Inborn error of carbohydrate metabolism

By

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Inborn errors of metabolism

Definition:- These are a group of rare genetic disorders in which the body cannot metabolize food components normally.

➢ These disorders are usually caused by defects in the enzymes involved in the biochemical pathways that break down very essential biochemical components.

What is a metabolic disease?

Garrod's hypothesis

What is a metabolic disease?

➢ According to ***Garrod's hypothesis*** A *genetically* determined *biochemical disorder* in which a specific *enzyme defect* produces a *metabolic block* that may have *pathologic* consequences at birth (e.g. *phenylketonuria*) or in later life (e.g. *diabetes mellitus*); also called *enzymopathy* and *genetotrophic* disease.

Inborn errors of Carbohydrate Metabolism

Categories

1) Hemolytic anemia's caused by deficiencies of-
   A. Hexokinase
   B. Pyruvate kinase
   C. Glucose-6-(P)-dehydrogenase
2) Pyruvate dehydrogenase deficiency.
3) Carbohydrate intolerance disorders-
   A. Lactose intolerance.
   B. Fructose intolerance.
4) Fructosuria.
5) Galactosemia.
6) Pentosuria.
7) Glycogen storage disorders.
8) Mucopolysaccharidoses.

3) Carbohydrate intolerance disorders

A. Hereditary Lactose intolerance :-

- It is a rare disorder, due to the deficiency of Lactase (β-Galactosidase) enzyme.
- Symptoms - Diarrhea, inadequate nutrition and fluid & electrolyte disturbances.
- Prominent feature is Lactosuria (Lactose in urine).
- Milk is not digested in the individuals so milk products are preferred.

B. Hereditary Fructose intolerance :-

- It is an autosomal recessive disorder.
- Incidence is 1 in 20,000.
- 1 in 70 persons are carriers of abnormal gene.
- The defect is Adolase-B (fructose-1-(P) aldolase)
- Fructose -1(P) cannot be metabolized.
- Fructose-1(P)  Glyceraldehyde + DHAP.

- It leads to accumulation of fructose-1-(P),
  - severe hypoglycemia, vomiting, hepatic failure and jaundice.
- Fructose-1-(P) allosterically inhibits liver phosphorylase and blocks glycogenolysis leading to hypoglycemia.
- Treatment :- Early detection and intake of diet free from fructose and sucrose, are advised to overcome fructose intolerance.

4) Essential fructosuria :-

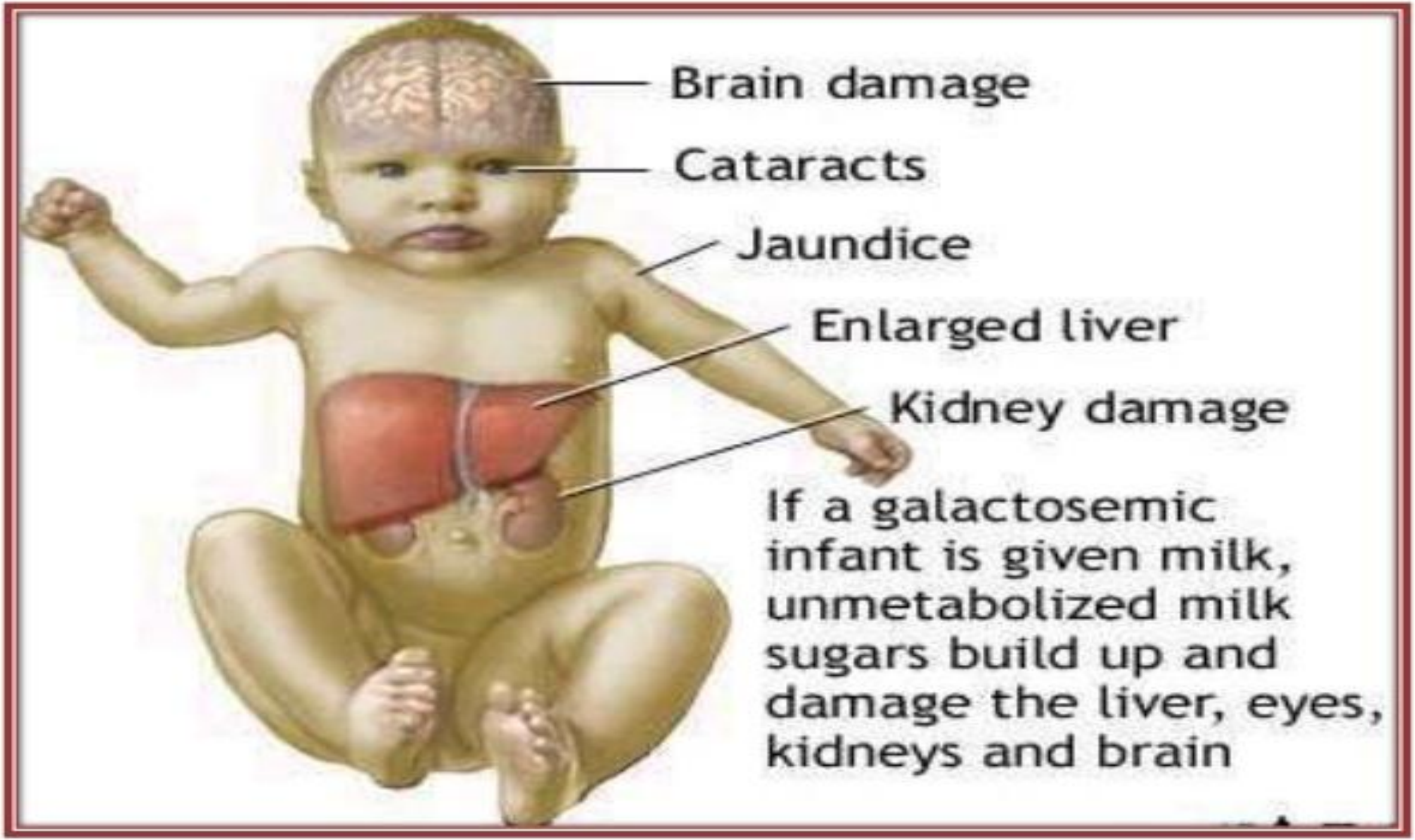
- Due to the deficiency of fructokinase, fructose is not converted to fructose-1-(P).
- Fructose  Fructose-1-(P).
- This is an asymptomatic condition with excretion of fructose in urine.

