Fructose & galactose metabolism

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Objectives

- Sources of fructose
- Biomedical importance
- Conversion of fructose to sorbitol.
- Complications due to sorbitol
- Disorders of fructose metabolism.

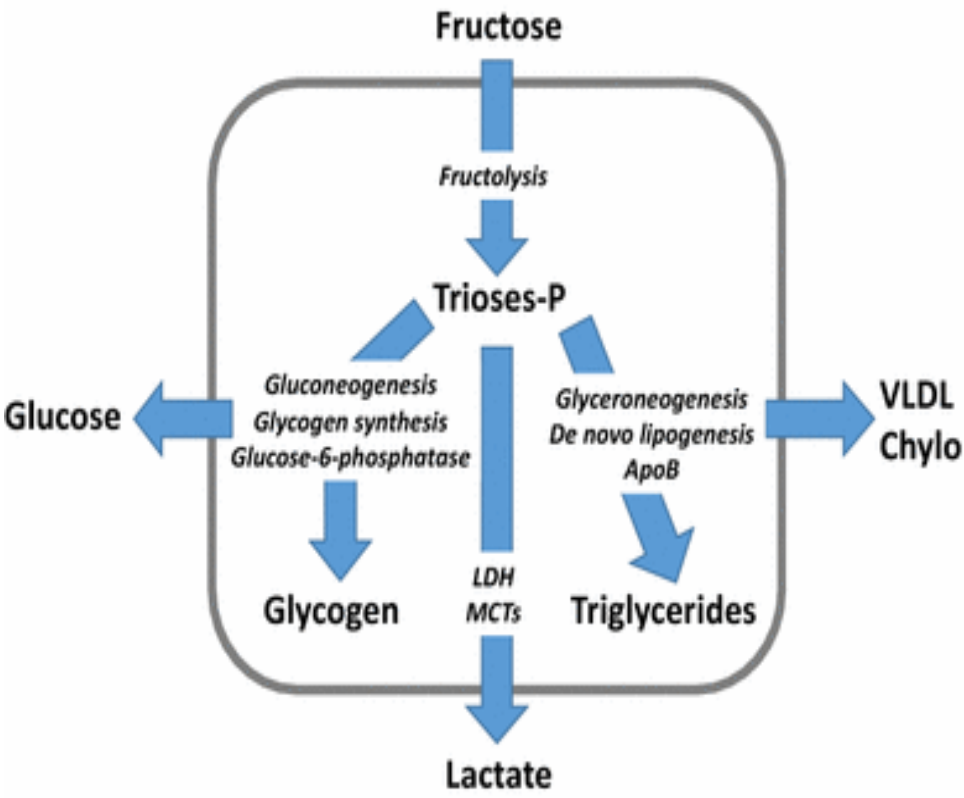
FRUCTOSE METABOLISM

- Major source of fructose is disaccharide SUCROSE
- Sucrose is cleaved in the intestines to form GLUCOSE & FRUCTOSE
- Found in many fruits , HONEY & high fructose corn syrup
- Entry into cells is not insulin dependent.
- Absorbed by facilitated diffusion.
- Taken by portal circulation to liver, there it is converted to glucose.

Biomedical importance

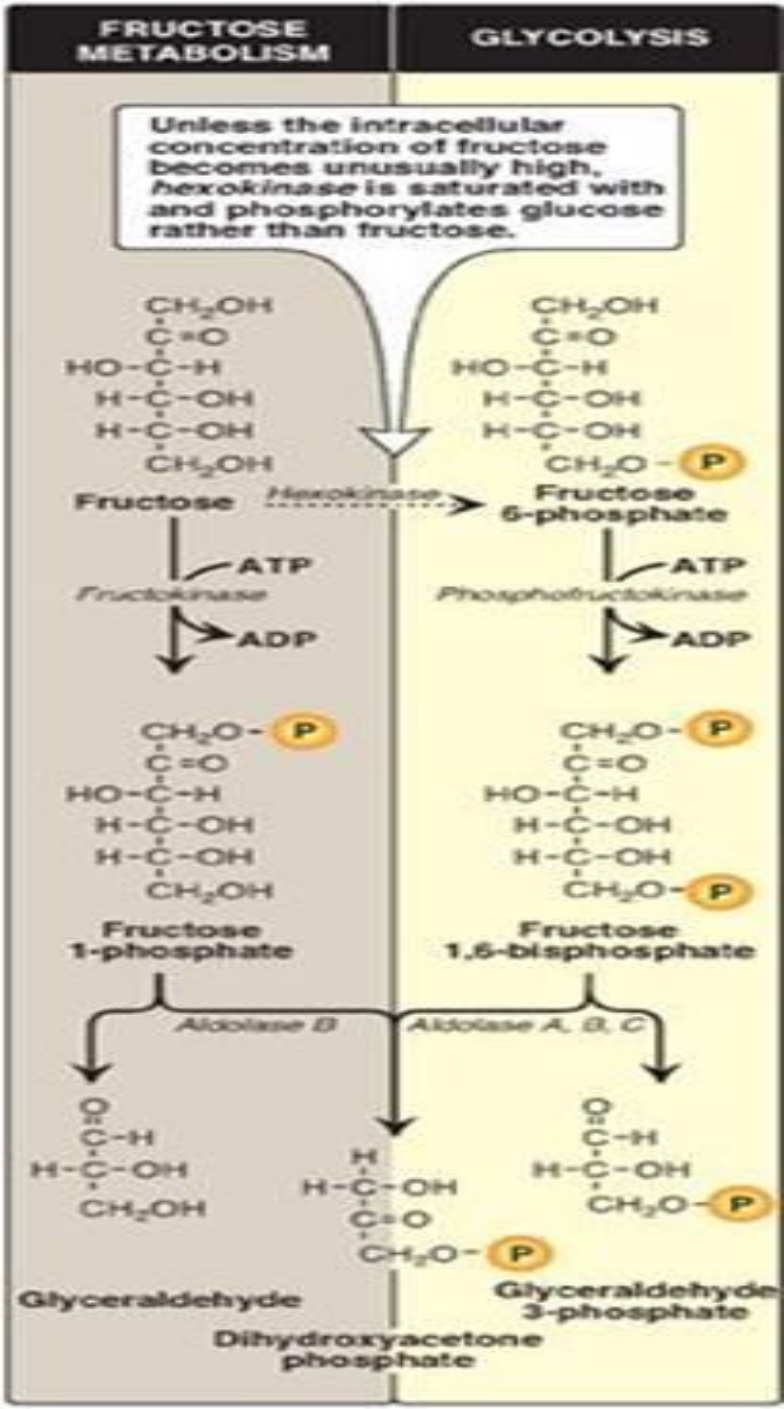
- Good source of energy.
- Source of energy for spermatozoa.

