metabolic disorders

it’s Caused by an absence or deficiency in an enzyme (protien)

Rey’s syndrome

- Extremely rare can affect the brain and liver
- • Most commonly in kids between 4 and 14 years old recovering from a viral infection
- studies have linked the use of aspirin
- we can treat it in its earliest stages.
- pathophysiology; mitochondrial dysfunction
- Treatment ; there is no cure for RS
- Successful management aimed at protecting the brain against irreversible damage by reducing brain swelling, preventing complications in the lungs, and anticipating cardiac arrest.
- • When RS is diagnosed and treated in its early stages, chances of recovery are excellent. When diagnosis and treatment are delayed, the chances for successful recovery and survival are severely reduced.
- Symptomes;
- No fever,persistent vomiting, lethargy or sleepiness and severe weakness.

Wilson disease

- It is autosomal recessive genetic disease that prevents the body from getting rid of extra copper.
- • People who get Wilson disease inherit two abnormal copies of the ATP7B gene, one from each parent.
- • In WD when the copper storage capacity of the liver is exceeded, copper is released into the bloodstream and travels to other organs –including the brain, kidneys, and eyes. Over time, high copper levels can cause life-threatening organ damage.
- • . It equally affects men and women. Symptoms usually appear between ages 5 to 35.
- symptoms In Liver or spleen: swelling, yellowing of the skin and whites of the eyes. Rarely, acute liver failure
- • In CNS: problems with speech, swallowing, or physical coordination.
- • Other signs and symptoms: anemia, low platelet or white blood cell count, slower blood clotting, measured by a blood test.
- • Kayser-Fleischer rings is the most unique sign of Wilson disease
- requires lifelong treatment to reduce copper in the body.

Hemochromatosis

- Caused by too much absorption and storage of iron.
- Healthy people absorb about 10 percent of the iron in the food, People with hemochromatosis absorb up to 30 percent of iron. Over time, they absorb and retain between 5 to 20 times more iron than the body needs.
- Our body has no natural way to rid itself of the excess iron
- Causes;
- Hemochromatosis is an autosomal recessive disease results from defect in a gene called HFE (human factors engineering).
- •The HFE protein regulates the production of a protein called hepcidin which is produced by the liver, and it determines how much iron is absorbed from the diet and released from storage sites in the body.
- .The most known mutation of HFE is C282Y
- Treatment ;
- Phlebotomy, which means removing blood the same way it is drawn from donors at blood banks.
- Diagnosis
- 1. Serum transferrin saturation: A plasma protein that transport iron in blood. Transferrin saturation values greater than 45 percent are considered too high.
- 2. Ferritin : This test measures the amount of iron stored in your body (most of ferritin is in liver).
- 3. Genetic testing to confirm the diagnosis blood test to detect the HFE mutation.

Glycogen Storage disease

type 1 of glycogen storage disease

- also known as von Gierke's disease, is the most common form of glycogen storage disease.
- • Cause inherited deficiency of liver Glucose 6- phosphatase (release free glucose & phosphate).
- • The absence of glucose 6-phosphatase in the liver causes hypoglycemia due to inability to release free glucose.
- • The microsomal G6Pase system consists of membrane- bound phosphohydrolase and various translocases for G6P (T1), phosphate (T2), and glucose (T3).
- 1-GSD type Ia caused by G6Pase defect
- 2- GSD type Ib resulting from deficiency of a specific translocase T1 which is a transporter of glucose-6-phosphate (G6P) into the microsomal compartment
- 3-GSD type Ic is deficiency of translocase T2 that carries inorganic phosphates from microsomes into the cytosol
- 4- GSD type Id is deficiency in a T3 that translocates free glucose molecules from microsomes into the cytosol.

