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BIOCHEMISTRY

UNIT 2

TOPIC :

- **Carbohydrate metabolism**

  Glycolysis– Pathway, energetics and significance

  Citric acid cycle- Pathway, energetics and significance

  HMP shunt and its significance; Glucose-6-Phosphate dehydrogenase

  (G6PD) deficiency

  Glycogen metabolism Pathways and glycogen storage diseases (GSD)

  Gluconeogenesis- Pathway and its significance

  Hormonal regulation of blood glucose level and Diabetes mellitus

Metabolism of Carbohydrates

→ Biochemical processes involved in synthesis, breakdown, and inter-conversion of carbohydrates in living organisms, are collectively called as carbohydrate metabolism

→ Glucose (a monosaccharide metabolised by nearly all organisms) is the essential molecule of carbohydrate metabolism which participates in various metabolic pathways. Insulin is the primary metabolic hormone synthesised in pancreas and regulates glucose level in blood.

→ The metabolism of carbohydrate is simplest than other like protein , and fat , that is why it is used as immediate source of energy.

→ The unused glucose stored in the liver in the form of Glycogen.

Some Pathways of Metabolism of Carbohydrate

❖ Glycolysis : Break Down of glucose into ATP (energy) and Pyruvate and Lactate.

❖ Citric Acid Pathway or Cycle (Krebs Cycle , Tricarboxylic Acid Cycle (TCA)) : It is the common metabolic Pathway for Carbohydrates , Fats and protein Oxidation.

❖ Glycogenesis : In this pathway , The glycogen is synthesised from Glucose.

❖ Glycogenolysis : In this pathway glycogen is converted into Glucose.

❖ Gluconeogenesis : In this pathway glucose is Synthesised from a non-carbohydrate source , (fats and proteins)

Glycolysis

- Glycolysis is an important pathway of Carbohydrate metabolism and it occurs in the Cytoplasm of a living cell.
- Glycolysis is important to maintain ATP balance.
- The Enzymes involved in Glycolysis are present in Cytosol of cell.

Steps of Glycolysis Pathway

① Glucose is converted into Glucose-6-phosphate (G6P)

- Enzyme: Hexokinase
- ATP is broken into ADP + Pi (energy investment step)

② Glucose-6-phosphate is isomerized into Fructose-6-phosphate (F6P)

- Enzyme: Phosphoglucose isomerase

③ Fructose-6-phosphate is converted into Fructose-1,6-bisphosphate (F1,6BP)

- Enzyme: Phosphofructokinase-1 (PFK-1)
- Another ATP is used and converted into ADP

④ Fructose-1,6-bisphosphate is broken into two 3-carbon molecules

- Enzyme: Aldolase
- The products are:
  - Glyceraldehyde-3-phosphate (G3P)
  - Dihydroxyacetone phosphate (DHAP)

⑤ DHAP is isomerized into G3P

- Enzyme: Triose phosphate isomerase
- So now, 2 molecules of G3P are formed from one glucose

⑥ **Glyceraldehyde-3-phosphate (G3P) is converted into 1,3-Bisphosphoglycerate (1,3-BPG)**

- Enzyme: G3P dehydrogenase
- NAD^+ is reduced to NADH

⑦ **1,3-Bisphosphoglycerate is converted into 3-Phosphoglycerate (3PG)**

- Enzyme: Phosphoglycerate kinase
- ATP is generated (substrate-level phosphorylation)