- Excess is harmful bcz it increase synthesis of TG.
- In diabetes through sorbitol pathway causes development of cataract.



Fructose metabolism

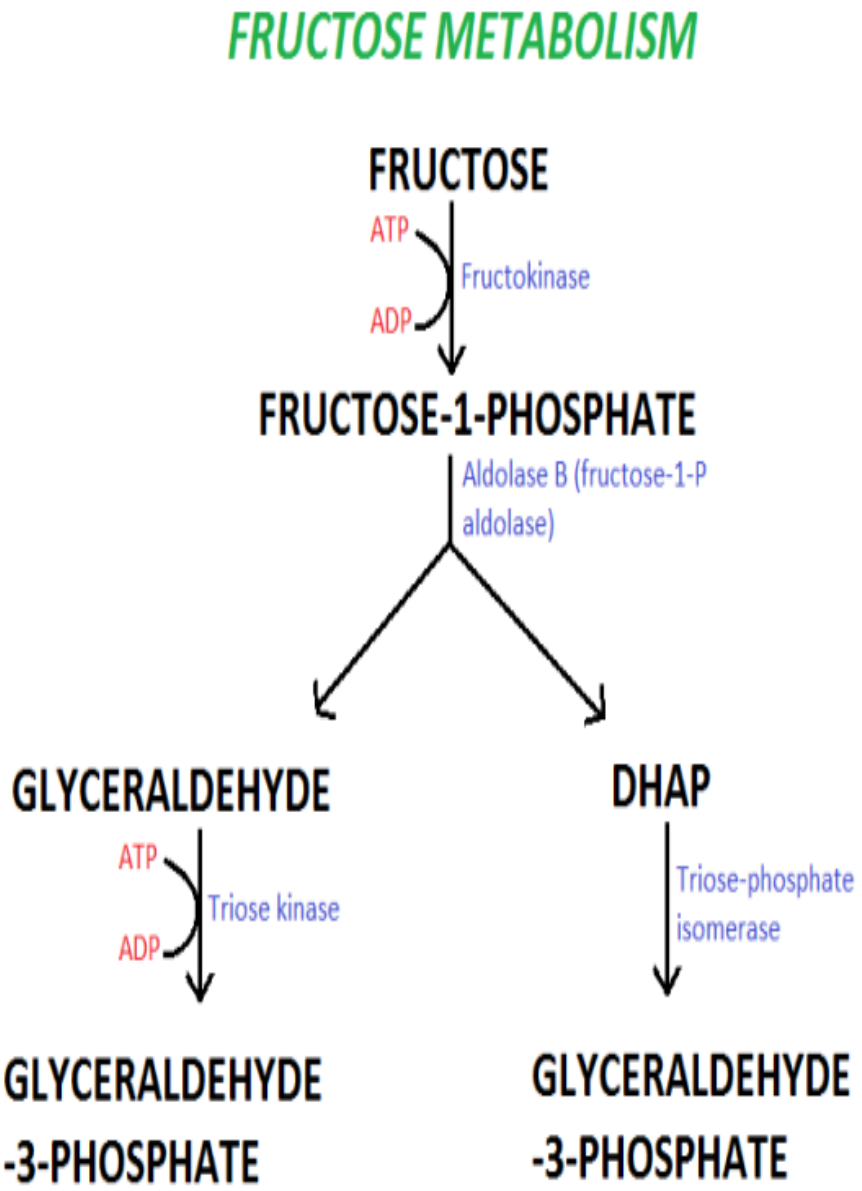
- Fructose is mostly phosphorylated by fructokinase to fructose -1-phosphates, present in liver, muscles , kidneys & intestine.



This enzyme cannot phosphorylates glucose.

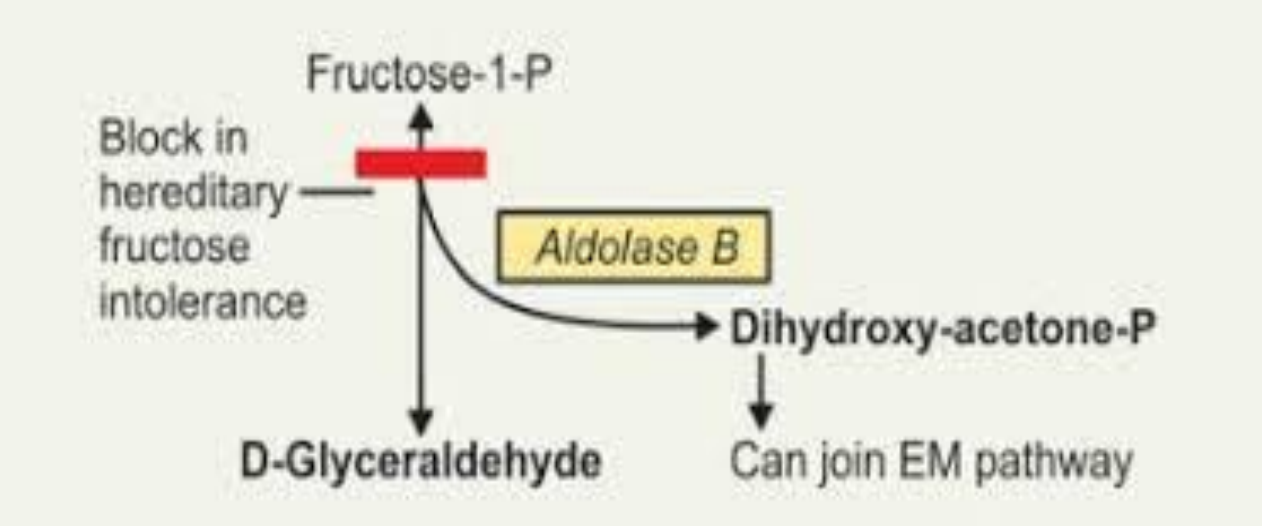
Its activity is Insulin independent.

This is the major pathway for fructose phosphorylation.