5) Galactosemia:-

- It is a serious serious autosomal recessive disorder resulting from the deficiency of galactose-1-(P) uridyltransferase, leads to accumulation of Galactose-1-(P) in the liver and becomes toxic.
- Incidence is one in 35,000 births.
- Galactose -1-(P)  UDP Galactose.

Symptoms:

- The build up of galactose and the other chemicals can cause serious health problems like
  - Swollen and inflamed liver,
  - Kidney failure,
  - Stunted physical and mental growth, and
  - Cataracts in the eyes.
- If the condition is not treated there is a 70% chance that the child could die.
- Treatment :- Galactose free diet is preferred i.e. milk will be avoided.


Brain damage
Cataracts
Jaundice
Enlarged liver
Kidney damage
If a galactosemic infant is given milk, unmetabolized milk sugars build up and damage the liver, eyes, kidneys and brain

6) Essential pentosuria :

- It is a rare autosomal recessive disorder and benign condition, asymptomatic.
- Individuals does not show any ill-effects.
- Incidence is one in 2,500 births.
- Primarily in Jewish population.

7) Glycogen storage diseases :

- The metabolic defects concerned with the glycogen synthesis and degradation are collectively called as GSD.
- All Glycogen storage disorders are Autosomal recessive disorders (except Type-VIII)
- Incidence estimated to be between 1 in 1 lack to 1 million births per year in all ethnic groups.

Disorder	Enzyme	Affected Tissue
Type I (von Gierke's disease)	Glucose-6-phosphatase	Liver, kidney, intestine
Type II (Pompe's disease)	Lysosomal α 1,4- glucosidase (Acid maltase)	All organs
Type III (Cori's disease)	Amylo α 1,6- glucosidase (debranching enzyme)	Liver, muscle, heart, leukocytes
Type IV (Anderson's disease)	Glucosyl 4,6-transferase	Most tissues
Type V (Mc Ardle's disease)	Muscle glycogen phosphorylase	Skeletal muscle
Type VI (Her's disease)	Liver glycogen phosphorylase	Liver
Type VII (Tauri's disease)	Phosphofructokinase	Skeletal muscle, erythrocytes.

Disorder	Incidence in births (1 out of)	Chromosome location
Type I (von Gierke's disease)	1,00,000	17
Type II (Pompe's disease)	1,75,000	17
Type III (Cori's disease)	1,25,000	1
Type IV (Anderson's disease)	1 million	3
Type V (Mc Ardle's disease)	1 million	11
Type VI (Her's disease)	1 million	14
Type VII (Tauri's disease)	1 million	1

Disorder	Features
Type I (von Gierke's disease)	Hypoglycemia, Hepatomegaly, Cirrhosis, Ketosis, Hyperuricemia.
Type II (Pompe's disease)	Generalized glycogen deposit; lysosomal storage disease.
Type III (Cori's disease)	Hepatomegaly, Cirrhosis
Type IV (Anderson's disease)	Hepatomegaly, Cirrhosis
Type V (Mc Ardle's disease)	Exercise intolerance
Type VI (Her's disease)	Hepatomegaly, Hyperuricemia.
Type VII (Tauri's disease)	

GSD Type-VIII :

- It is an X linked recessive disorder.
- Frequency is one in 1,25,000 births.
- Enzyme deficiency is Phosphorylase kinase.

Clinical Features

- Hepatomegaly and fibrosis in childhood, these symptoms improve with age and usually disappear after puberty.
- Fasting hypoglycemia (40-50 mg/dl)
- Hyperlipidemia
- Growth retardation, Growth often normalizes by adulthood as well.
- Elevated serum transaminase levels (Aspartate aminotransferase and alanine aminotransferase > 500 units/ml)

Overview of Carbohydrate metabolism

Enzyme Deficiency	Disease
Hexokinase Pyruvate kinase Glucose-6-(P) dehydrogenase	Hemolytic Anemia
Pyruvate dehydrogenase	Muscular hypotonia, Lactic acidosis.
Lactase Aldolase B (fructose-1-(P) aldolase)	Hereditary Lactose intolerance Hereditary fructose intolerance
Fructokinase	Essential Fructosuria
Galactose-1-(P)-Uridyl transferase Galactokinase Uridine di-(P)-galactose-4-epimerase	Galactosemia
L-Xylitol dehydrogenase	Essential Pentosuria
	Glycogen storage disorders And Mucopolysaccharidoses