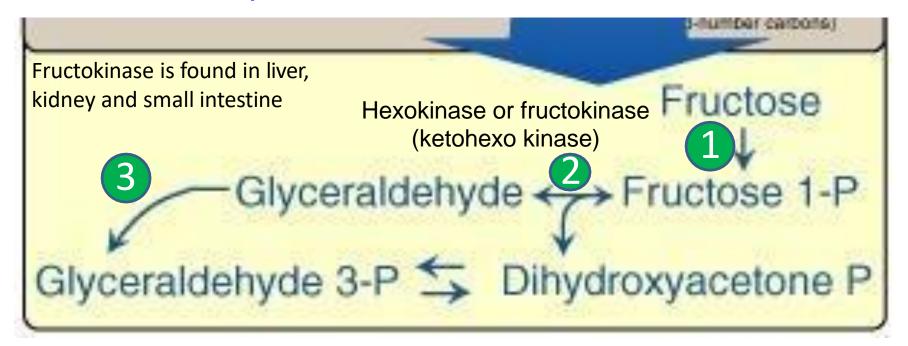


Dr. Diala Abu-Hassan, DDS, PhD

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



CH₂OH CH₂OH C=0 C=O HO-C-H HO-C-H H-C-OH H-C-OH H-C-OH H-C-OH CH₂OH CH3O - P Hexokinase Fructose Fructose 6-phosphate **Fructokinase** Phosphotructokinase CH2O-P CH₀O-P C=O C=O HO-C-H HO-C-H H-C-OH H-C-OH H-C-OH H-C-OH CH₂O-P CH₂OH Fructose Fructose 1-phosphate 1,6-bisphosphate Aldolase A Aldolase B Aldolase B H-C-OH H-C-OH CH₂O-CH₂OH CH₂O~ Glyceraldehyde Glyceraldehyde 3-phosphate Dihydroxyacetone phosphate

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

Human expresses three forms of aldolase

Aldolase B

Liver, kidney, small intestine

Substrate

Fruc. 1 phopsphate

Also

Fruc. 1,6 bisphospate

Aldolase A

In most tissues

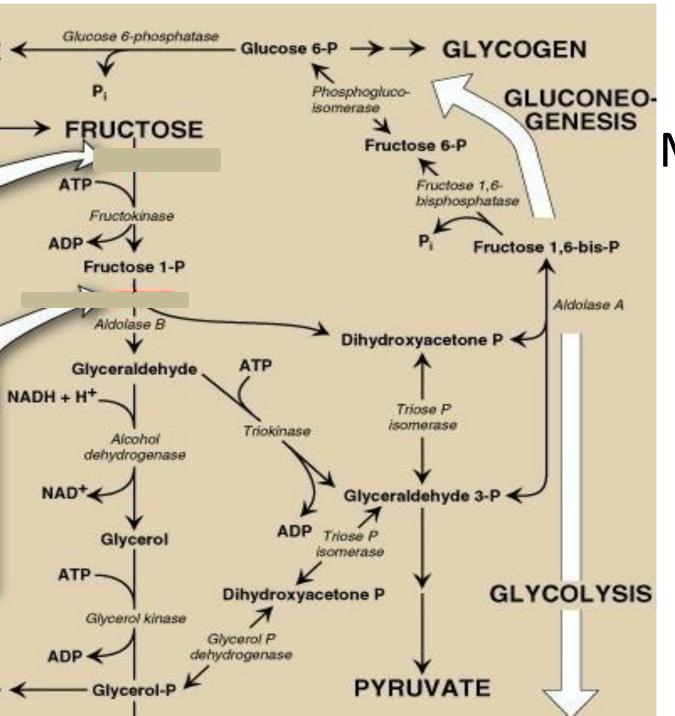
Substrate

Fruc. 1,6 bisphospate

Not

Fruc. 1 phpsphate

↓activity → fructose intolerance



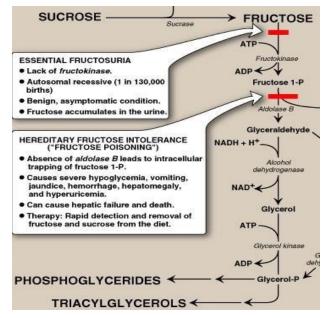
Fructose Metabolism and Interaction with other **Pathways**