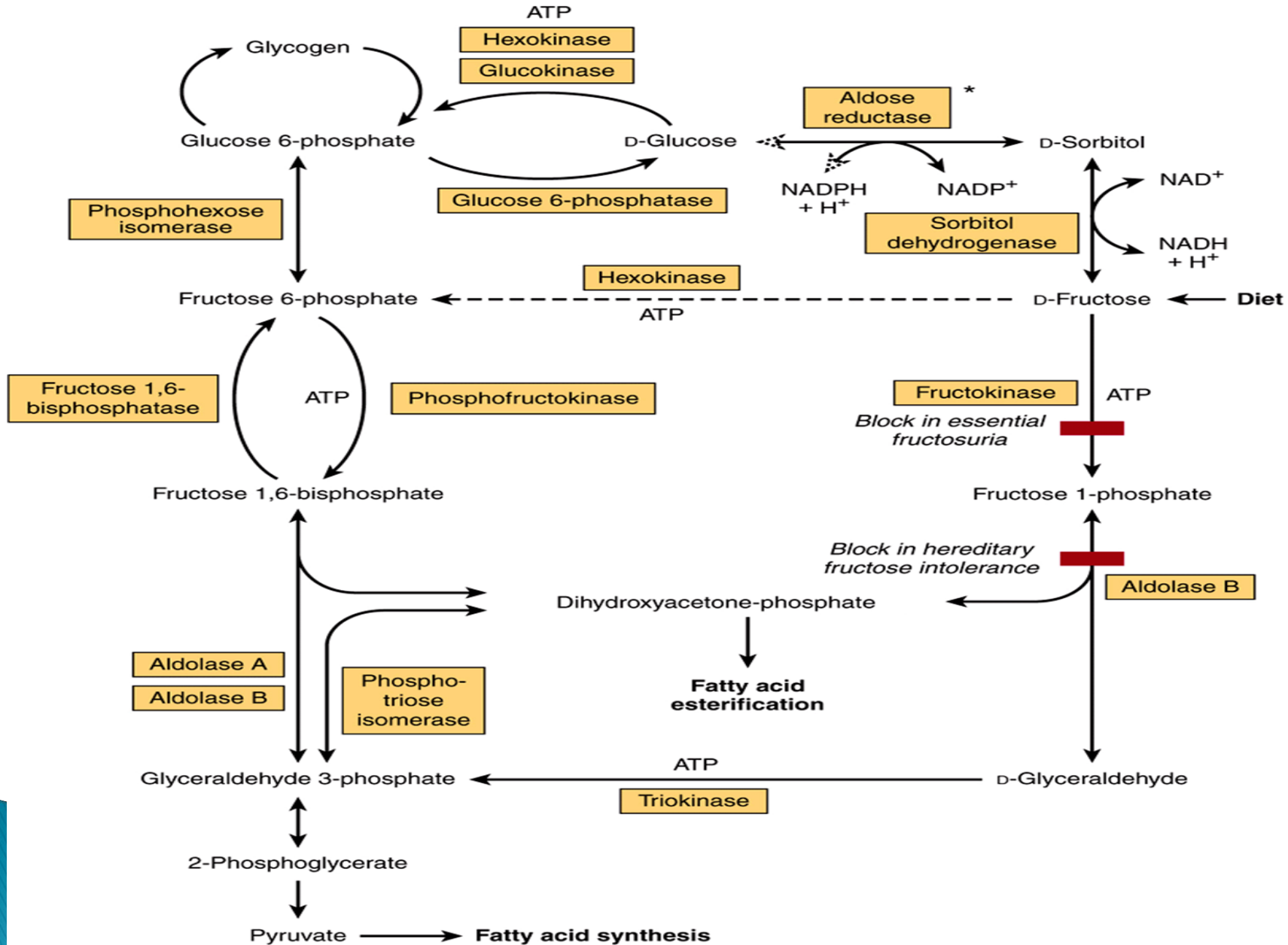


- Conversion of fructose-1-phosphate to D-glyceraldehyde is catalyzed by aldolase B.

  Hereditary fructose intolerance occurs due to deficiency of this enzyme.



Fate of D-Glyceraldehyde



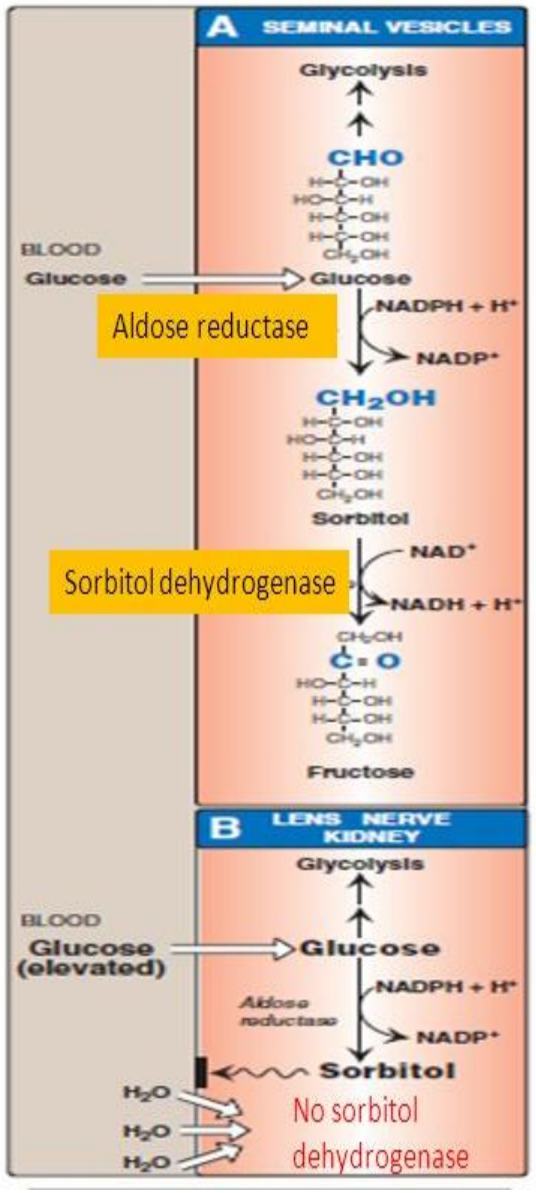
CONVERSION OF GLUCOSE TO FRUCTOSE VIA SORBITOL:

- SITES OF SYNTHESIS OF SORBITOL:
- Lens, retina, schwann cells of peripheral nerves, liver, kidney, placenta, red blood cells and cells of the ovaries and seminal vesicles.