⑧ **3-Phosphoglycerate is converted into 2-Phosphoglycerate (2PG)**

- Enzyme: Phosphoglycerate mutase

⑨ **2-Phosphoglycerate is converted into Phosphoenolpyruvate (PEP)**

- Enzyme: Enolase
- Water is removed

⑩ **Phosphoenolpyruvate (PEP) is converted into Pyruvate**

- Enzyme: Pyruvate kinase
- ATP is generated

⑪ **Under anaerobic conditions**, pyruvate is converted into **lactate**

- Enzyme: Lactate dehydrogenase
- NADH is used to regenerate NAD^+

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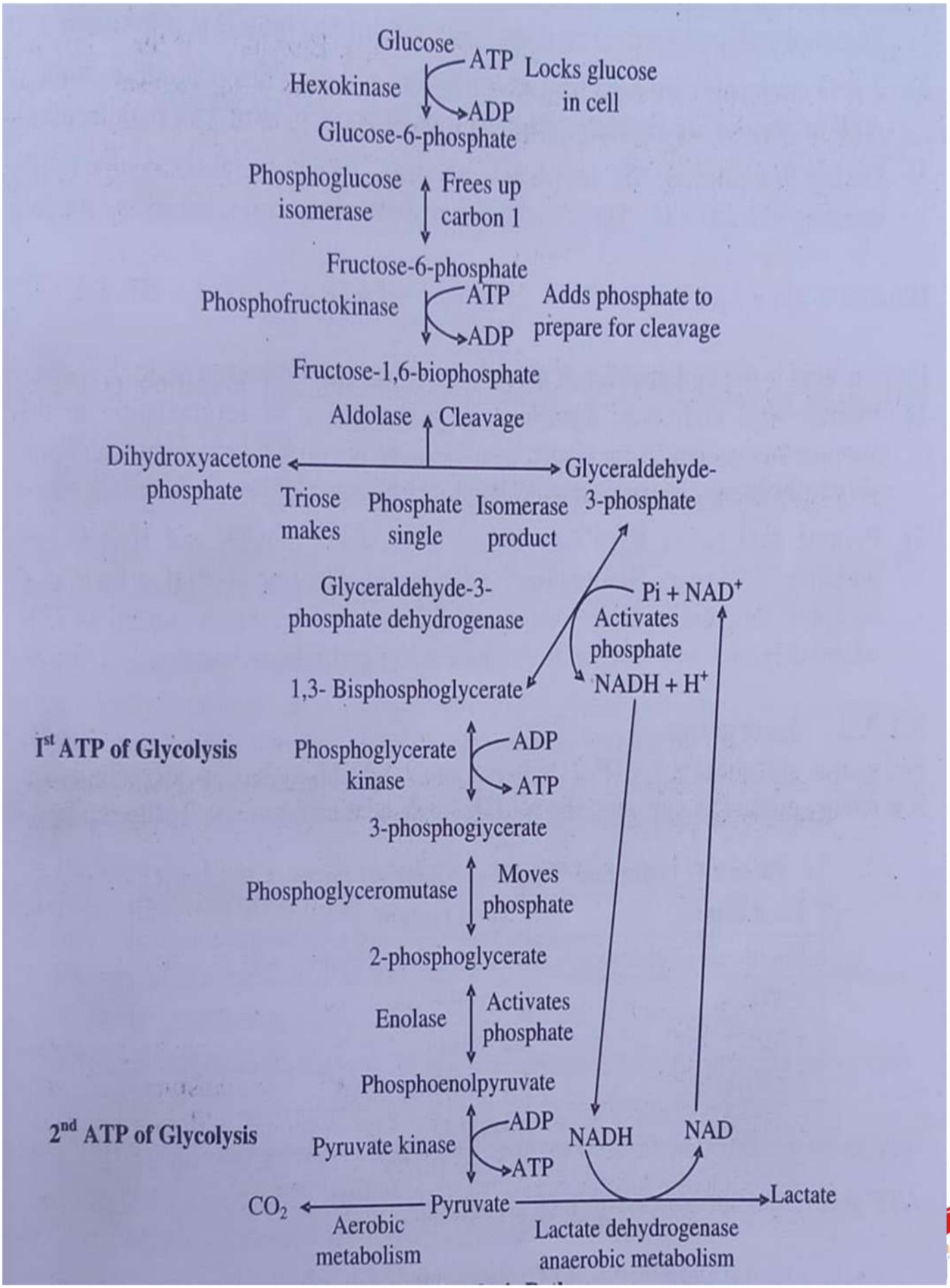

Glucose
ATP
Hexokinase
ADP
Locks glucose in cell
Glucose-6-phosphate
Phosphoglucose isomerase
Frees up carbon 1
Fructose-6-phosphate
Phosphofructokinase
ATP
ADP
Adds phosphate to prepare for cleavage
Fructose-1,6-biophosphate
Aldolase
Cleavage
Dihydroxyacetone phosphate
Triose makes
Phosphate single
Isomerase product
Glyceraldehyde-3-phosphate
Glyceraldehyde-3-phosphate dehydrogenase
Pi + NAD+
Activates phosphate
NADH + H+
1,3- Bisphosphoglycerate
I st ATP of Glycolysis
Phosphoglycerate kinase
ADP
ATP
3-phosphogiycerate
Phosphoglyceromutase
Moves phosphate
2-phosphoglycerate
Enolase
Activates phosphate
Phosphoenolpyruvate
2nd ATP of Glycolysis
Pyruvate kinase
ADP
ATP
NADH
NAD
CO2
Pyruvate
Lactate
Aerobic metabolism
Lactate dehydrogenase anaerobic metabolism

Significance

- ✓ It is the only pathway that occurs in all cells of the body, including those without mitochondria (e.g., RBCs).
- ✓ From glycolysis, energy is obtained in the form of ATP, which is used in various metabolic activities of the cell.
- ✓ Glycolysis is the only source of energy in red blood cells (RBCs), because RBCs lack mitochondria.
- ✓ During vigorous exercise, when oxygen supply is low in muscle tissue, anaerobic glycolysis occurs and becomes a major source of ATP for working muscles.
- ✓ Glycolysis provides intermediates that are used for the synthesis of non-essential amino acids.
- ✓ Glyceraldehyde-3-phosphate (G3P) produced in glycolysis is also used in the synthesis of triglycerides and phospholipids (important for fat metabolism and membrane formation).
- ✓ Glycolysis is the first step in the complete oxidation of glucose to carbon dioxide and water via the TCA cycle and electron transport chain (ETC).
- ✓ It helps in the regeneration of NAD^+ under anaerobic conditions, allowing glycolysis to continue in the absence of oxygen.