type 2 of glycogen storage disease

- known as acid maltase deficiency or Pompe disease, is a lysosomal disease.
- • It is an autosomal recessive disease
- • Deficiency of a lysosomal enzyme, alpha-1,4-glucosidase, causes accumulation of glycogen known as GSD type II.
- • Alpha-1,4-glucosidase is important for the degradation glycogen in the lysosome.
- • The most abundant deposits are in the cardiac and skeletal muscles and liver,
- infantile form is characterized by heavy deposits of glycogen in the heart, liver, and tongue.
- • The hypotonia (low muscle tone tension or resistance to stretch) and muscle weakness (myopathy) involve skeletal and respiratory muscles as well with progressive respiratory insufficiency.
- • In the CNS, the disease primarily affects the nuclei of the brainstem and the cells of the ventral horn of the spinal cord. Mental functions are preserved.
- = Juvenile and adult forms, is characterized by glycogen deposition in skeletal muscles. The involvement of the cardiac muscle varies in the juvenile form, whereas the muscle is unaffected in the adult form

type 3 of glycogen storage disease

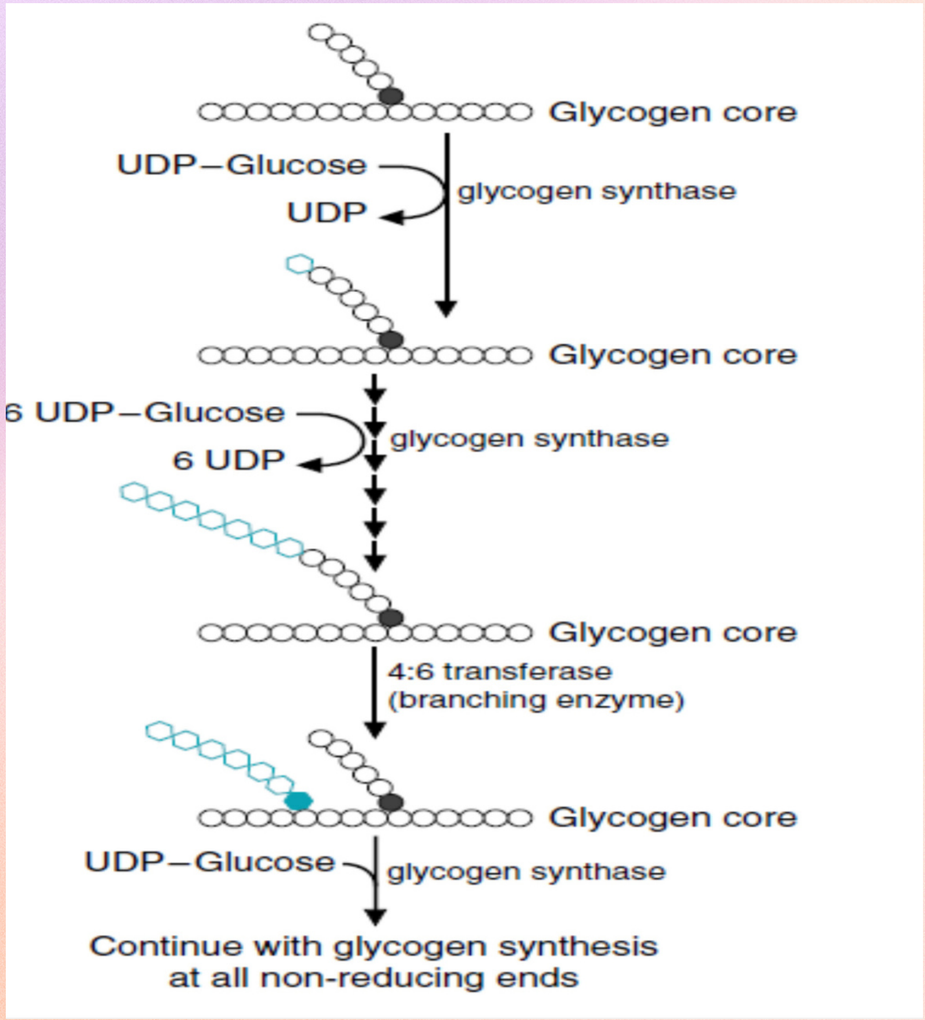
- also known as Forbes-Cori disease or limit dextrinosis.
- • Both liver and skeletal muscles are involved in GSD type III.
- • Deficiency of the cytosolic debrancher enzyme
- • Abnormal glycogen with short external branches is stored in the liver, heart, and skeletal muscle cells.
- • 2 forms of the disease exist.
- 1- In GSD type IIIa, the liver, skeletal muscles, and cardiac muscle are involved.
- 2- In GSD type IIIb, only the liver is involved.
- The debrancher enzyme, catalyzes the removal of the last branched four residues. It has two catalytic activities it acts as a:
- 1- As a transferase, it first removes the three glucose residues, and adds it to the end of a longer chain.
- 2- Alpha amylo-1,6- glucosidase activity resulting in the release of free glucose.

