GLYCOGENESIS

Introduction

- Glycogen is a homo polysaccharide with 1-4 linkage and alpha 1-6 linkage
- Branching makes more globular and less space consuming .

Definition of glycogenesis:

- It is the formation of glycogen, which occurs in all tissues of the body, but in large amount in liver and muscles.
- There are very small amount of glycogen synthesis and storage in the central nervous system; this is why it is completely dependent on blood glucose as a source of energy.
- **Site:** Cytosol of all cells particularly liver and muscles.

STRUCTURE AND FUNCTION OF GLYCOGEN

Main stores of glycogen:

1. Skeletal muscle

2. Liver

Main function of:

Muscle Glycogen: Fuel reserve for the synthesis of ATP during muscle

Liver Glycogen: Maintain the blood glucose concentration, particularly during the early stages of a fast

- Storage form of carbohydrate in liver and muscle
- Provide glucose during fasting.
- The glycogen content of liver is 10g/100g tissue and 1-2 g/100g in skeletal muscle
- When blood glucose lowers, liver glycogen is broken down and helps to maintain glucose level
- About 5 hours after taking food, the blood sugar tends to fall. Glycogen is lyzed to glucose so that energy needs are met

- After 18 hrs fasting, most of the liver glycogen is depleted, when depot fats are hydrolyzed and energy requirement is met by fatty acid oxidation
- The function of muscle glycogen is to act as reserve fuel for muscle contraction
- All the enzyme related to glycogen metabolism are cytoplasmic

AMOUNTS OF LIVER AND MUSCLE GLYCOGEN

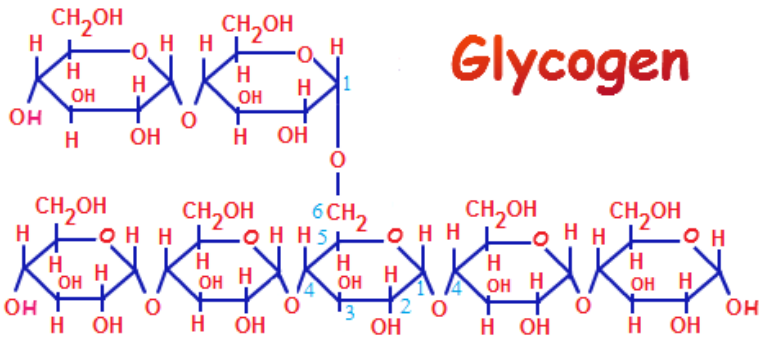
• Resting Muscle: Approximately 400 g i.e. 1–2% of the fresh weight of resting muscle

• Well-Fed Liver: Approximately 100 g of glycogen i.e.10% of the fresh weight of a well-fed adult liver.

STRUCTURE OF GLYCOGEN:

• Polysaccharide made exclusively from α -D – glucose • Primary glycosidic bond is an α (1→ 4) linkage. After an average of eight to ten glucosyl residues, there is a branch containing an α (1→ 6) linkage

• Molecular mass of up to 108 daltons



FLUCTUATION OF GLYCOGEN STORES

• Increase during the well-fed state and are depleted during a fast

• Muscle glycogen is not affected by short periods of fasting (a few days) and is only moderately decreased in prolonged fasting (weeks)

Synthesized from molecules of α-D- glucose

• Process occurs in the cytosol

• Requires energy supplied by ATP (for the phosphorylation of glucose) and uridine triphosphate (UTP)

Glycogenesis pathway:

- Glucose 6-phosphate isomerizes to **glucose 1-phosphate** by the action of phosphoglucomutase.
- **Synthesis of an activated form of glucose (UDP-glucose) :**from glucose 1-phosphate and UTP (uridine triphosphate) in a reaction catalyzed by UDP-glucose pyrophosphorylase