Energetics of Glycolysis Pathway

- Glycolysis is the process in which one molecule of glucose (6C) is broken down into two molecules of pyruvate (3C) in the cytoplasm. During this process, energy is both used and generated in the form of ATP and NADH.

ATP Used (Investment Phase)

Step	Reaction	ATP Used
1	Glucose → Glucose-6-phosphate (by Hexokinase)	**1 ATP**
2	Fructose-6-phosphate → Fructose-1,6-bisphosphate (by PFK-1)	**1 ATP**

ATP Produced (Payoff Phase)

→ Since 2 molecules of G3P are formed per glucose, the following steps happen twice:

Step	Reaction	ATP Produced
1	1,3-Bisphosphoglycerate → 3-Phosphoglycerate (by Phosphoglycerate kinase)	**2 ATP (1 per G3P × 2)**
2	Phosphoenolpyruvate → Pyruvate (by Pyruvate kinase)	**2 ATP (1 per G3P × 2)**

Total ATP generated = 4 ATP

Citric Acid Cycle (Krebs Cycle / TCA Cycle)

- ✓ The Citric Acid Cycle was discovered by Sir Hans Krebs in 1937, which is why it is also called the Krebs Cycle.
- ✓ Another name for this cycle is the TCA Cycle, which stands for Tricarboxylic Acid Cycle.
- ✓ The cycle takes place inside the mitochondria and is a major energy-producing pathway in the body.
- ✓ It is the next step after aerobic glycolysis. The end product of glycolysis, pyruvate, is converted into Acetyl-CoA, which enters the TCA cycle.
- ✓ The main function of the citric acid cycle is the oxidation of Acetyl-CoA into carbon dioxide (CO_2), while producing NADH, $FADH_2$, and GTP/ATP.
- ✓ These high-energy molecules (NADH & $FADH_2$) enter the Electron Transport Chain (ETC) to generate more ATP.
- ✓ About 65–70% of ATP needed by the body is produced through the citric acid cycle and the processes linked to it.
- ✓ The TCA cycle only occurs under aerobic conditions, because it depends on the regeneration of NAD^+ and FAD, which require oxygen indirectly.
- ✓ The Citric Acid Cycle is one of the most important metabolic pathways for energy production, and it also provides precursors for biosynthetic pathways (amino acids, heme, fatty acids).

Steps of the Citric Acid Cycle (Krebs Cycle)

Step I: Formation of Citrate

- Acetyl-CoA (2C) reacts with Oxaloacetate (4C) to form Citrate (6C).
- Enzyme: Citrate synthase

Step II: Isomerization of Citrate

- Citrate is isomerized into Isocitrate.
- Enzyme: Aconitase

Step III: Oxidation & Decarboxylation of Isocitrate

- Isocitrate is oxidized and loses 1 CO_2 to form α-Ketoglutarate (5C).
- NAD^+ is reduced to NADH.
- Enzyme: Isocitrate dehydrogenase

Step IV: Formation of Succinyl-CoA

- α-Ketoglutarate loses another CO_2 and is converted into Succinyl-CoA (4C).
- NAD^+ is reduced to NADH.
- Enzyme: α-Ketoglutarate dehydrogenase

Step V: Conversion to Succinate

- Succinyl-CoA is converted into Succinate.
- One molecule of GTP (or ATP) is formed by substrate-level phosphorylation.
- Enzyme: Succinyl-CoA synthetase

