

## Fructose Intolerance

Fructose intolerance is an error in fructose metabolism caused by deficiency of the enzyme aldolase B. After ingestion, fructose is degraded to fructose-1-phosphate in the liver by fructokinase. Then, fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde. A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells and phosphate trapping. This accumulation has downstream effects on gluconeogenesis and glycogenolysis and the regeneration of ATP. Symptoms include hypoglycemia, vomiting, jaundice, cirrhosis and potentially kidney failure. This disease is inherited in an autosomal recessive fashion. Diagnosis is aided by dietary history, especially in infants who become symptomatic after breast feeding is supplemented by fructose containing foods. Treatment is based around strict avoidance of fructose in the diet. It is important to distinguish this disease from essential fructosuria, which causes a clinically benign elevation of fructose in the blood and urine.



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### Pathophysiology

#### Deficiency of Aldolase B

[Down-arrow Aldo-lace \(B\) Bee](#)

Fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde (GA). A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells and phosphate trapping.

#### Fructose 1-P To DHAP And GA

[Fruit-toast \(1\) Wand-Fonz-fairy to Dhapper Dog-hat or Glitter-pie](#)

Fructose-1-phosphate is degraded by aldolase B into dihydroxyacetone-phosphate (DHAP) and glyceraldehyde (GA).

#### Accumulation Of Fructose-1-Phosphate

[Fruit-toast \(1\) Wand-Fonz-fairy](#)

A deficiency of aldolase B results in the accumulation of fructose-1-phosphate in cells. This traps phosphate in an unusable form that does not return to the general phosphate pool, resulting in depletion of phosphate and ATP stores. This has downstream effects on gluconeogenesis and glycogenolysis and the regeneration of ATP.

#### Inhibition Of Glycogenolysis

[Inhibiting-chains with Glider-lights](#)

Glycogenolysis is the breakdown of glycogen to glucose-1-phosphate and glucose. In hereditary fructose intolerance, the accumulation of fructose-1-phosphate in cells leads to trapping of phosphate which decreases the amount of ATP available to cells. Decreased ATP leads to inhibition of glycogenolysis and gluconeogenesis.

#### Inhibition Of Gluconeogenesis

[Inhibiting-chains with Glue-genie](#)

Gluconeogenesis is a metabolic pathway that results in the generation of glucose from substrates such as lactate, glycerol, and glucogenic amino acids. In hereditary fructose intolerance, the accumulation of fructose-1-phosphate in cells leads to the trapping of phosphate which decreases the amount of ATP available to cells. Decreased ATP leads to inhibition of glycogenolysis and gluconeogenesis.

### Clinical Features

## **Hypoglycemia**

### **Hippo-glue-bottle**

Due to inhibition of glycogenolysis and gluconeogenesis, individuals with hereditary fructose intolerance suffer from hypoglycemia.

## **Vomiting**

### **Vomit**

Vomiting is a common nonspecific symptom in hereditary fructose intolerance. Vomiting can also be seen secondary to hypoglycemia in this disorder.

## **Jaundice**

### **Jaundice-janitor**

Jaundice is yellowing of the skin and conjunctival membranes caused by hyperbilirubinemia, and it is often caused by liver disease. Aldolase B is preferentially expressed in the liver and deficiency can cause liver damage with presentation of jaundice.

## **Cirrhosis**

### **C-roses-on-liver**

Cirrhosis is characterized by fibrosis and scarring of the liver, leading to loss of function. Because aldolase B is expressed in the liver, deficiency can cause liver damage and cirrhosis.

## **Autosomal Recessive**

### **Recessive-chocolate**

This disease is inherited in an autosomal-recessive fashion.