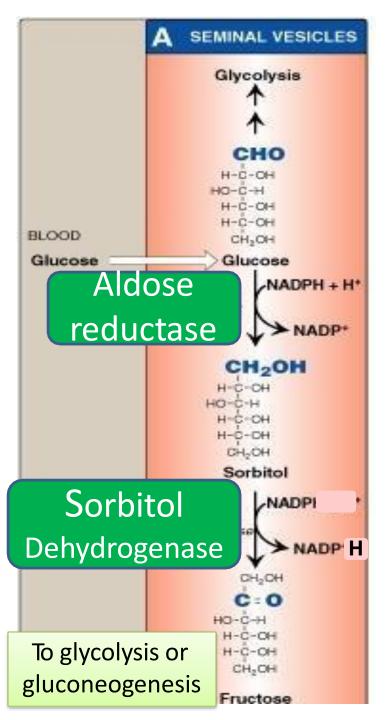
Disorders of Fructose Metabolism

- Fructokinase Deficiency sessential 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





Conversion of glucose to fructose via sorbitol

Aldose Reductase:

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

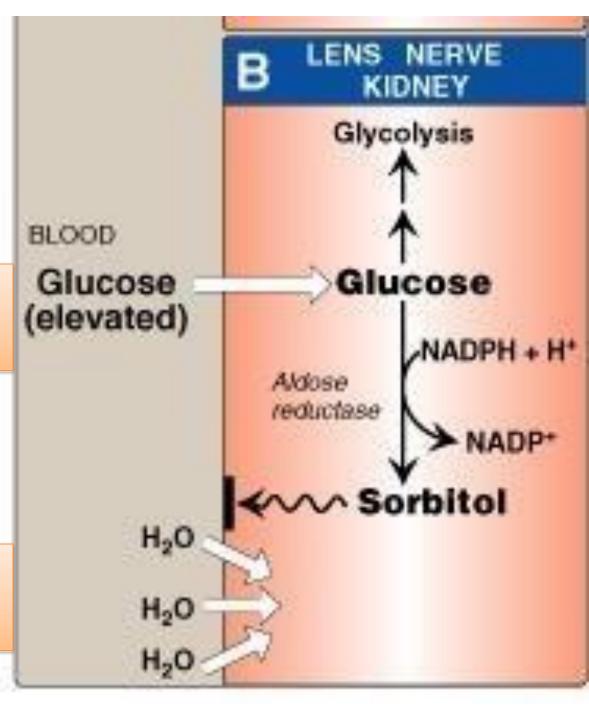
Sorbitol Dehydrogenase: Liver, ovaries and seminal vesicles

Fructose: the major energy source for sperm cells

Conversion of glucose to sorbitol and Diabetic Complications

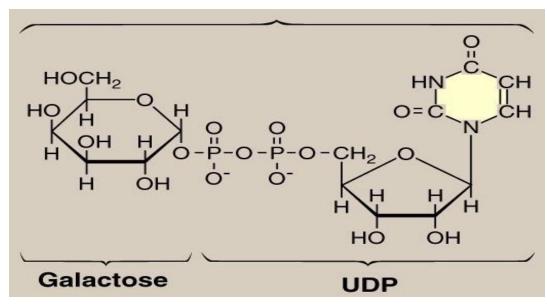
Glucose entry is insulin independent in these tissues

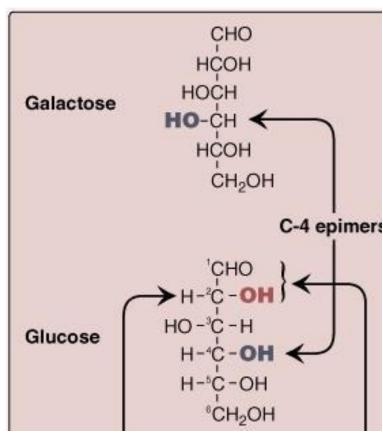
Water retention and cell swelling leading to diabetic complications