Step VI: Oxidation of Succinate

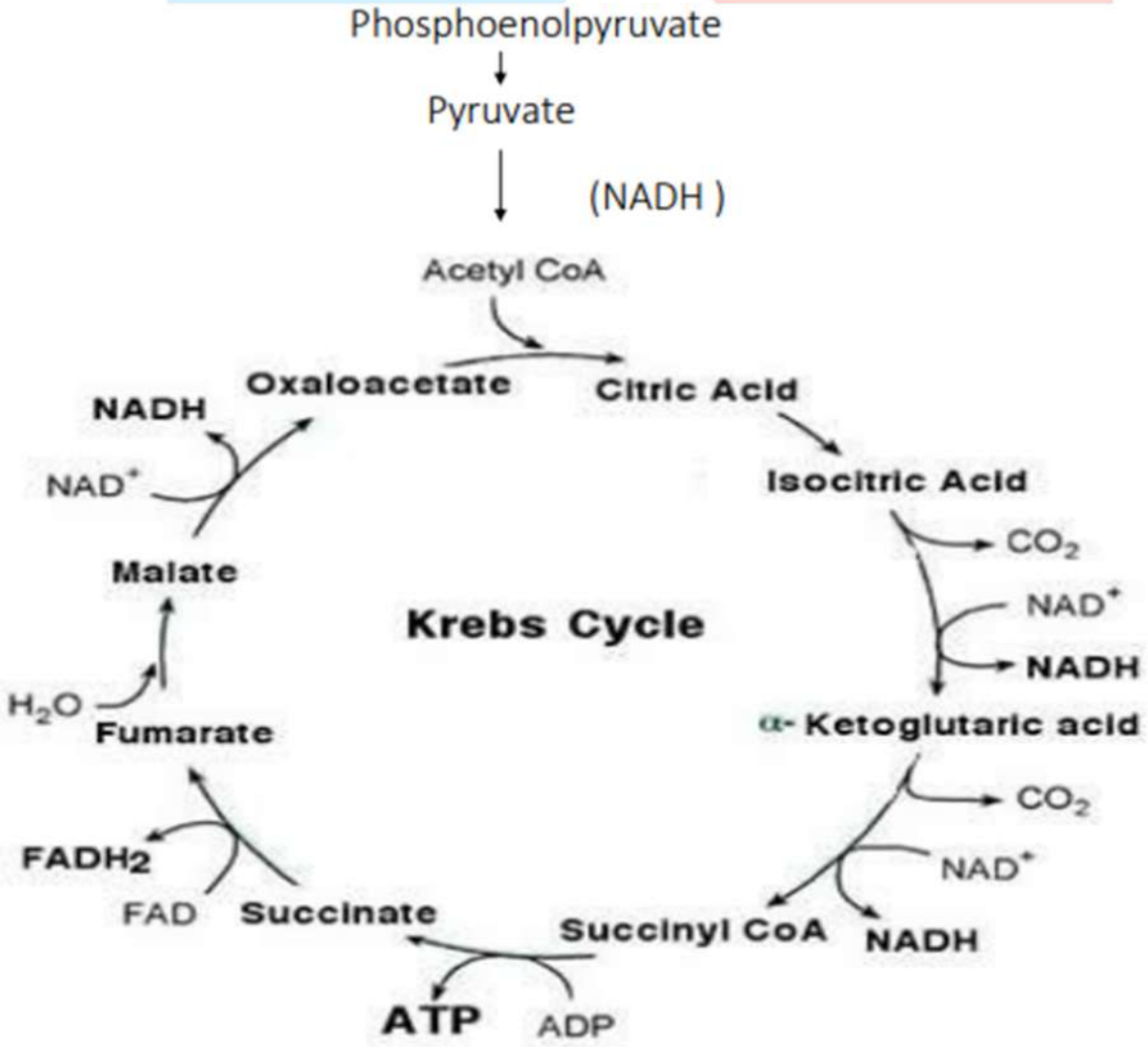
- Succinate is oxidized to Fumarate.
- FAD is reduced to $FADH_2$.
- Enzyme: Succinate dehydrogenase

Step VII: Hydration of Fumarate

- Fumarate is converted into Malate.
- Enzyme: Fumarase

Step VIII: Oxidation of Malate

- Malate is oxidized to regenerate Oxaloacetate, completing the cycle.
- NAD^+ is reduced to NADH.
- Enzyme: Malate dehydrogenase



Significance of the Citric Acid Cycle

- ✓ It is the major source of energy (ATP) for the body.
- ✓ It is the final common oxidative pathway for the metabolism of carbohydrates, fats, and proteins.
- ✓ During the TCA cycle, there is complete oxidation of Acetyl-CoA into carbon dioxide (CO_2) and water, releasing energy.
- ✓ Excess carbohydrates are converted into fat (lipogenesis) through intermediates like citrate.
- ✓ It provides intermediates for the synthesis of non-essential amino acids, such as α-ketoglutarate and oxaloacetate.
- ✓ A high amount of ATP is generated via NADH and $FADH_2$ through the Electron Transport Chain (ETC).
- ✓ The cycle is amphibolic in nature — meaning it functions in both catabolic (breakdown) and anabolic (biosynthetic) processes.

Energetics of the Citric Acid Cycle (Krebs Cycle)

→ Although the conversion of pyruvate to Acetyl-CoA is not directly part of the Krebs cycle, it is included in energy calculations.

→ ATP Yield from One Pyruvate Molecule:

Step	Reaction	Coenzyme Produced	ATP Equivalent
1	Pyruvate → Acetyl-CoA	1 NADH	**3 ATP**
2	Isocitrate → α-Ketoglutarate	1 NADH	**3 ATP**
3	α-Ketoglutarate → Succinyl-CoA	1 NADH	**3 ATP**
4	Succinyl-CoA → Succinate	1 GTP	**1 ATP**
5	Succinate → Fumarate	1 $FADH_2$	**2 ATP**
6	Malate → Oxaloacetate	1 NADH	**3 ATP**

Total ATP from 1 Pyruvate = 15 ATP

HMP Shunt (Hexose Monophosphate Shunt)

- The HMP Shunt is an alternative oxidative pathway of glucose metabolism that generates NADPH and pentose sugars (ribose-5-phosphate) without producing ATP.
- Other Names of HMP Shunt:
    1. Pentose Phosphate Pathway (PPP)
    2. Phosphogluconate Pathway
    3. Warburg–Dickens Pathway
- It is an alternative pathway to glycolysis and the TCA cycle for the oxidation of glucose.
- It occurs in the cytosol (cytoplasm) of cells, especially in liver, fat cells, adrenal glands, and RBCs.
- This pathway is more complex than glycolysis.
- The HMP shunt is anabolic in nature, as it produces compounds used in biosynthesis.
- It is mainly concerned with the synthesis of:
    - NADPH – used in fatty acid synthesis, cholesterol synthesis, and antioxidant defense.
    - Pentose sugars (like Ribose-5-phosphate) – used in the synthesis of nucleotides and nucleic acids (DNA & RNA).