type 4 of glycogen storage disease

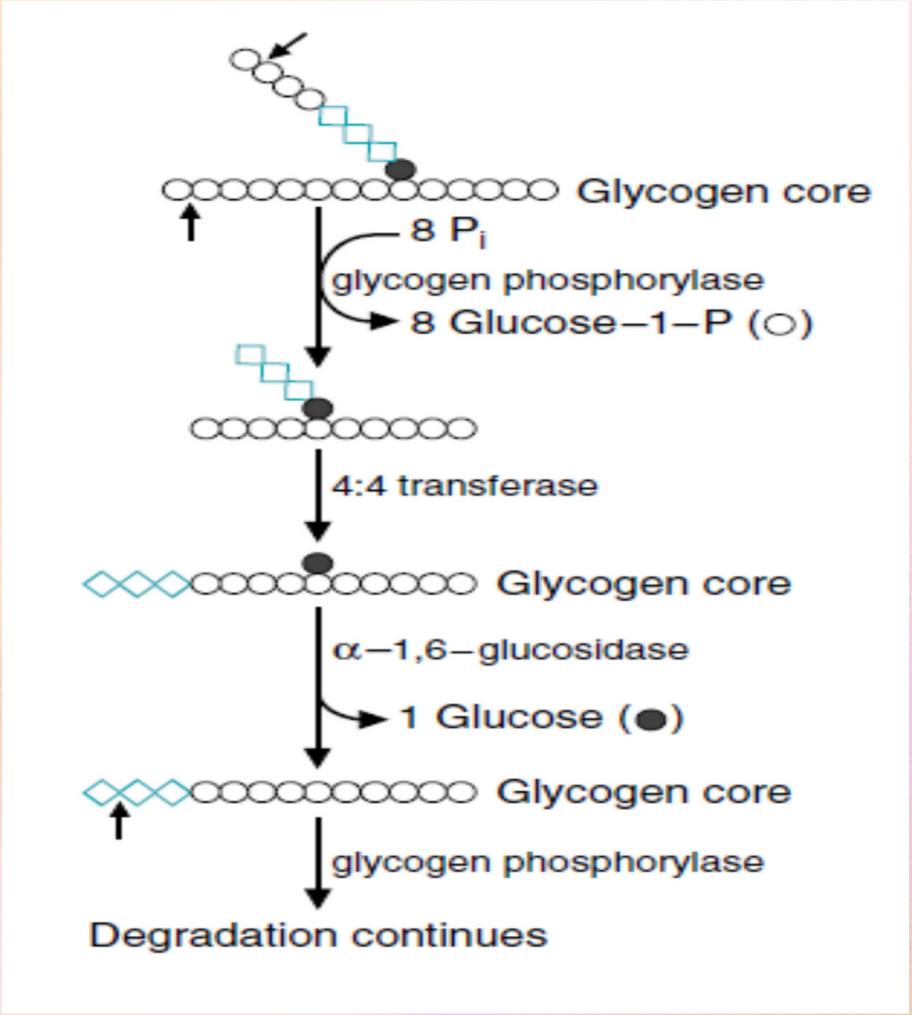
also known as amylopectinosis or Andersen disease .

• Causes deficiency in amylo-4:6-transferase (branching enzyme).
• Accumulation of abnormally structured glycogen in the liver, heart, and neuromuscular system characterizes this disease.
• The abnormal glycogen has long external branches that resemble amylopectin.
• This form of glycogen is less soluble; liver cirrhosis probably arises as a reaction to this insoluble material.

Deficiency in amylo- 4:6-transferase
When the chain reaches 11 residues or more in length, then 6 to 8 residue piece is cleaved by amylo-4:6- transferase and reattached to a glucose unit by an α- 1,6 bond.


Glycogen core
UDP–Glucose
UDP
glycogen synthase
Glycogen core
6 UDP–Glucose
6 UDP
glycogen synthase
Glycogen core
4:6 transferase
(branching enzyme)
Glycogen core
UDP–Glucose
glycogen synthase
Continue with glycogen synthesis
at all non-reducing ends

Type 4


Glycogen core
8 P_i
glycogen phosphorylase
8 Glucose–1–P (○)
4:4 transferase
Glycogen core
α–1,6–glucosidase
1 Glucose (●)
Glycogen core
glycogen phosphorylase
Degradation continues

Type 3