Clinical symptoms

- Growth failure, failure to thrive, weight loss
- Ambiguous genitalia, delayed puberty, precocious puberty
- Developmental delay, seizures, dementia, encephalopathy, stroke
- Deafness, blindness, pain agnosia
- Skin rash, abnormal pigmentation, lack of pigmentation, excessive hair growth, lumps and bumps
- Dental abnormalities
- Immunodeficiency, thrombocytopenia, anemia, enlarged spleen, enlarged lymph nodes
- Many forms of cancer

Classification

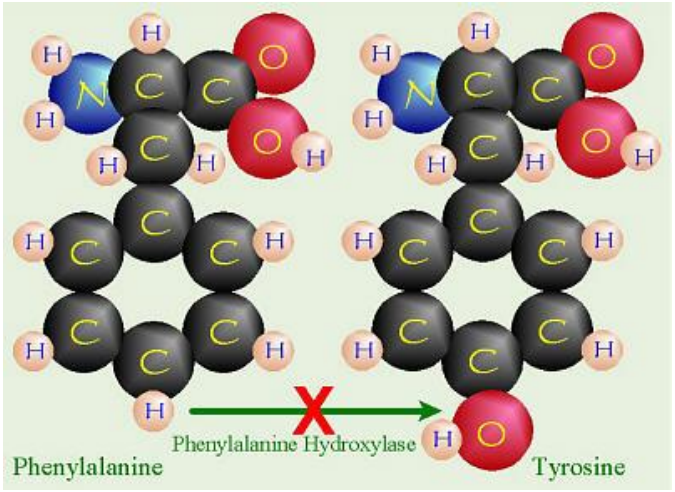
Amino acid metabolism	phenylketonuria, maple syrup urine disease, glutaric acidemia type 1, homocystinuria
Carbohydrate metabolism	Glycogen storage disease, galactosaemia
Urea cycle disorder - urea cycle defects	OTC deficiency, carbamoyl phosphate synthetase I deficiency
Disorders of organic acid metabolism (organic acidurias)	alkaptonuria, propionic acidaemia, methyl malonic aciduria, isovaleric acidaemia
Lysosomal storage disorders	Gaucher's disease, Niemann Pick disease, Fabry disease mucopolysaccharidoses
Transport protein defects	cystic fibrosis, cystinuria, cystinosis
Disorders of fatty acid oxidation and mitochondrial metabolism	Medium-chain acyl-coenzyme A dehydrogenase deficiency (often shortened to MCADD.)
Porphyrin metabolism	Acute intermittent porphyria
Disorders of purine or pyrimidine metabolism	Lesch-Nyhan syndrome
Steroid metabolism	Lipoid congenital adrenal hyperplasia, congenital adrenal hyperplasia
Mitochondrial function	Kearns-Sayre syndrome, Pearson syndrome
Peroxisomal function	Zellweger syndrome, adrenoleukodystrophy
Metals metabolism	Wilson disease
Connective tissue defects	Hypophosphatasia
Hereditary hyperbilirubinemia	Crigler-Najjar syndrome

I. Amino acid metabolism

Phenylketonuria (PKU)

- **Definition**:

  PKU is a metabolic disorder caused by a deficiency of the liver enzyme phenylalanine hydroxylase.



- **Inheritance**:

  Autosomal recessive

Diagnosis of HPA

- **Biochemical testing**
  - quantitative plasma amino acid analysis
  - urine pterin studies
  - dihydropterin reductase measurement

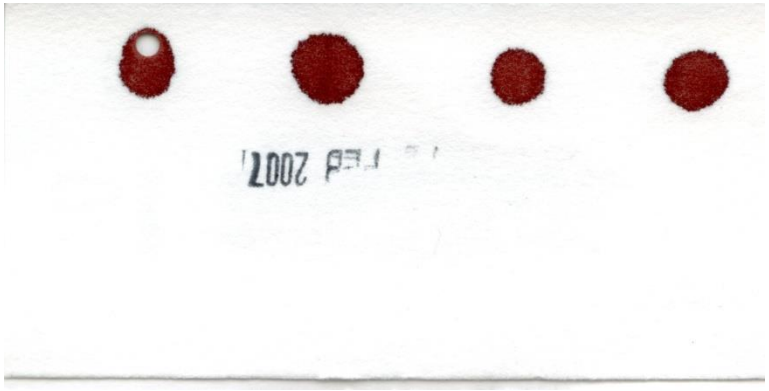
  Note: Enzyme analysis is not usually indicated for PAH, because it is a hepatic enzyme.

- **Genetic diagnosis**
  - Targeted mutation analysis - sequence analysis of select exons
  - Sequence analysis /mutation scanning
  - Duplication/deletion analysis
  - Linkage analysis

Good sample

The blank must fill the circle completely with one drop of blood.
Circle must be filled and evenly saturated.