Phases of the HMP Shunt:

① *Oxidative Phase* ***(Irreversible)***

- Glucose-6-phosphate is oxidized to Ribulose-5-phosphate
- NADPH is produced in this phase

② *Non-Oxidative Phase* ***(Reversible)***

- Ribulose-5-phosphate is converted into Ribose-5-phosphate (used in nucleotide synthesis)

- Also produces intermediates like Fructose-6-phosphate and Glyceraldehyde-3-phosphate (link to glycolysis)

Steps of HMP Shunt (Hexose Monophosphate Shunt)

The HMP Shunt has **two phases**:

- **Oxidative Phase** – Produces **NADPH** and **Ribulose-5-phosphate**
- **Non-Oxidative Phase** – Produces **Pentose sugars** and links back to glycolysis

Oxidative Phase (Irreversible):

1. **Glucose-6-phosphate** (from glycolysis) is converted into **6-phosphoglucono-δ-lactone**

   - Enzyme: Glucose-6-phosphate dehydrogenase
   - $NADP^+ \rightarrow NADPH$

2. **6-phosphoglucono-δ-lactone** is hydrolyzed to form **6-phosphogluconate**

   - Enzyme: Lactonase (also called Gluconolactonase or Gluconolactone hydrolase)

3. **6-phosphogluconate** is oxidatively decarboxylated to form **Ribulose-5-phosphate**

   - Enzyme: 6-Phosphogluconate dehydrogenase
   - CO_2 is released
   - $NADP^+ \rightarrow NADPH$

Non-Oxidative Phase (Reversible):

4. **Ribulose-5-phosphate** is converted into:

- Ribose-5-phosphate (by Phosphopentose isomerase)
- Xylulose-5-phosphate (by Phosphopentose epimerase)

5. **Transketolase Reaction**

- Ribose-5-phosphate + Xylulose-5-phosphate → Glyceraldehyde-3-phosphate (G3P) + Sedoheptulose-7-phosphate
- Enzyme: Transketolase
- Cofactor: Thiamine pyrophosphate (TPP)

6. **Transaldolase Reaction**

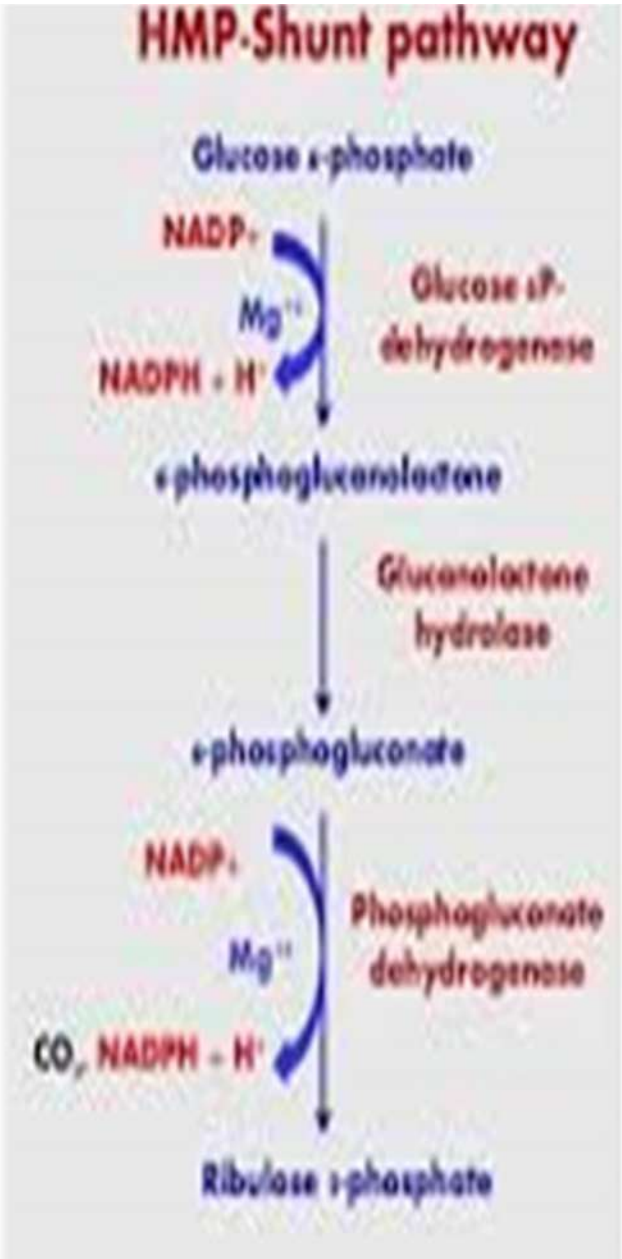
- Glyceraldehyde-3-phosphate + Sedoheptulose-7-phosphate → Fructose-6-phosphate + Erythrose-4-phosphate