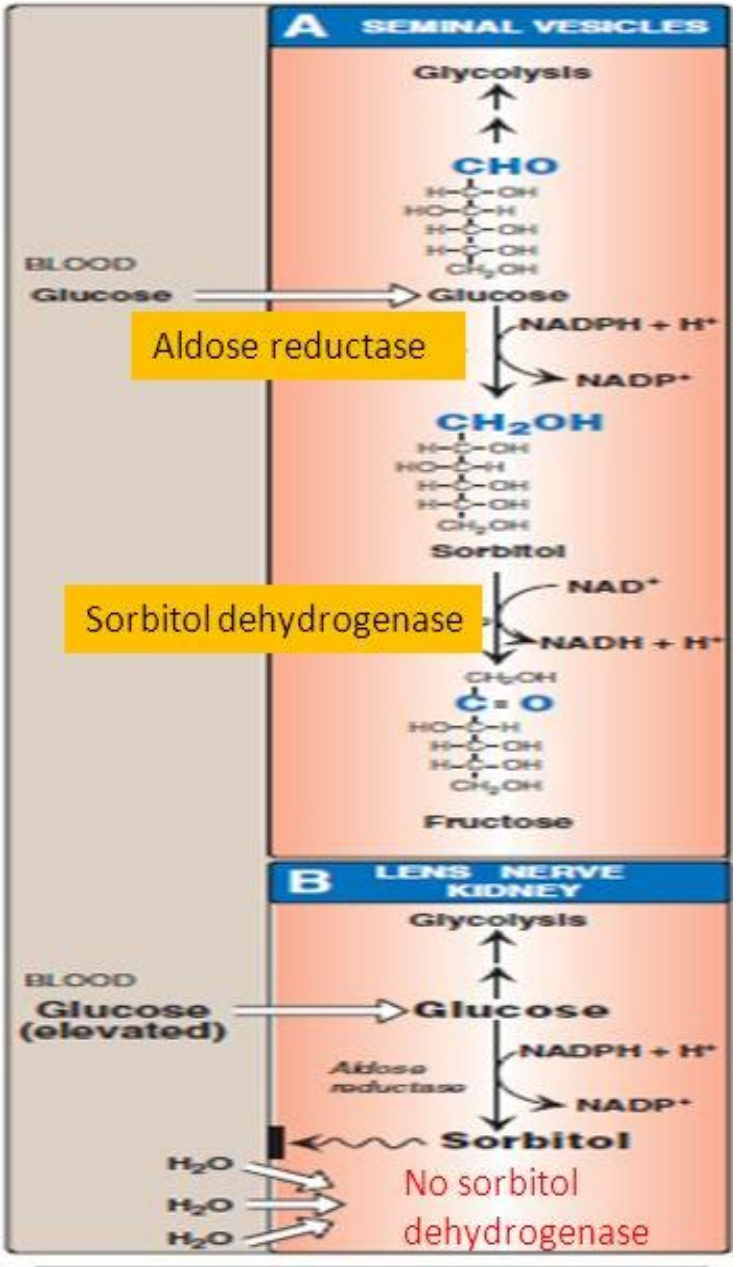
Sorbitol pathway

- Fructose is major source of energy for spermatozoa.
- It is formed from glucose in seminal vesicles.
- Pathway involve

1. Reduction of D-glucose to D-sorbitol.
2. Oxidation of sorbitol to D-fructose.



- Aldose reductase is absent in liver but present in lens,retina of eye, kidney,placenta, schwann cells of peripheral nerves. erythrocytes and seminal vesicals.
- Enzyme sorbitol dehydrogenase is either low in activity or absent in these cells.



EFFECT OF HYPERGLYCEMIA ON SORBITOL METABOLISM:

Elevated intracellular glucose concentration and adequate supply of NADPH cause aldose reductase to produce significant increase in the amount of sorbitol , which cannot pass efficiently through the cell membranes and in turn remain trapped in the cell.

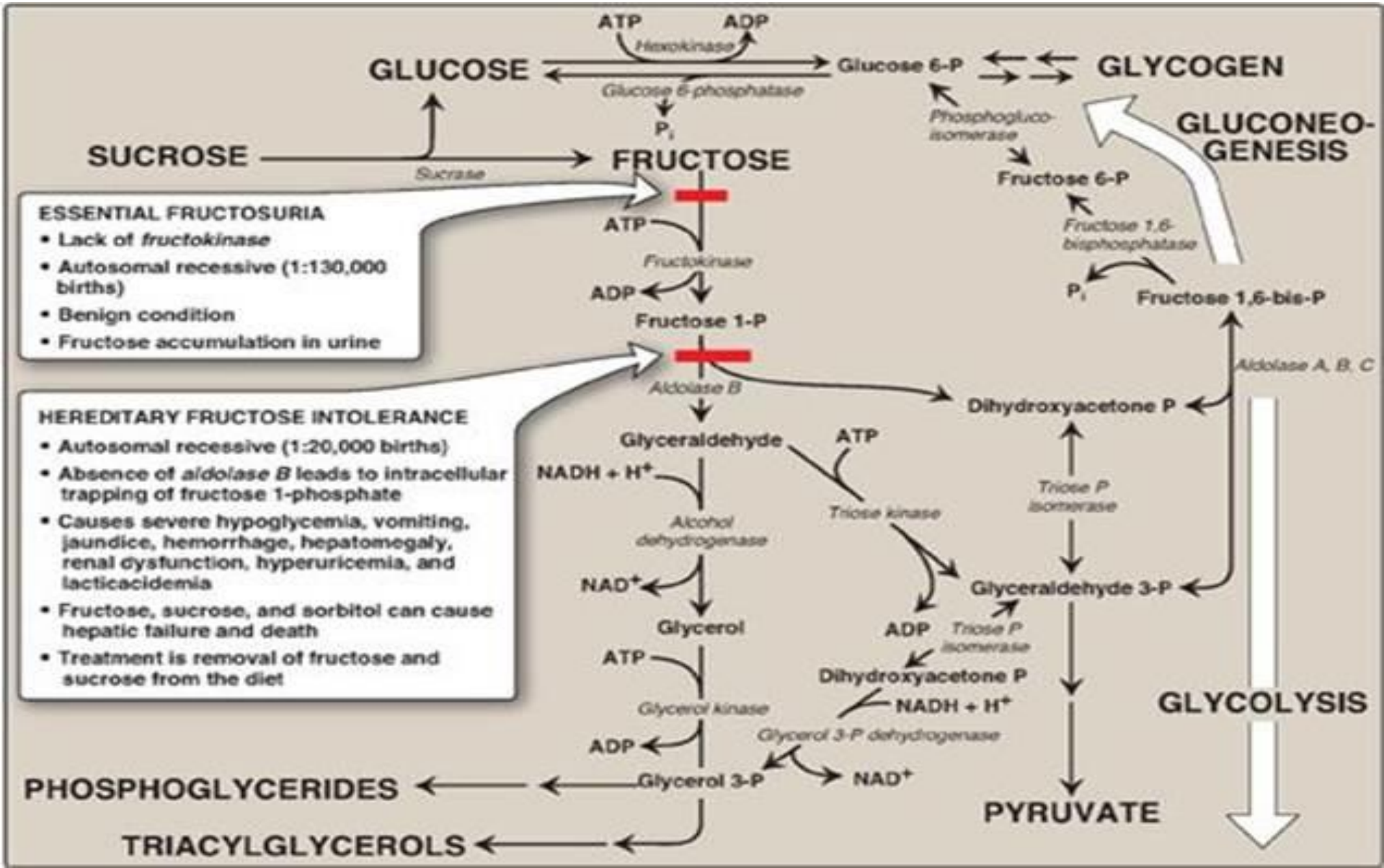
EFFECT OF HYPERGLYCEMIA ON SORBITOL METABOLISM:

- This is exacerbated when sorbitol dehydrogenase is low or absent(in lens , retina , kidney, nerve cells).
- As a result sorbitol accumulates in these cells causing strong osmotic effects and therefore cell swelling as a result of water retention.