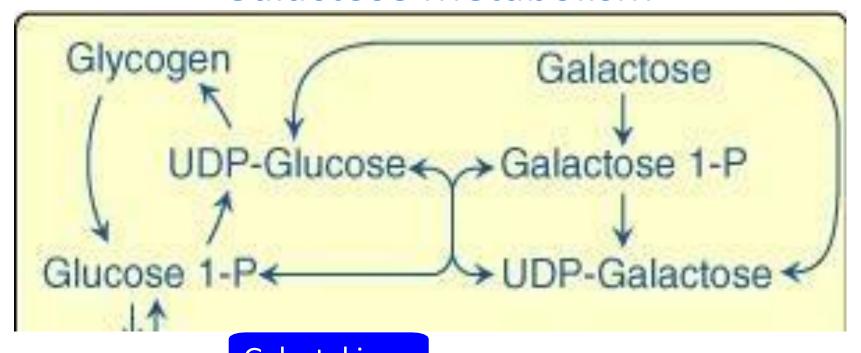
Galactose Metabolism

- 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





Galactose Metabolism



Galactokinase
Galactose + ATP ______ Gal. 1-Phosph ADP

transferase

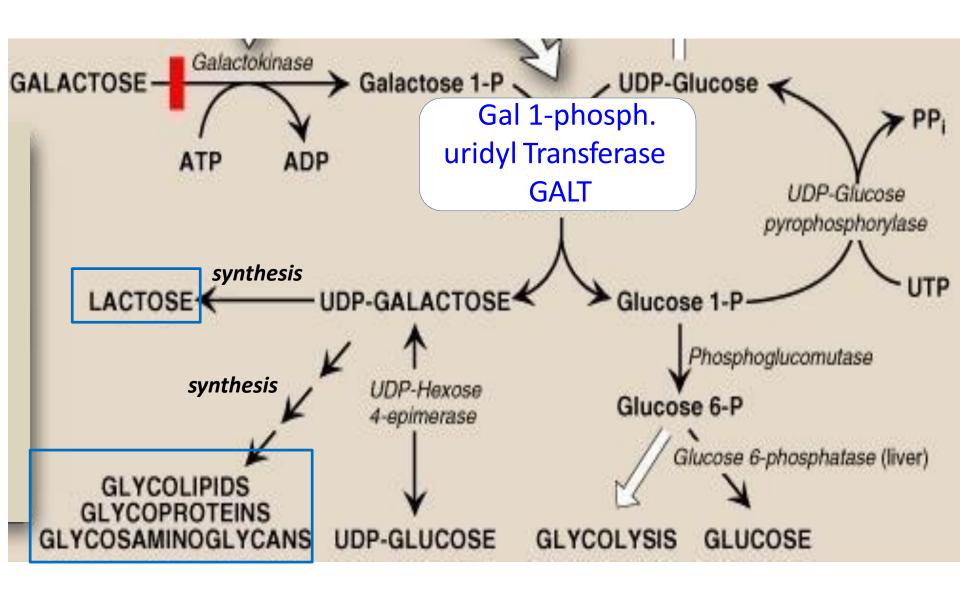
Gal 1-Phosph + UDP Glc. UDP- Galactose + Glc1-Phosph