7. **Another Transketolase Reaction**

- Erythrose-4-phosphate + Xylulose-5-phosphate → Fructose-6-phosphate + Glyceraldehyde-3-phosphate

Final Products:

- Fructose-6-phosphate and Glyceraldehyde-3-phosphate re-enter glycolysis
- NADPH is used in biosynthesis and antioxidant defense
- Ribose-5-phosphate is used for DNA/RNA synthesis


HMP-Shunt pathway
Glucose 6-phosphate
NADP+
Mg++
NADPH + H+
Glucose 6P-dehydrogenase
6-phosphoglucanolactone
Gluconolactone hydrolase
6-phosphogluconate
NADP+
Mg++
CO2 NADPH + H+
Phosphogluconate dehydrogenase
Ribulose 5-phosphate

Significance of HMP Shunt

1. **Production of NADPH**
   - Essential for:
     - **Fatty acid synthesis**
     - **Cholesterol synthesis**
     - **Detoxification reactions**
     - Maintaining **glutathione** in reduced form
2. **Ribose-5-phosphate Synthesis**
   - For synthesis of **nucleotides** and **nucleic acids** (DNA, RNA)
3. **Antioxidant Defense**
   - In **RBCs,** NADPH is used to regenerate **reduced glutathione (GSH)** which protects cells from **oxidative stress.**
4. **Non-ATP Pathway**
   - Allows cells to use glucose for biosynthesis, not just for energy.
5. **Clinical Marker**
   - **Transketolase** activity (dependent on vitamin B_1) is used to assess **thiamine deficiency.**

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Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency

G6PD

- **G6PD (Glucose-6-Phosphate Dehydrogenase)** is the **rate-limiting enzyme** of the **Hexose Monophosphate (HMP) Shunt**.
- It catalyzes the reaction:
- Glucose-6-phosphate + NADP+ → 6-phosphogluconolactone + NADPH
- **NADPH** is essential for:
    - Reductive biosynthesis (fatty acid and cholesterol synthesis)
    - Maintaining reduced glutathione (GSH) in cells
    - Protecting red blood cells (RBCs) against oxidative damage

G6PD Deficiency

- G6PD deficiency is a genetic enzymopathy where the body lacks or produces a defective form of G6PD.
- It leads to reduced production of NADPH, which compromises the cell's ability to combat oxidative stress.
- Primarily affects RBCs, which rely solely on the HMP shunt for NADPH.
- Result: Hemolysis (destruction of RBCs) when exposed to oxidative stress.

Symptoms of G6PD Deficiency

- May be **asymptomatic** until exposed to oxidative stress.
- During hemolytic episode:
    - Sudden fatigue, weakness
    - Dark-colored urine (hemoglobinuria)
    - Jaundice (yellowing of skin and eyes)

- Rapid heartbeat
- Back or abdominal pain

Prevention and Management

- **Avoid known triggers** (e.g., drugs, foods, chemicals)
- During a hemolytic episode:
  - **Supportive care** (hydration, oxygen)
  - **Blood transfusion** in severe cases
- **Genetic counseling** for affected families

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Glycogen Metabolism

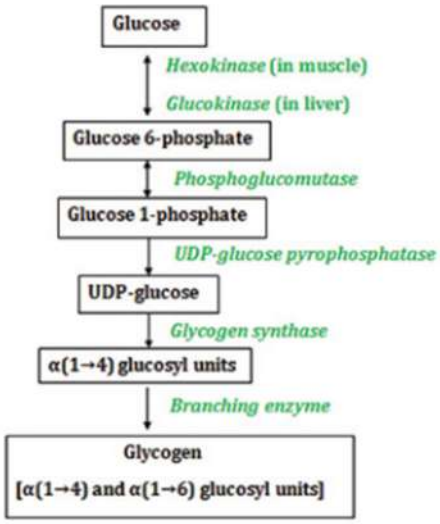
- Glycogen is a highly branched polysacharide (polymer of carbohydrates) , and 8-10 glucose units present at per branch.
- Glucose is stored in animal in the form of Glycogen.
- Glycogen is mainly stored in liver (6-8 %) and in muscles cells (1-25)
- According to NCBI about (500g) glycogen stored in muscles and (100g) in liver.
- Glycogen stored in the form of granules in cell cytosol , where most of the enzymes are found which required for glycogen synthesis and breakdown.
- First of all liver glycogens are consumed for energy.

