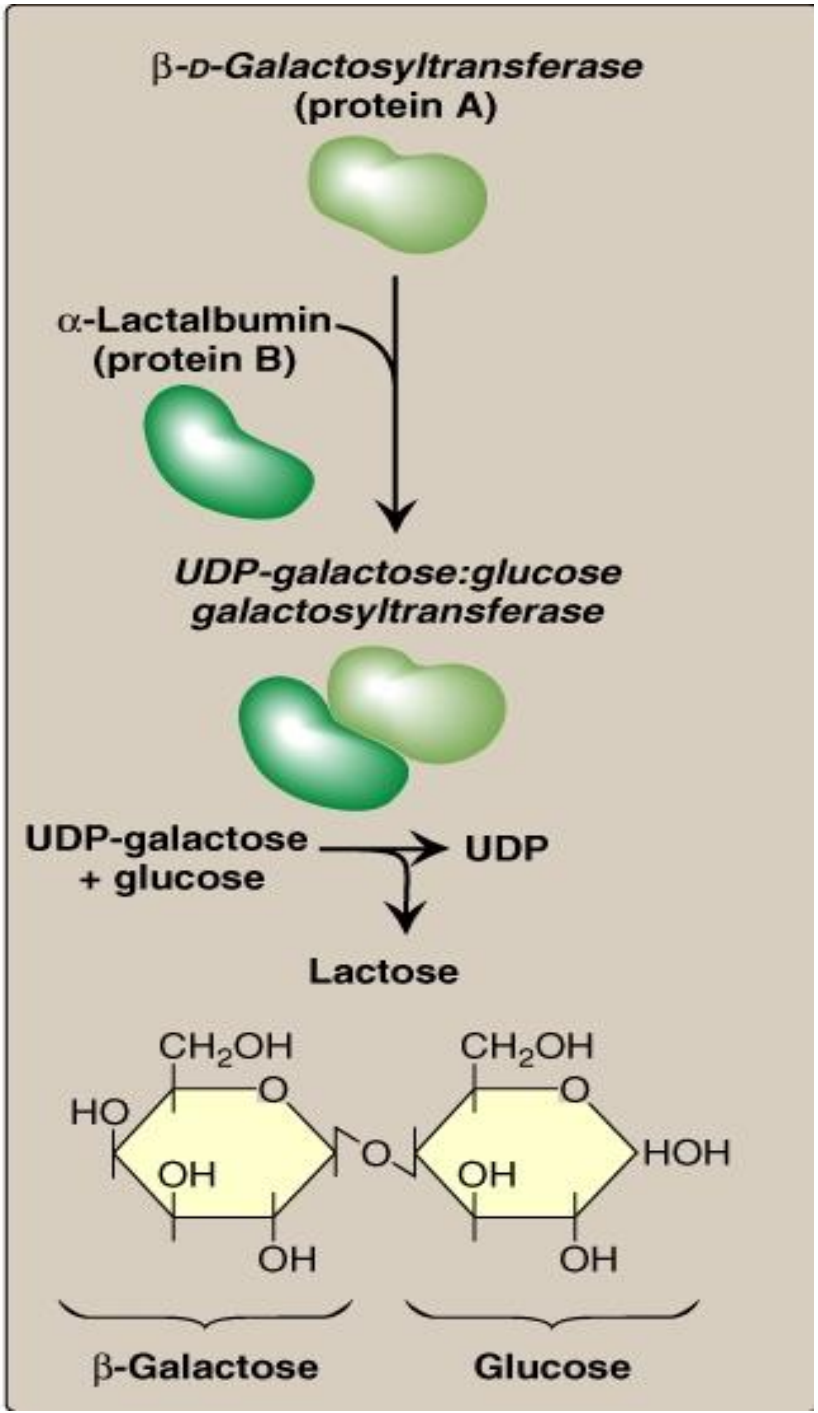
Galactosyl transferase (Protein A)

α-lactalbumin (Protein B)



In glycolipids synthesis

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


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
OH
HOH
OH
β-Galactose
Glucose

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- Benign, asymptomatic condition.
- Fructose accumulates in the urine.

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