Hexose Monophosphate shunt [HMP shunt]
OR
Pentose Phosphate Pathway

→ It takes place in the cytosol of cell membrane

→ Tissues : adipose tissue, mammary gland, thyroid, erythrocytes (RBCs).

→ Activity of this pathway is very low in skeletal muscle.

→ very important pathway to generating NADPH

∵ NADH → Regenerating ATP from ADP.

∵ NADPH → used to synthesis of fatty acids, cholestrol, steroids.

→ converting hexoses into pentoses

- Pentoses imp. substrate for DNA & RNA

Nucleotides
↓
Nitrogenous Bases
+
Phosphate
+
5 C sugar.
(Ribose / Deoxyribose)

→ Pathway has 3 stages :

(i) oxidative reaction –

Glucose-6-Phosphate → Ribulose-5-Phosphate + 2 NADPH

Glucose-6-Phosphate

$\downarrow$ Glucose-6-Phosphate Dehydrogenase ($NADP^+ \rightarrow NADPH$)

6-phosphogluconolactone

$\downarrow$ lactonase ($H_2O \rightarrow H^+$)

6-phosphogluconate

$\downarrow$ 6-phosphogluconate dehydrogenase ($NADP^+ \rightarrow NADPH$, CO_2)

Ribulose 5-phosphate.

(ii) Isomerization of Ribulose-6-P to Ribose-5-P.

Ribulose-5-P $\xrightleftharpoons[\text{Phosphopentose isomerase}]{}$ Ribose-5-P.

(iii) linkage of PP pathway to Glycolysis

Ribulose 5-P $\underset{\text{phosphopentose isomerase}}{\rightleftharpoons}$ Xylulose 5-P.

=> Xylulose 5-P (C5) + Ribose 5-P (C5)

$\rightleftharpoons$ Transketolase

Glyceraldehyde 3-P [C3] + sedoheptulose 7-P [C7]

$\rightleftharpoons$ Transaldolase

Fructose 6-P [C6] + Erythrose 4-P [C4]

$\rightleftharpoons$ Transketolase

Glyceraldehyde 3-P [C3] + Fructose 6-P [C6]

Control of Pathway

Note: If cell need Ribose 6-P then they take Glyceraldehyde 3-P & Fructose 6-P then do ~~bac~~ reversible to form Ribose 6-P.

If cell need NADPH then after form Glyceraldehyde 3-P & Fructose 6-P cycle enters in glycolysis.

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Glucose 6-phosphate dehydrogenase deficiency

[G6PD Deficiency]

=> Inherited disease (generation by generation)

=> Deficiency occurs in all cell but more severe in RBC. so, that means NADPH doesn't synthesize.

HMP shunt $\xrightarrow{\text{doesn't provide}}$ NADPH → cause G6PD deficiency

↓

Accumulation of methemoglobin in RBCs

Hemolysis [Breakdown of RBCs] ←

=> Those patient who suffer from G6PD deficiency

⇓

some drugs [oxidant nature] like => Primaquine (antimalarial)

Sulphamethoxazole (Antibacterial)

Acetanilid (Antipyretic)

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II Glycogen Metabolic Pathways

- Glycogen is a polymer of glucose residues linked by alpha-(1,4)-& alpha-(1,6) - glycosidic bond.

- Glycogen is the storage form of glucose in liver and muscle.

Glycogen metabolic Pathway

↓ Glycogenesis [Synthesis of glycogen from glucose]

↓ Glycogenolysis [Breakdown of glycogen into glucose]

* Glycogenesis:

Glucose $\xrightarrow[\text{ATP} \to \text{ADP}]{\text{Hexokinase}}$ Glucose 6-P $\xrightarrow{\text{Phosphogluco Mutase}}$ Glucose 1-P

Glucose 1-P $\xrightarrow{\text{UDPG phosphorylase}}$ Urine Diphosphate glucose

Urine Diphosphate glucose $\xrightarrow[\text{UDP}]{\text{Glycogen synthase}}$ Glycogen primer $\xrightarrow{\text{Branching Enzymes}}$ $\boxed{\text{Glycogen}}$

→ Glycogenolysis:

Glycogen $\xrightarrow{\text{phosphorylase}}$ Glucose 1-P $\xrightarrow{\text{phosphogluco mutase}}$ Glucose 6-P $\xrightarrow{\text{Hexokinase}}$ Glucose

Glycogen storage disease: (GSD)

- Those problems occurs during glycogenesis (during synthesis) & during glycogenolysis (during breakdown) collectively refer to as glycogen storage disease.
- It is characterised by deposition of normal or abnormal type of glycogen in one or more tissue.