Front



Back

II. Carbohydrate metabolism

Galactosemia

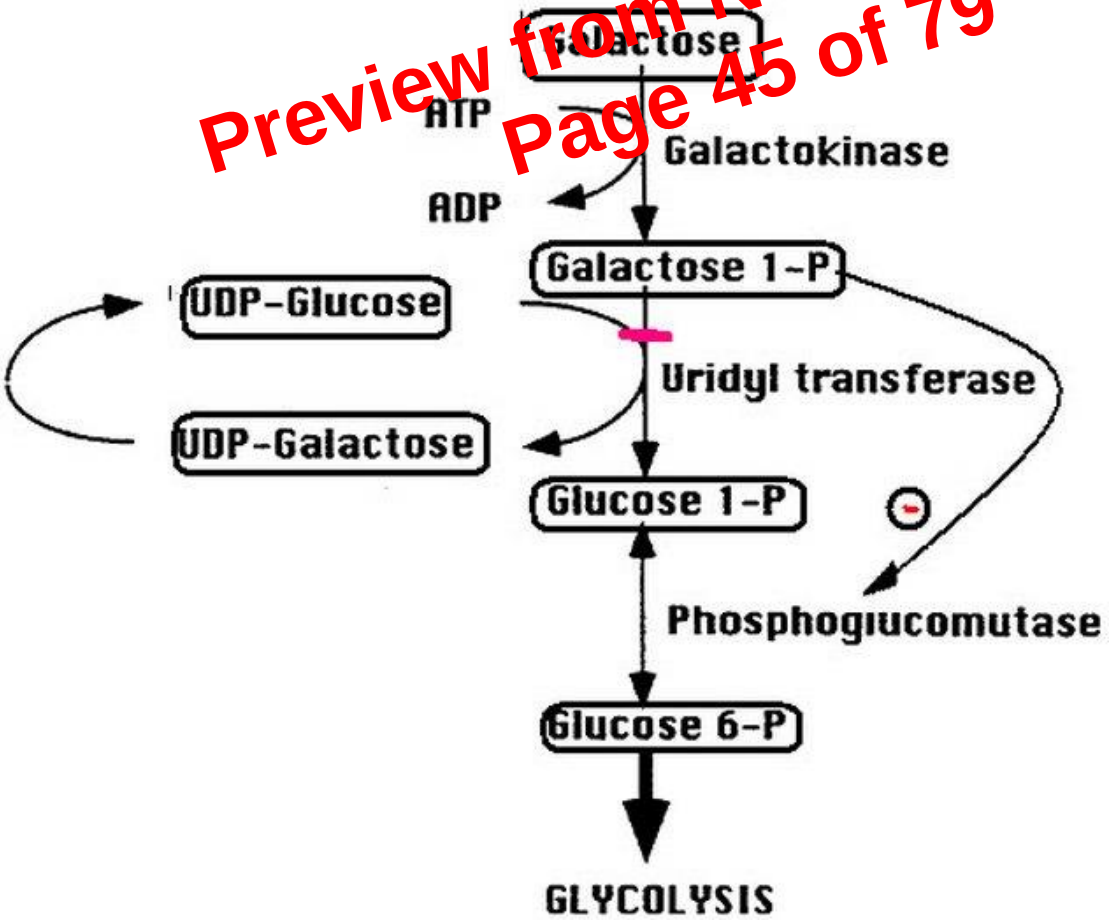
- **Definition**:

  Galactosemia is a rare genetic metabolic disorder that affects an individual's ability to metabolize the sugar galactose properly.

- **Inheritance**:

  Autosomal recessive

Galactose metabolism



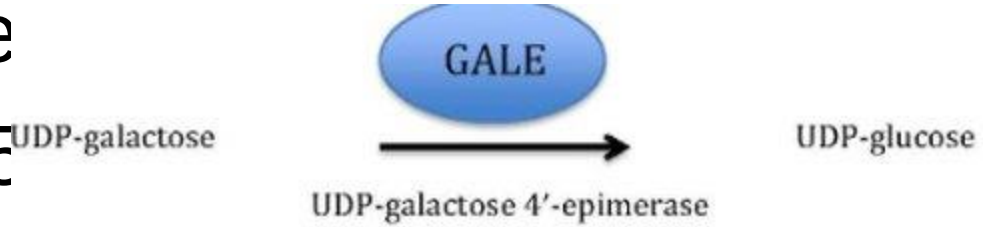
Galactose is converted into glucose by the action of three enzymes:

- galactose-1-phosphate uridyl transferase
- galactokinase
- UDP galactose epimerase

Type III galactosemia (UDP galactose epimerase)

- **Gene:** *GALE1* gene
- **Location**: 1p36-p35
- **Gene product**:

  UDP-galactose-4-epimerase
- **Function:** conversion of UDP-glucose to UDP-galactose



Clinical characteristics

- Hypotonia
- Poor feeding
- Vomiting
- Weight loss
- Jaundice
- Hepatomegaly
- Liver dysfunction
- Aminoaciduria
- Cataracts.

Prevention of Galactosemia

- **Prenatal Testing**
  - chorionic villus sampling – 10-12 weeks' gestation
  - amniocentesis – 15-18 weeks' gestation

- **Preimplantation genetic diagnosis (PGD)**

Diagnosis and treatment of alkaptonuria

- Diagnosis
  - gas chromatography-mass spectrometry analysis (detection of a significant amount of HGA in the urine by gas chromatography-mass spectrometry analysis)
  - molecular genetic testing
    - Targeted mutation analysis
    - Sequence analysis

- Treatment

  symptomatic

Diagnosis and treatment of Gaucher' disease

- Diagnosis
  - Clinical
  - Enzyme testing
  - Genetic (sequencing)

- Treatment
  - Enzyme replacement with i.v. recombinant glucocerebrosidase – 200 000$ annualy

Diagnosis and treatment of adrenoleukodystrophy

- Diagnosis
  - Clinical
  - Plasma very long chain fatty acid (VLCFA) determination by gas chromatography-mass spectrometry
  - Molecular genetic analysis
  - Newborn screening
- Treatment
  - Dietary therapy
  - Transplant
  - Gene therapy
  - Treatment of the adrenal insufficiency