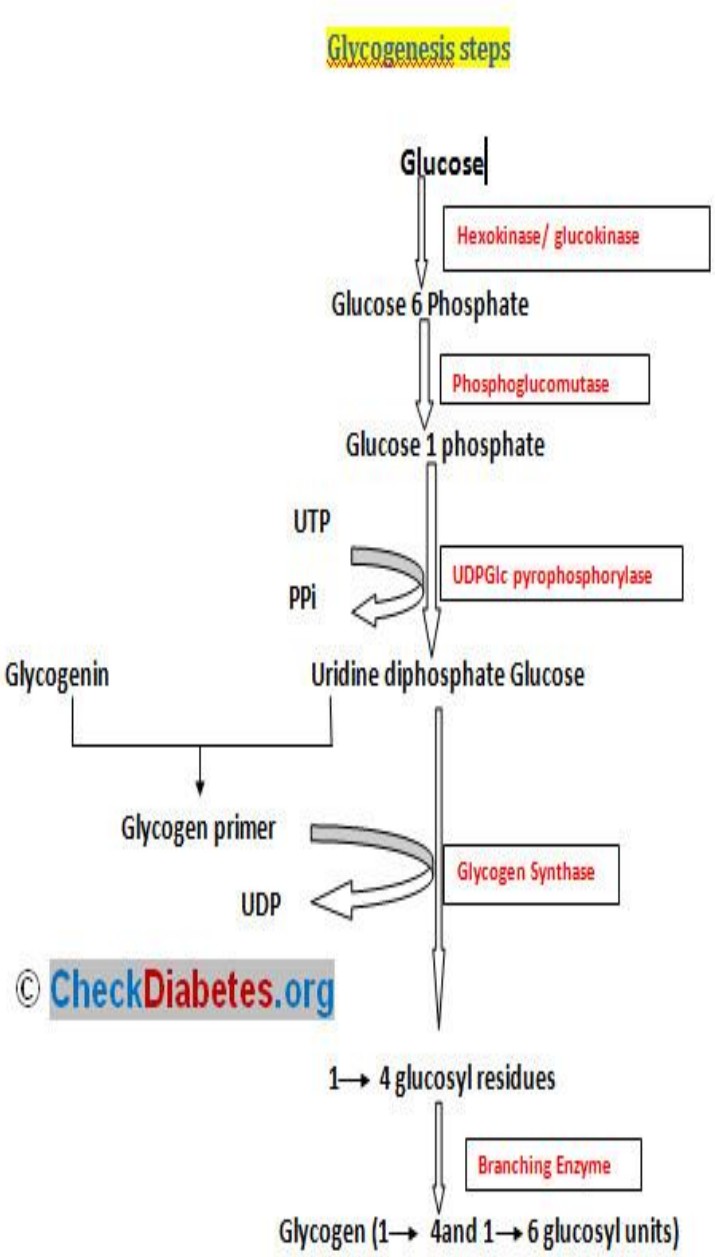
Elongation of glycogen chain

- ***Glycogen synthase* – the key regulatory enzyme in glycogenesis**
- catalyses formation of an α-1,4-glycosidic bonds by the transfer of glucosyl from activated UDP-glucose to an existing chain (a primer)

*The **branching in glycogen***

- ❑ After around 8 residues, branching begins and the branches provide more number of activated glucose residual ends for the UDP glucose to get attached to.
- ❑ This branching is brought about by branching enzyme called amylo-α(1→4) → α(1→6)-**transglucosidase**.
- forms α-1,6-linkages that make glycogen a branched polymer.

- Branching is important because it increases the solubility of glycogen and increases the velocity of glycogen synthesis and breakdown (creating a large number of non-reducing ends).



Glycogen Storage Diseases

- Glycogen storage diseases are groups of inherited disorders characterized by deposition (over-storage) of an abnormal type or quantity of glycogen or failure of storage of glycogen in the tissues.
- They are mainly due to deficiency of one of enzymes of glycogenesis or glycogenolysis, phosphofructokinase, or lysosomal glycosidases.
- These include type I to type VIII glycogen storage diseases.

TABLE 21.1 Glycogen-storage diseases

Type	Defective enzyme	Organ affected	Glycogen in the affected organ	Clinical features
I Von Gierke disease	Glucose 6-phosphatase or transport system	Liver and kidney	Increased amount; normal structure.	Massive enlargement of the liver. Failure to thrive. Severe hypoglycemia, ketosis, hyperuricemia, hyperlipemia.
II Pompe disease	α-1,4-Glucosidase (lysosomal)	All organs	Massive increase in amount; normal structure.	Cardiorespiratory failure causes death, usually before age 2.
III Cori disease	Amylo-1,6-glucosidase (debranching enzyme)	Muscle and liver	Increased amount; short outer branches.	Like type I, but milder course.
IV Andersen disease	Branching enzyme (α-1,4 ⟶ α-1,6)	Liver and spleen	Normal amount; very long outer branches.	Progressive cirrhosis of the liver. Liver failure causes death, usually before age 2.
V McArdle disease	Phosphorylase	Muscle	Moderately increased amount; normal structure.	Limited ability to perform strenuous exercise because of painful muscle cramps. Otherwise patient is normal and well developed.
VI Hers disease	Phosphorylase	Liver	Increased amount.	Like type I, but milder course.
VII	Phosphofructokinase	Muscle	Increased amount; normal structure.	Like type V.
VIII	Phosphorylase kinase	Liver	Increased amount; normal structure.	Mild liver enlargement. Mild hypoglycemia.

Note: Types I through VII are inherited as autosomal recessives. Type VIII is sex linked.

Glycogen degradation

Glycogen digestion in the gastrointestinal tract

- It is essentially the same as the digestion of amylopectin.
- Both saliva and pancreatic secretion contain ***α-amylase***, which catalyses **hydrolytic splitting of α-1,4-glucosidic bonds** at random, unless they are near chain ends or branch points.
- The products are then **maltose, maltotriose** and a mixture of small branched fragments (with 5 - 9 glucose residues) called **α-dextrins**.
- Those products are **hydrolysed** to **free glucose** by the action of both ***maltase*** and ***saccharase-isomaltase***, found in the plasma membrane of mucosal cells of the duodenum and jejunum.

Energetics:

One ATP is utilised for glycogenesis