[I] Type 1 ⇒ (Von Gierke disease)

i) Fasting Hypoglycemia : Defect in glucose 6-phosphat

ii) lactic acidemia : Glucose is not synthesized from lactate produced in muscle (Accumulation of lactate in muscle).

iii) Hyperlipidemia :

- ↑ (inc.) plasma, free fatty acids & ketone bodies.

iv) Hyperuricemia :

- Accumulation of Glucose 6 - phosphate

↓

HMP shunt

↓

↑ phosphoribosyl pyrophosphate activity

↓

↑ metabolism of purine nucleotide to uric acid

↓

↑ uric acid.

[II] Type 2 (Pompe's disease)

- Accumulation of glycogen in lysosomes due to deficiency of lysosomal (1,4 or 1,6 glycosidase enzymes are not available to breakdown).

↓

- Heart enlargement
- Muscle weakness

Gluconeogenesis

- Synthesis of glucose from non-carbohydrate compounds.
- Non-carbohydrate compounds → Pyruvate, Amino acids, Proteins, Fatty acids, Lactate

→ location → Cytosol, Mitochondria, liver, kidney matrix.

→ Significance :

- Brain, Erythrocytes, kidney medulla, testes
  ⇓
  need glucose for energy
- Glucose is the only source that supplies energy to the skeletal muscle (Anaerobic condition).
- In fasting condition → gluconeogenesis is a process to form glucose which fulfil the basic requirements of body.
- Tissue accumulate : lactate, Glycerol
  ↓
  clear from blood by Gluconeogenesis.

$$\text{Lactate} \underset{NAD^+ \;\to\; NADH + H^+}{\overset{\text{Lactate Dehydrogenase}}{\rightleftharpoons}} \text{Pyruvate} \xrightarrow{CO_2,\ ATP \to ADP} \text{Oxaloacetate}$$

Oxaloacetate

$\downarrow$ PEP Carboxykinase ($GTP \to GDP$, CO_2)

Phosphoenol pyruvate [PEP].

$\uparrow\downarrow$ Enolase

2-phosphoglycerate

$\uparrow\downarrow$ Phosphoglycerate Mutase

3-phosphoglycerate

$\uparrow\downarrow$ Phosphoglycerate kinase (ADP, ATP)

1,3-bisphosphoglycerate

$\uparrow\downarrow$ Gly-3-P dehydrogenase ($NADH + H^+$, NAD^+, P_i)

Dihydroxy Acetone phosphate $\rightleftharpoons$ Glyceraldehyde 3-phosphate (phosphotriose isomerase)

$\uparrow\downarrow$ Aldolase

Fructose 1,6-bisphosphate.

$\uparrow\downarrow$ Fructose 1,6-bisphosphatase (H_2O, Pi)

Fructose-6-Phosphate.

$\uparrow\downarrow$ Phosphohexose isomerase

Glucose 6-phosphate.

$\uparrow\downarrow$ Glucose 6-phosphatase (H_2O, P_i)

Glucose.

✓

E.T.C ⇒ metabolic pathway at chain.
e^- transport one compound to another compound
& release of energy ATP form & the O_2 is convert into H_2O

Hormonal Regulation of blood glucose level

1) Insulin :- ↑ Glucose transport in cell from blood by inc. permeability of cell.

- inc. glycogen formⁿ in liver & muscles
- conversion of glucose into fat
- stimulate protein synthesis.
- Inhibit ketoneogenesis.
- ↓ gluconeogenesis & ↑ glycolysis

2) Anterior Pituitary Hormones (GH) :-
- Hyperglycemia
- Inhibition of insulin.
- breakdown of muscle protein.
- ↑ mobilizatⁿ of fat in form of free fatty acid from adipose tissue.

3) Epinephrine :-
- ↑ blood sugar & lactate
- Diminishe the uptake of glucose by cell.
- diminution in amount of Insulin

4) Glucagon :-
- Promotes glycogenolysis in liver
- ↑ gluconeogenesis
- breakdown of glycogen to lactic acid in muscle.