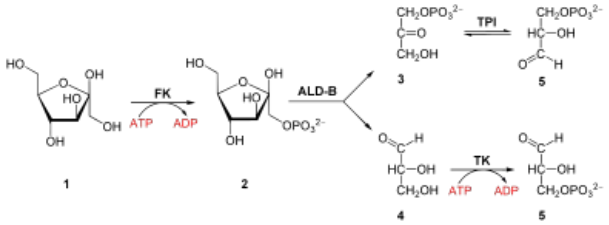
Disorders of fructose metabolism

Fructose is metabolised in the liver, kidneys and small intestine. Intravenous fructose in large doses is toxic.

Toxicity of fructose

Hyperuricemia, hyperlactacidemia, and ultrastructural changes in the liver develop. The utilization of fructose-1-phosphate is limited by triokinase, which converts the resulting D-glyceraldehyde to glyceraldehyde-3-phosphate (which is further converted to pyruvate). The triokinase-catalyzed reaction consumes ATP to form ADP, and AMP is also formed during interconversions of adenine nucleotides. Excess fructose-1-phosphate depletes ATP triokinase. *The hyperuricemic effect* of fructose is due to the degradation of adenine nucleotides to uric acid (AMP to IMP, etc.). *Hyperlactacidemia* promotes the development of acidemia, which in addition reduces the solubility of uric acid in the blood.

Hereditary fructose intolerance



1. Fructose, 2. Fructose-1-phosphate, 3. dihydroxyacetone phosphate, 4. glyceraldehyde, 5. glyceraldehyde-3-phosphate

- severe AR hereditary disease, incidence 1:20 000 - 1:40 000
- **Cause:** the enzyme fructose-1-phosphate aldolase (fructal aldolase B) is missing in the liver and cortex and intestinal mucosa
- **Pathogenesis**: fructose-1-phosphate accumulates in the liver and acts by competitive inhibition of phosphorylase, preventing the breakdown of glycogen into glucose and enzyme deficiency also prevents gluconeogenesis, which causes severe hypoglycemia
- **Clinical signs:** appear shortly after infants have been given milk and fruit that contain sucrose. Symptoms begin non-specifically with vomiting and diarrhoea with episodes of hypoglycemia after eating a diet containing fructose. Hypoglycaemia is caused by the blockade of glycogenolysis and gluconeogenesis.
- The symptoms are practically identical to classical galactosemia, only cataracts are missing. These include vomiting, hepatomegaly and jaundice (jaundice), and hyperaminoaciduria, which are among the trias identical for diff. tyrosinaemia, galactosaemia and hereditary fructose intolerance. Other symptoms include: bleeding, proximal tubular renal disorder, and liver failure with high aminotransferase levels (ALT, AST).
- fructose tolerance test is contraindicated - it could cause severe hypoglycemia, shock and death.
- **Diagnosis:** detection of a mutation in the A149P gene for aldolase B on chromosome 9.
- **Treatment:** complete elimination of fructose from the diet and at the same time supplementation with vitamin C, as a fructose-free diet, requires the avoidance of most natural and frequent sources of vitamin C.
- **Prognosis:** it is uncertain even when following the diet.
- patients have **strong resistance** to foods containing *fructose.*

Essential fructosuria

- also otherwise **benign fructosuria**
- fructokinase deficiency in the liver, kidneys and intestine
- **Occurrence:** 1: 120,000
- Fructose cannot be used in the body because it cannot phosphorylate and therefore become more involved in metabolism. It is a benign disease that is essentially asymptomatic. It is important only from the differential diagnostic point of view.

Fructose-1,6-bisphosphatase deficiency

- severe AR hereditary disease
- **Cause:** The function of the enzyme fructose-1,6-bisphosphatase is reduced
- **Pathogenesis:** lack of enzyme prevents gluconeogenesis, which causes severe hypoglycemia, but also accumulates an excess of compounds that enter gluconeogenesis (AMK, lactate, glycerol).
  - Thus, after depletion of glycogen, patients accumulate precursors of gluconeogenesis, such as lactate, which causes lactic (metabolic) acidosis.
  - Due to hypoglycemia and the inability to gluconeogenesis, multiple ketone bodies are also formed by essentially the same mechanism as in diabetic hypoglycemia, thus ketoacidemia occurs, which contributes to the overall metabolic acidosis.
- **Clinical signs:** episodes of hyperventilation caused by the body's ability to cope and metabolic acidosis through greater excretion of CO2, apnea, hypoglycemia, ketosis, lactic acidemia, hepatomegaly; in about half of all cases, the deficit manifests itself in the first 4 days of life
- **Diagnosis:** molecular analysis of DNA from peripheral leukocytes, if no mutation is found, determination of enzymatic activity in liver biopsy should be performed
- **Therapy:** therapy of ketoacidosis consists of administration of bicarbonate, therapy of hypoglycemia, and using glucose (both parenterally). Patients should not fast, especially during febrile seizures, and should

preferably be fed corn starch overnight,
- The diet should consist mainly of sugars, on the contrary, being rich in fats and proteins is not suitable.
- Growth, psychomotor and intellectual development are not affected and fasting tolerance improves with age to the point where the disorder is not a problem at a later age (explained by increasing hepatic glycogen storage capacity, which leads to less dependence of blood glucose on gluconeogenesis)
- Patients **have no resistance** to foods containing *fructose*

References

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Literature

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