PATHALOGICAL ALTERATIONS ASSOCIATED WITH DIABETES:

1. Cataract formation.
2. Peripheral neuropathy.
3. Diabetic nephropathy.
4. Diabetic retinopathy.

Disorders of fructose metabolism



Galactose metabolism

Objectives

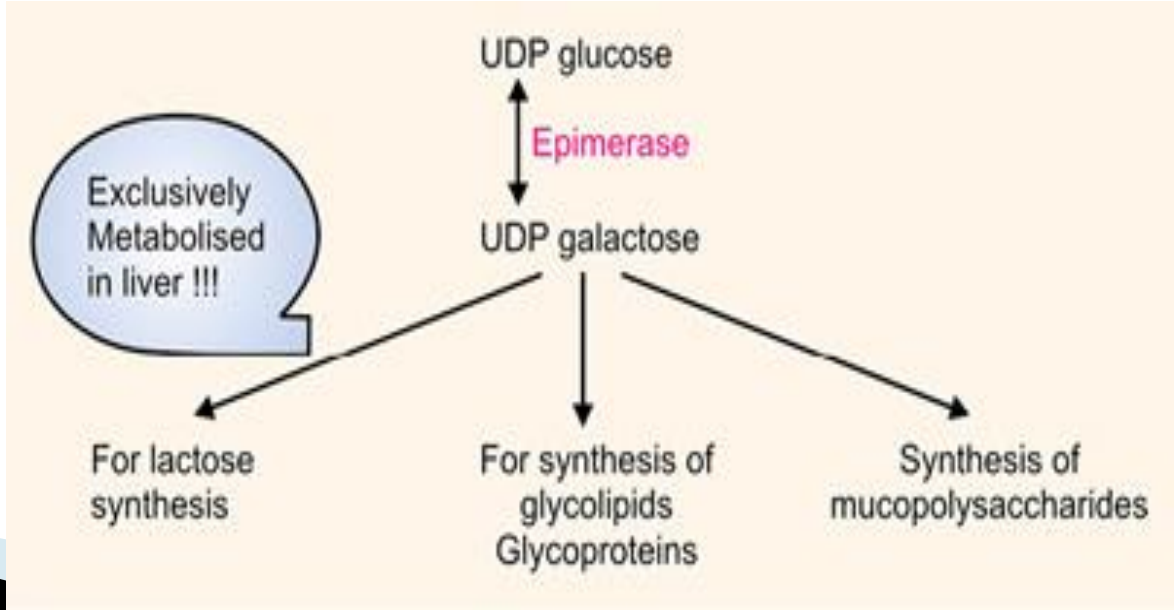
- Sources of galactose.
- Biomedical importance
- Metabolism of galactose
- Biosynthesis of lactose
- Regulation of lactose synthesis
- Disorders of galactose metabolism.

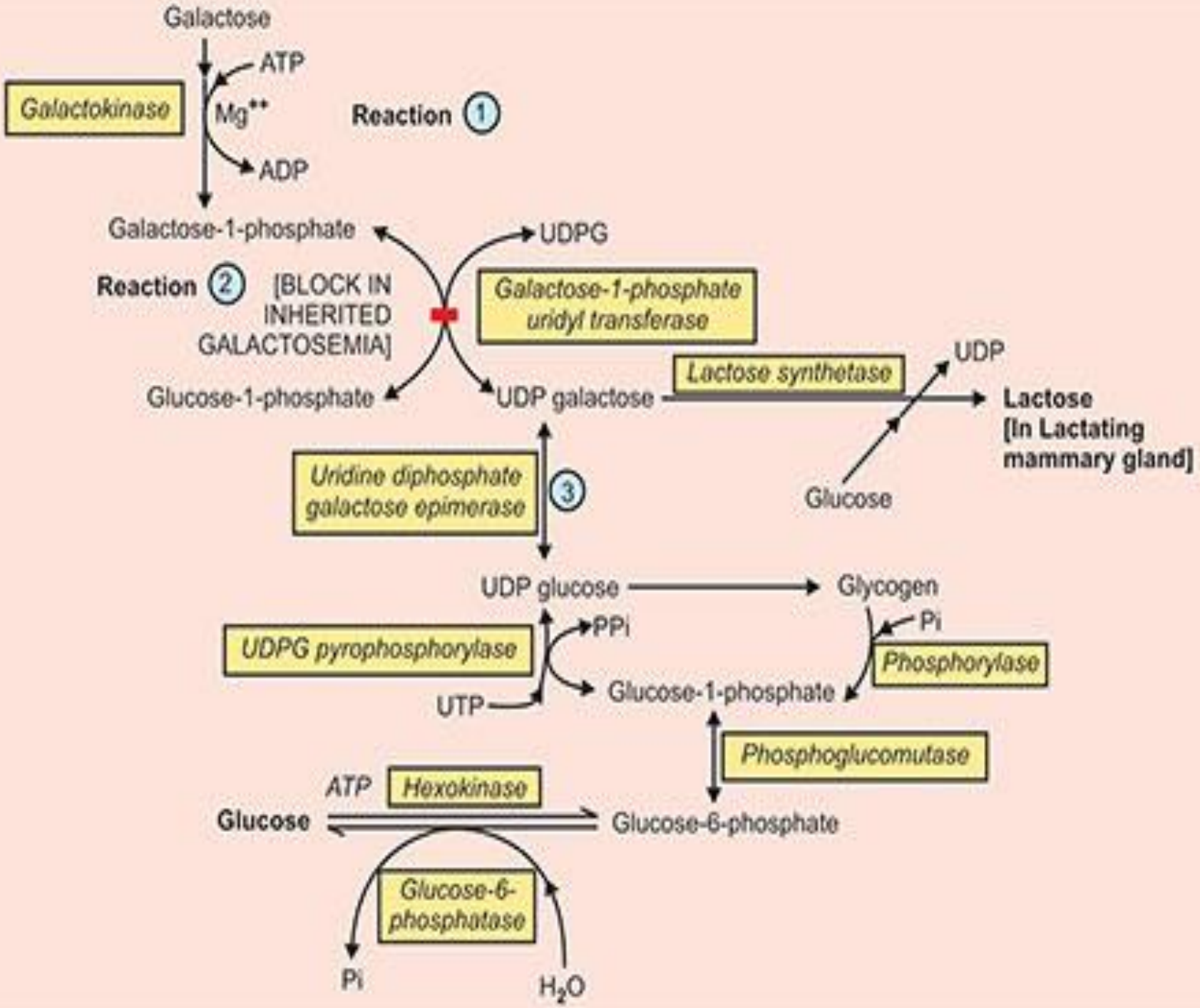
Sources of Galactose

- Major dietary source of galactose is LACTOSE
- Obtained from milk and milk products
- Galactose can also be obtained from lysosomal degradation of complex CHO like glycoproteins and glycolipids
- Entry into cells is not insulin dependent.