UDP Galactose



UDP Glucose

Galactose metabolism and fates



Disorders of Galactose Metabolism

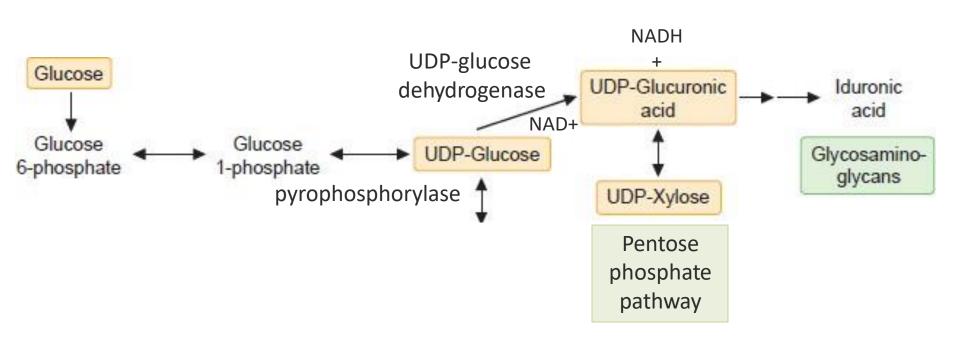
- Deficiency of GALT

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

- Galactose · · · · · → Galactitol production
- Deficiency of Galactokinase
- Accumulation of Galactose
 Galactitol

Disorders of Galactose CLASSIC GALACTOSEMIA Uridyltransferase deficiency. Metabolism Autosomal recessive disorder (1 in 23,000 births). It causes galactosemia and galactosuria, vomiting, diarrhea, and jaundice. GALACTOKINASE DEFICIENCY This causes galactosemia and Accumulation of galactose 1-phosphate and galactitol galactosuria. in nerve, lens, liver, and kidney tissue causes liver damage, severe mental retardation, and cataracts. It causes galactitol accumulation if galactose is present in the diet. Antenatal diagnosis is possible by chorionic villus Sugar alcohol sampling. NADP+ Therapy: Rapid diagnosis and removal of Galactitol galactose (therefore, lactose) from the diet. NADPH + H+ Glycogen Aldose reductase Galactokinase Galactose 1-P GALACTOSE-UDP-Glucose -ALDOSE REDUCTASE ADP Galactose 1-phosphate UDP-Glucose uridyltransferase The enzyme is present in pyrophosphorylase liver, kidney, retina, lens, nerve tissue, seminal vesicles, and ovaries. UDP-GALACTOSE Glucose 1-F **LACTOSE ←** It is physiologically unimportant Phosphoglucomutase in galactose metabolism unless galactose levels are high (as in UDP-Hexose Glucose 6-P 4-epimerase galactosemia). Glucose 6-phosphatase (liver) Elevated galactitol can cause **GLYCOLIPIDS** cataracts. GLYCOPROTEINS UDP-GLUCOSE **GLYCOLYSIS** GLYCOSAMINOGLYCANS GLUCOSE

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 (Galactosyl β (1 \rightarrow 4) glucose) Synthesis

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

Lactose

UDP Gal. + Glucose

synthase 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

Lactose

Lactose

CH₂OH

OH

OH

OH

Glucose

Lactose synthesis in mammary glands

β-D-Galactosyltransferase (protein A)

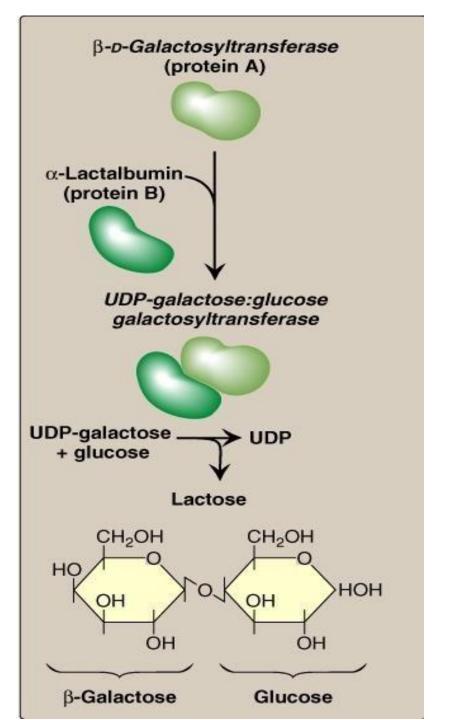
UDP-galactose:glucose galactosyltransferase

α-Lactalbumin

(protein B)

In glycolipids and N-linked glycoprotein synthesis

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



Lactose Synthesis in Mammary Glands