Glycogen Metabolism is also in two types :

- Glycogenesis
- Glycogenolysis

Glycogenesis

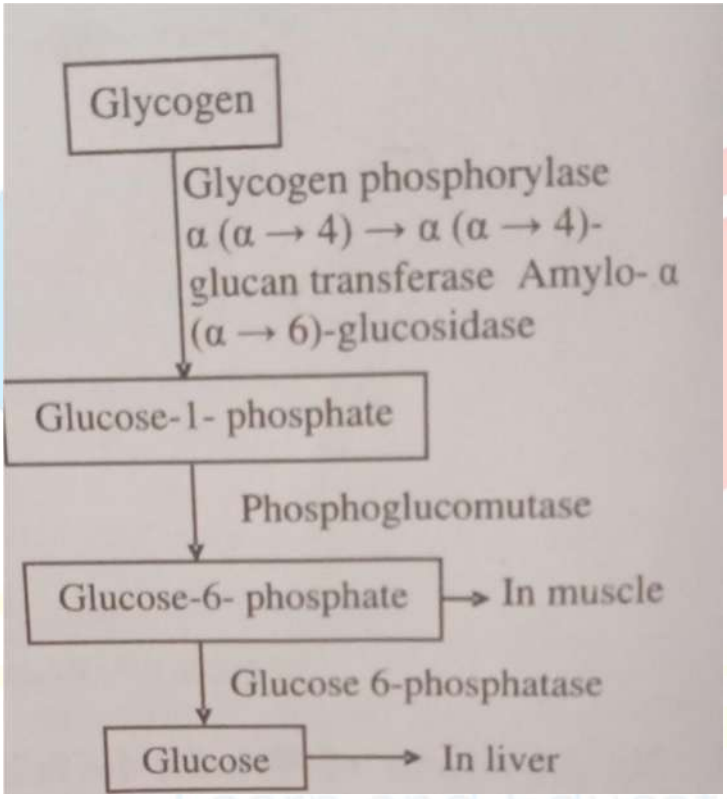
- The formation (synthesis) of glycogen from glucose is called Glycogenesis . Glycogen is a highly branched polysacharide (polymer of carbohydrates) , and 8-10 glucose units present at per branch .



Glycogenesis

Glycogenolysis

- The process of conversion of stored Glycogen into glucose is called glycogenolysis.



Significance of Glycogen Metabolism

- ❖ Maintains blood glucose levels, especially during fasting.
- ❖ Provides quick energy during exercise (especially in muscles).
- ❖ Prevents hyperglycemia and hypoglycemia.
- ❖ Liver glycogen is used for whole-body glucose supply; muscle glycogen is used locally in muscle cells.
- ❖ Regulated by hormones (insulin, glucagon, epinephrine) for metabolic balance.

Glycogen Storage Diseases (GSDs)

Glycogen Storage Diseases (GSDs) are a group of **inherited metabolic disorders** caused by **defects in enzymes** involved in **glycogen synthesis or breakdown**.

- Result in **abnormal quantity or structure of glycogen** in liver, muscles, kidneys, or other tissues.
- Lead to **energy production issues**, **hypoglycemia**, **muscle weakness**, or **organ enlargement** depending on the enzyme and tissue involved.

Classification of GSDs

GSDs are classified by **Roman numerals (I to IX)** based on the **specific enzyme deficiency**.

GSD Type	Name	Enzyme Deficiency	Affected Organ	Major Features
Type I	**Von Gierke's disease**	Glucose-6-phosphatase	Liver, kidney	Severe hypoglycemia, hepatomegaly, lactic acidosis
Type II	**Pompe's disease**	Lysosomal α-1,4-glucosidase	All tissues (esp. heart, liver, muscle)	Cardiomegaly, muscle weakness, fatal in infancy
Type III	**Cori's disease**	Debranching enzyme	Liver, muscle	Milder hypoglycemia, hepatomegaly, muscle weakness
Type IV	**Andersen's disease**	Branching enzyme	Liver, heart, muscle	Cirrhosis, liver failure, usually fatal in early childhood

Type V	**McArdle's disease**	Muscle glycogen phosphorylase	Skeletal muscle	Muscle cramps, exercise intolerance, myoglobinuria
Type VI	**Hers' disease**	Liver glycogen phosphorylase	Liver	Mild hypoglycemia, hepatomegaly
Type VII	**Tarui's disease**	Muscle phosphofructokinase	Muscle	Similar to McArdle's disease; hemolysis may occur
Type IX	—	Phosphorylase kinase	Liver, muscle	Hepatomegaly, growth delay, muscle weakness

Diagnosis

- Blood glucose levels
- Liver enzymes (ALT, AST)
- Muscle/liver biopsy
- Enzyme assay (specific to type)
- Genetic testing

Management

- Depends on the type of GSD
- Frequent feeding with cornstarch in hepatic GSDs
- Avoidance of strenuous exercise in muscle GSDs
- Gene therapy being investigated (especially for Type I and II)

Gluconeogenesis – Pathway and Significance

- Gluconeogenesis is the metabolic process by which glucose is synthesized from non-carbohydrate precursors.
- It occurs mainly in the liver and to a lesser extent in the renal cortex.
- It is an anabolic process and is essentially the reverse of glycolysis, but with key bypass reactions.