Biomedical importance

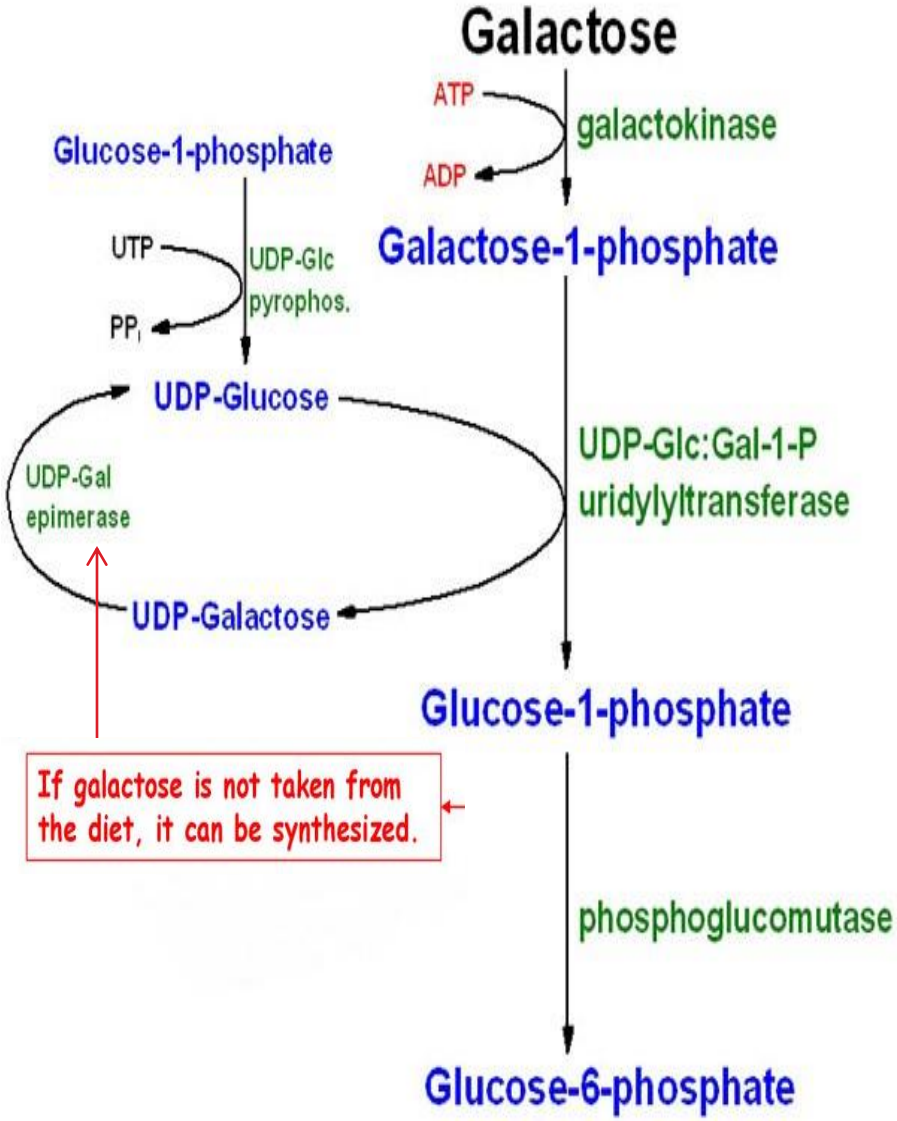
- Required by mammary glands for synthesis of milk.
- Brain require for synthesis of glycolipids -- cerebrosides and gangliosides.
- Synthesis of chondroproteins & mucoproteins.
- Galactosemia inheretid disorder due to deficiency of enzyme in pathway




Galactose
ATP
Galactokinase
Mg++
ADP
Reaction 1
Galactose-1-phosphate
UDPG
Reaction 2
[BLOCK IN INHERITED GALACTOSEMIA]
Galactose-1-phosphate uridyl transferase
Glucose-1-phosphate
UDP galactose
Lactose synthetase
UDP
Lactose [In Lactating mammary gland]
Glucose
Uridine diphosphate galactose epimerase
3
UDP glucose
Glycogen
Pi
PPi
UDPG pyrophosphorylase
Phosphorylase
UTP
Glucose-1-phosphate
Phosphoglucomutase
ATP
Hexokinase
Glucose
Glucose-6-phosphate
Glucose-6-phosphatase
Pi
H2O

