جامعة الملك سعود
King Saud University

MED437
KING SAUD UNIVERSITY

BIO TEAM

Major Metabolic Pathways of Glucose and Glucose Transport

437 Biochemistry Team

Color index:
Doctors slides
Notes and explanations
Extra information
Highlights

Objectives:

- **Define a metabolic pathway.**
- **Describe the general metabolic pathways for glucose (production and utilization)**
- **Briefly describe the HMP**
- **Recognize the mechanisms of glucose transport**

Metabolic pathways

Pathway: Series of chemical reactions that have one goal.
Reaction: Substrate+Substrate = Product.

Definition

Pathway for glucose happens in almost every cell, starting by oxidation of glucose and ending with pyruvate (or lactate).

Regulatory mechanism(s)

1- Rapid short-term
-Covalent modification
-Allosteric
2- Slow long-term (hormone)
-Induction\repression

Reaction

Few are rate-limiting enzymes (They are found only in irreversible pathways).

Site

- Cellular tissue
- Subcellular
Inside the cell (Mitochondrial)

Metabolic pathways of glucose

Production

Glycogeno**lysis**
Catabolic

Gluco-**neo**-**genesis**
Anabolic

Hexose interconversion

Catabolic Cycles	Anabolic Cycles
• Glycolysis & Kreb (mainly) • Glycogenolysis • HMP	Gluconeogenesis Glycogenesis

To understand ☺
You DON'T have to know this

Prefix:
Glyco-: glucose
Glycogeno-: glycogen
*except in synthesis of glycogen: we say **glycogensis** instead of saying glycogeno-genesis.

To differentiate: the synthesis of glucose is **glucoNEOgenesis***

Utilization

HMP / PPP
Catabolic

Glyco-**lysis**
Catabolic

Krebs cycle
Catabolic

Hexose interconversion

Glyco**genesis**
Anabolic

Suffix:
-genesis: process of producing
-lysis: breaking down.

Glycolysis

*Aerobic: with oxygen
*Anaerobic: without oxygen

- Oxidation (breaking down) of glucose to provide energy.

The kind of glycolysis	Aerobic glycolysis	Anaerobic glycolysis
When	If there is enough(adequate supply) oxygen, Cells that has mitochondria	In absence of oxygen , cells that lack mitochondria
The end product	**Pyruvate(s)** + 8ATP	**Lactate** + 2 ATP

Glycogenesis and Glycogenolysis

Glycogenesis

- Synthesis of glycogen from glucose .
- Occurs when glucose and ATP are present in relatively high amounts (This process is: storage)

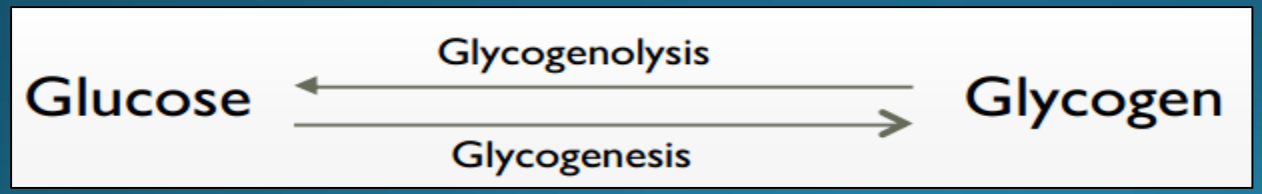
(اذا زاد الجلوكوز في الجسم و كانت الطاقة موجودة يتم تخزين الجلوكوز على شكل جلايكوجين عشان يحرقه و يستخدمه بعدين)

Glycogenolysis

- Degradation (تكسير) of glycogen into glucose
- Occurs in response to hormonal and neural signals

هرمونات او إشارات كهربائية (اذا احتاج الجسم جلوكوز يرسل إشارات للجلايكوجين لكي يتحول)

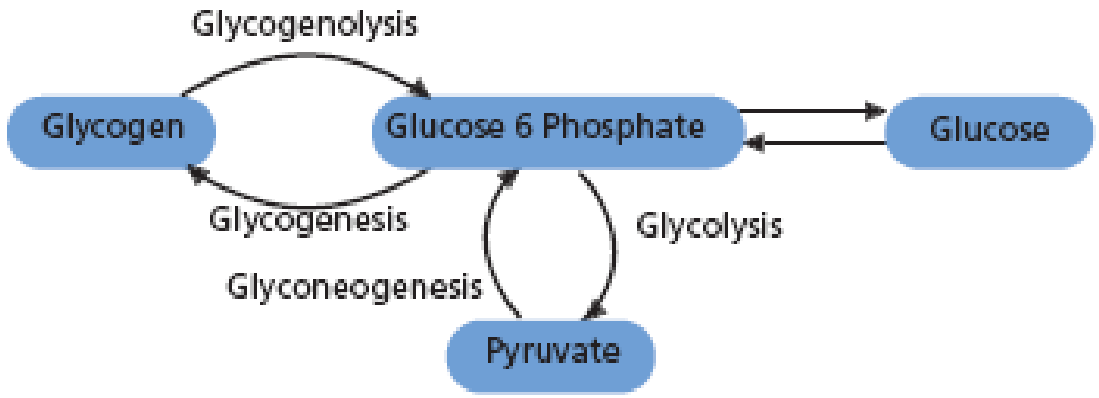
Both the same location: Mainly in **liver** and **muscle** → Cytosol



Gluconeogenesis

- Synthesis of glucose from non-carbohydrate precursors.
- The precursors could be **lactate**(Anaerobic), **pyruvate**(Aerobic), **glycerol** and **alpha-keto acids**.
- It requires both **mitochondria** and **cytosolic enzymes**.
- It occurs in **Liver** and **kidney.**

Figure 1. Glycogen and glucose homoeostasis



Glycerol: is a part of the triacylglycerol molecule which is the main constituent of body fat.