Location:

Organ	Cellular Site
Liver (primary), Kidney (during starvation)	**Cytosol and mitochondria**

Steps of Gluconeogenesis Pathway

→ Gluconeogenesis bypasses 3 irreversible steps of glycolysis using four key enzymes:

Bypass 1: Pyruvate → Phosphoenolpyruvate (PEP)

(Mitochondria → Cytosol)

1. **Pyruvate → Oxaloacetate**
   - **Enzyme**: Pyruvate carboxylase
   - **Cofactor**: Biotin
   - **Location**: Mitochondria
2. **Oxaloacetate → PEP**
   - **Enzyme**: PEP carboxykinase (PEPCK)
   - **Location**: Cytosol

Bypass 2: Fructose-1,6-bisphosphate → Fructose-6-phosphate

- **Enzyme**: Fructose-1,6-bisphosphatase
- **Location**: Cytosol
- Opposes PFK-1 in glycolysis

Bypass 3: Glucose-6-phosphate → Glucose

- **Enzyme**: Glucose-6-phosphatase
- **Location**: Endoplasmic reticulum (only in liver and kidney)
- Absent in **muscle**, hence muscle **cannot perform gluconeogenesis**.

Significance of Gluconeogenesis

✓ **Maintains Blood Glucose Levels**

- Vital during fasting, starvation, intense exercise, or low carbohydrate intake.
- Prevents hypoglycemia.

✓ **Supports Brain and RBCs**

- These tissues rely heavily on glucose as their primary energy source.

✓ **Liver's Role in Metabolic Homeostasis**

- Liver converts lactate (from muscle) and glycerol (from adipose) into glucose.

✓ **Clears Metabolic Byproducts**

- Lactate from anaerobic glycolysis (Cori cycle) is recycled.
- Alanine from muscles (Glucose-Alanine cycle) is converted to glucose.

✓ **Key During Starvation and Diabetes**

- In prolonged starvation or Type I diabetes, gluconeogenesis becomes the major source of glucose.

Hormonal Regulation of Blood Glucose Level

→ Regulation of blood glucose is essential for maintaining homeostasis.
→ Glucose is the primary energy source for tissues, especially the brain and red blood cells, which rely exclusively on glucose.
→ The normal fasting blood glucose level is approximately 70–110 mg/dL.

Abnormal Blood Glucose Levels

1. **Hyperglycemia**:
    - Blood glucose level **above normal**
    - Seen in **diabetes mellitus**
    - Symptoms: frequent urination, increased thirst, fatigue
2. **Hypoglycemia**:
    - Blood glucose level **below normal**
    - Can occur due to **excess insulin, starvation**, or **alcohol**
    - Symptoms: dizziness, confusion, sweating, unconsciousness

Hormonal Regulation

⇨ The blood glucose level is regulated by two hormones Insulin and Glucagon , both are secreted by Pancreas.

Insulin

- The ß cells of pancreas secret insulin hormone.
- The secretion of insulin increases when concentration of glucose increased in blood , and its secretion deceases when concentration of glucose decreased.
- Insulin helps the glucose for entering into cells , by this way increase the consumption of glucose.
- A fasting glucose level of 99 mg/dl or less is normal . but less than 70 mg/dl is not normal (may lead to hypoglycemia)

Glucagon

- The α cells of pancreas secrets glucagon.
- The secretion of glucagon increases when concentration of glucose decreases in blood , and its secretion decline when blood glucose level increased.
- The glucose stored in liver in the form of glycogen , released in blood under influence of glucagon.
- Glucagon also stimulates the liver and other cells to synthesis glucose from proteins and fats, when it required.

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Diabetes Mellitus

→ Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels (hyperglycemia) due to deficient insulin action (secretion or resistance).

Types of Diabetes

Type 1 Diabetes Mellitus (IDDM)

- **Cause**: Autoimmune destruction of **β-cells**
- **Insulin**: Absent
- **Onset**: Childhood or adolescence
- **Features**:
  - Polyuria, polydipsia, polyphagia
  - Weight loss, fatigue
  - Requires lifelong insulin therapy

Type 2 Diabetes Mellitus (NIDDM)

- **Cause: Insulin resistance** ± impaired insulin secretion
- **Onset:** Adult (usually >40 years)
- **Risk factors**: Obesity, sedentary lifestyle, genetics
- **Management**: Diet, exercise, oral antidiabetic drugs ± insulin

Gestational Diabetes

- Occurs during pregnancy
- Increased risk of developing Type 2 diabetes later

Symptoms of Diabetes Mellitus

- **Polyuria** (excess urination)
- **Polydipsia** (excess thirst)
- **Polyphagia** (excess hunger)
- **Unexplained weight loss**

- **Fatigue and blurred vision**

Management of Diabetes

1. **Lifestyle changes**
   - Balanced diet (low sugar, high fiber)
   - Regular exercise
   - Weight control
2. **Medications**
   - **Type 1**: Insulin only
   - **Type 2**: Oral hypoglycemics (e.g., metformin, sulfonylureas)
3. **Monitoring**
   - Regular blood glucose checks
   - Routine check-ups for complications

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