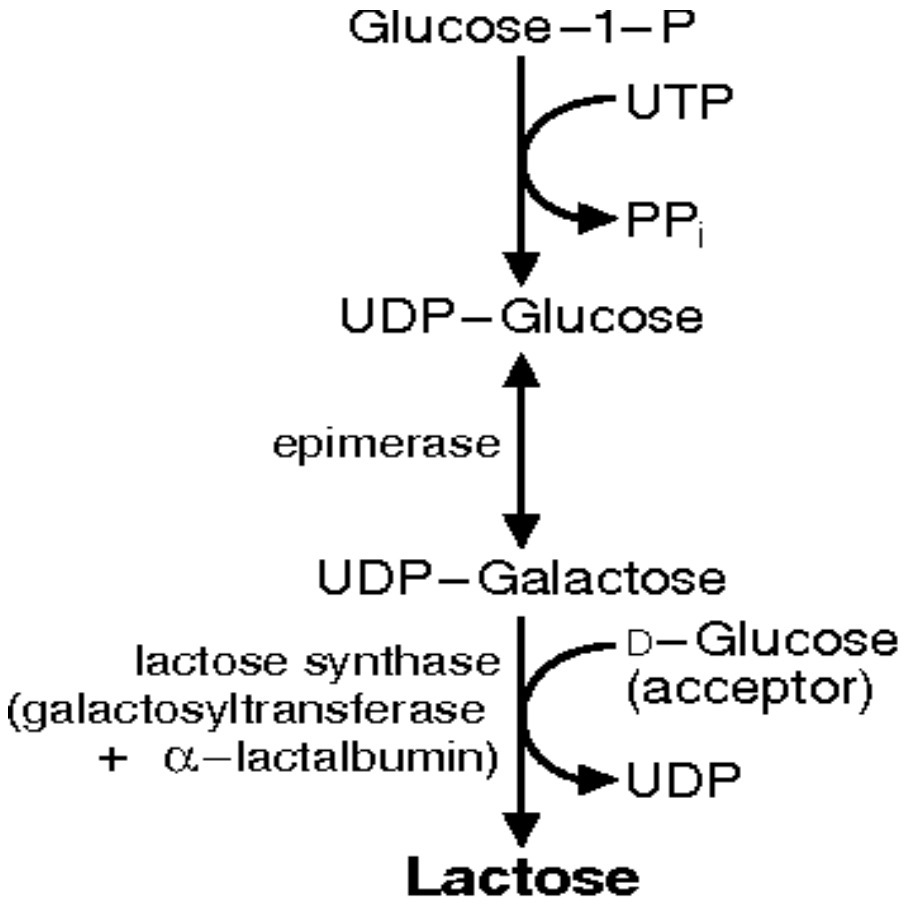
Metabolic pathway

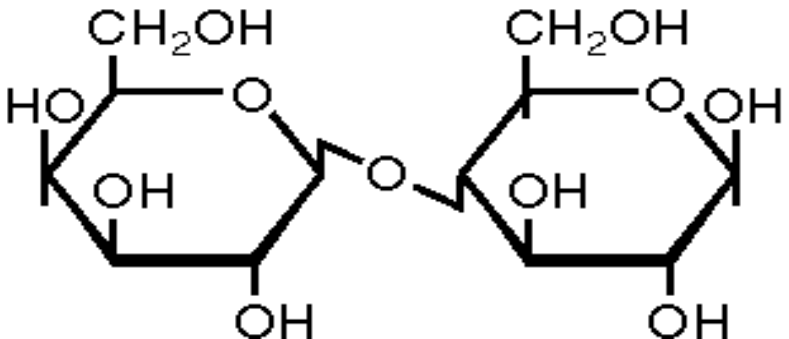
- First galactose is phosphorylated by Enzyme galactokinase to Galactose-1-phosphate.
- Galactose-1-P combine with UDP-glucose to form UDP-galactose.
- UDP-galactose & UDP-glucose are interconvertable by enzyme epimerase .



Biosynthesis of lactose

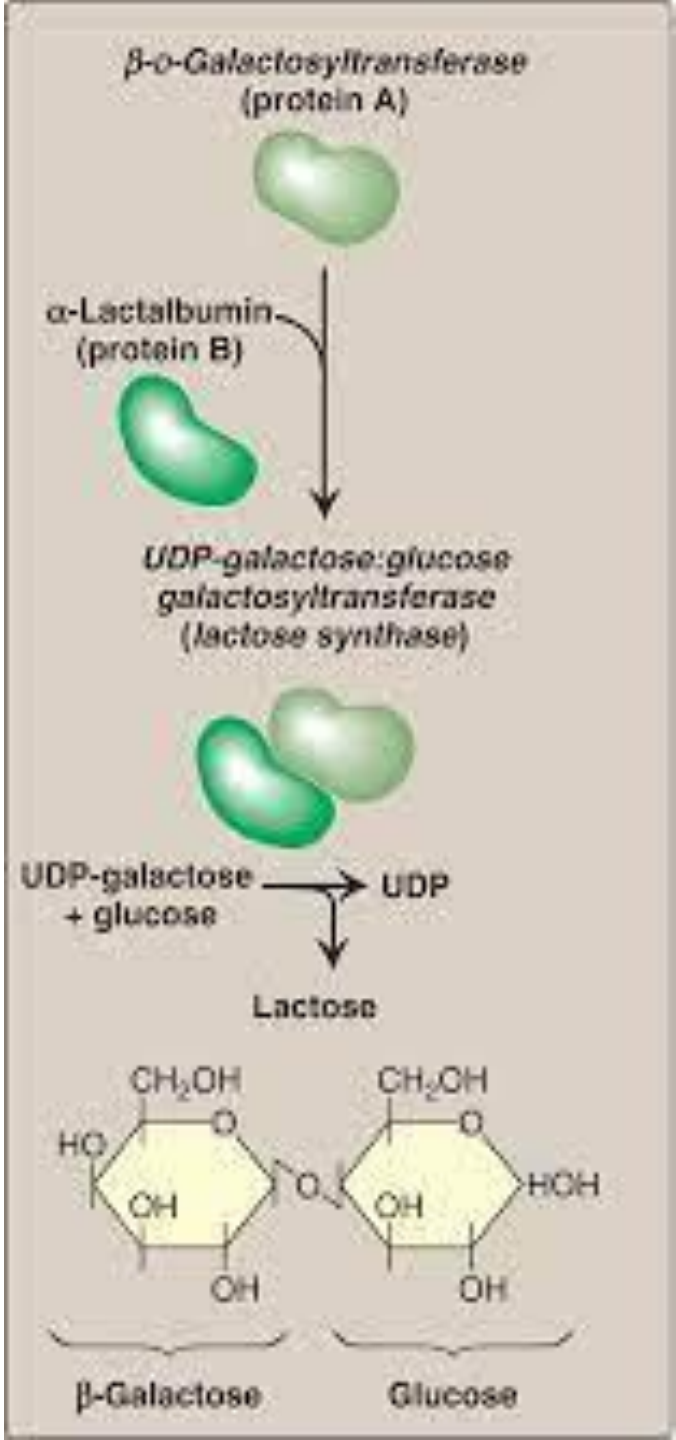
- UDP-galactose condenses with glucose to form lactose in mammary glands.



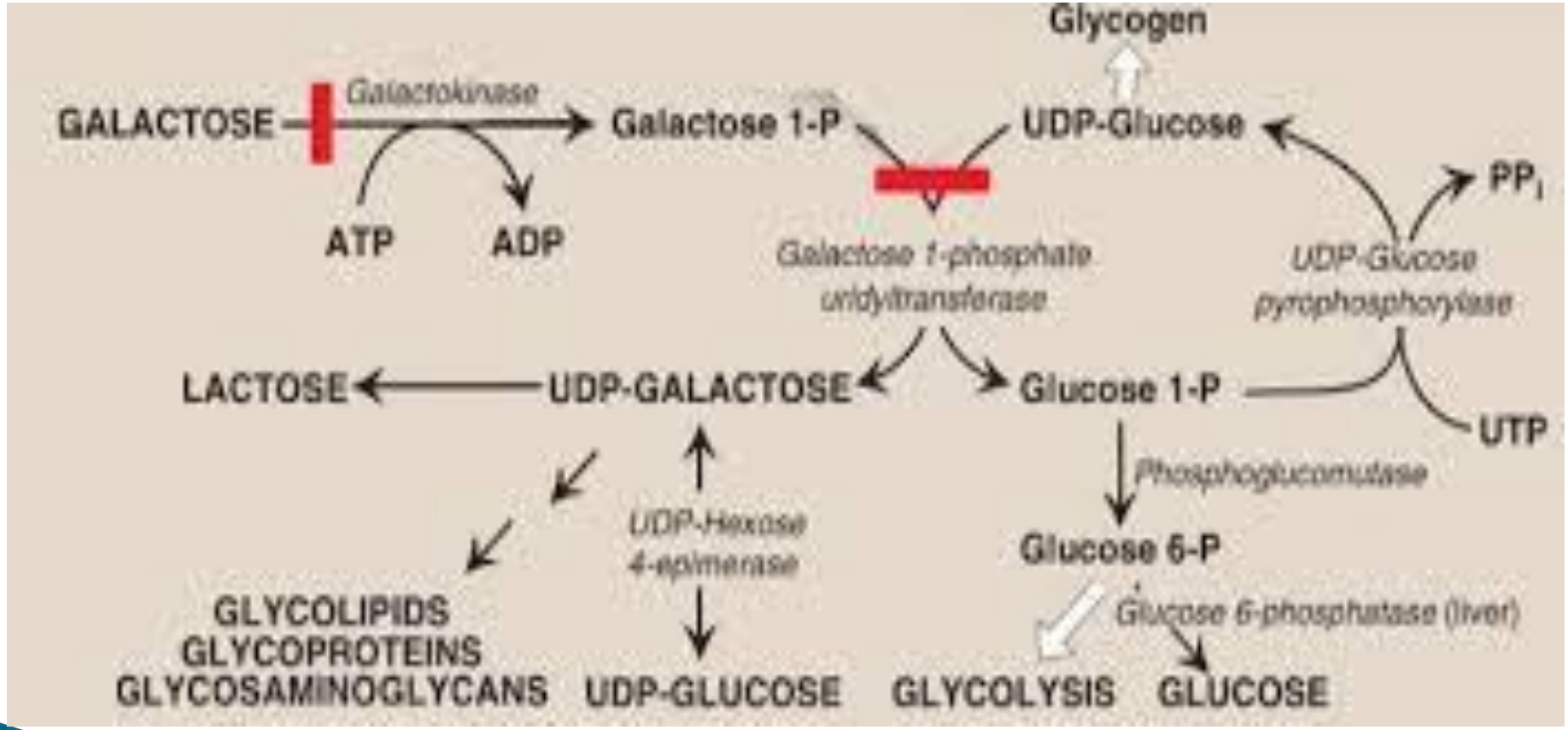


Regulation of lactose synthesis

- Lactose synthase has two subunits
- **Catalytic subunit:** galactosyl transferase
- **Modifier subunit:** α-lactalbumin.
- Only in mammary glands α-lactalbumin binds with catalytic unit and transfer the galactosyl moiety to glucose forming lactose.



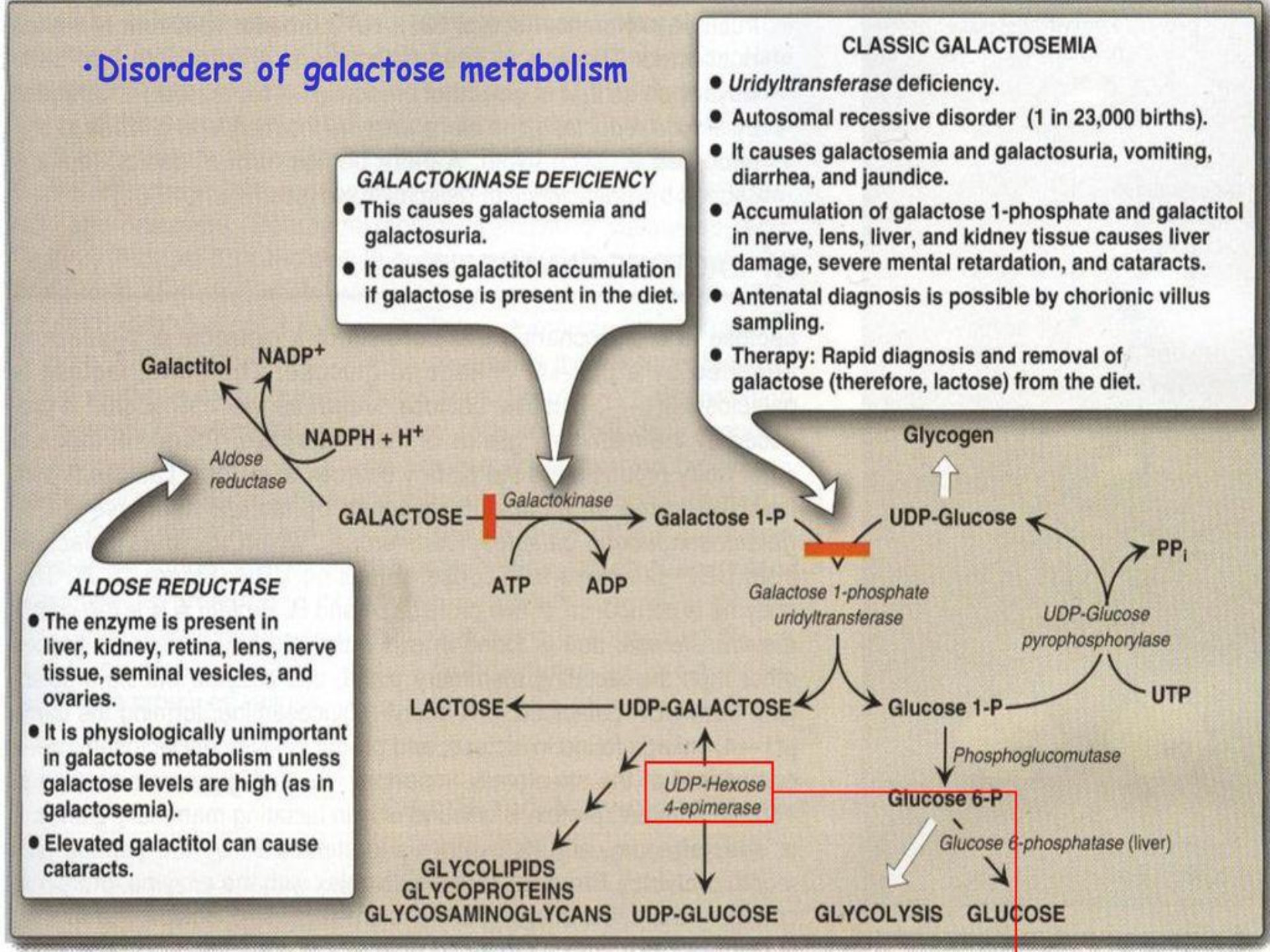
- Galactosyl transferase in other tissues is involved in transfer of galactosyl moiety for synthesis of glycosamines,



Regulation of lactose synthesis

- α-lactalbumin in mammary tissue is under the control of hormones.
- Prolactin: increases synthesis of both subunits.
- Progesterone: inhibits synthesis of α-lactalbumin.

•Disorders of galactose metabolism



References

- Medical biochemistry by Chatterjea
- Lipincott
- Satayanayaryn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