Keto acids: are organic compounds that contain a carboxylic acid group and a ketone group. The alpha-keto acids are especially important in biology as they are involved in the Krebs citric acid cycle and in glycolysis.

cytosolic enzymes: present in cytosol

Hexose Monophosphate shunt (**HMP**) or Pentose Phosphate Pathway (**PPP**)

- HMP shunt is an alternative pathway of glucose oxidation.
- It is **not** involved in the generation of energy.
- Around **10%** of glucose is entered in this pathway.
- In liver and kidney, this percentage is up to **30%**.

PPP is a metabolic pathway parallel to glycolysis.

Biomedical Importance of HMP

- It has two main functions:

1. Provides **NADPH** which is required for:
   - synthesis of fatty acids, steroids and some amino acids
   - Detoxification of drugs by Cytochrome P450.
   - In scavenging the free radicals.

2. Provides Pentoses, e.g. **ribose**
   - This pentose and its derivatives are useful in the synthesis of:
     - Nucleic acids (DNA and RNA)
     - Nucleotides (ATP, NAD, FAD and CoA)

Note: Cytochrome P450: enzymes also function to metabolize potentially toxic compounds, including drugs and products of endogenous metabolism such as bilirubin

Tissue Distribution of HMP

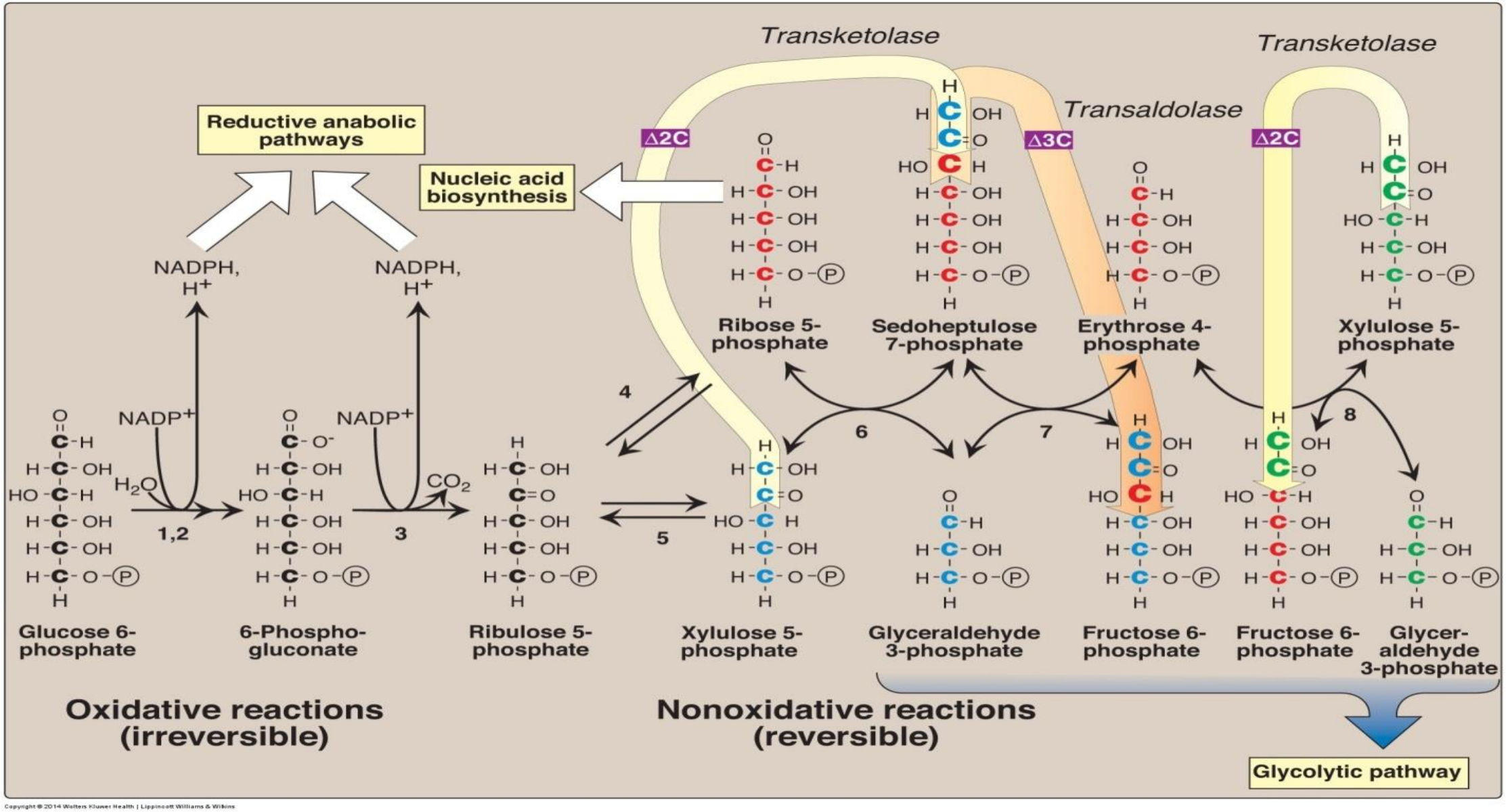
➢ **in the Cytosol of the following locations:**

- Liver
- Lactating mammary gland
- Adrenal cortex
- Gonads
- Adipose tissue
- Erythrocytes (RBC) *to reduce glutathione*
- Lens and cornea

Phases of HMP Shunt

- It has two phases:
  1. Oxidative phase (**irreversible**)
  2. Non-oxidative phase (**reversible**)

There are two distinct phases in the pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5-carbon sugars.



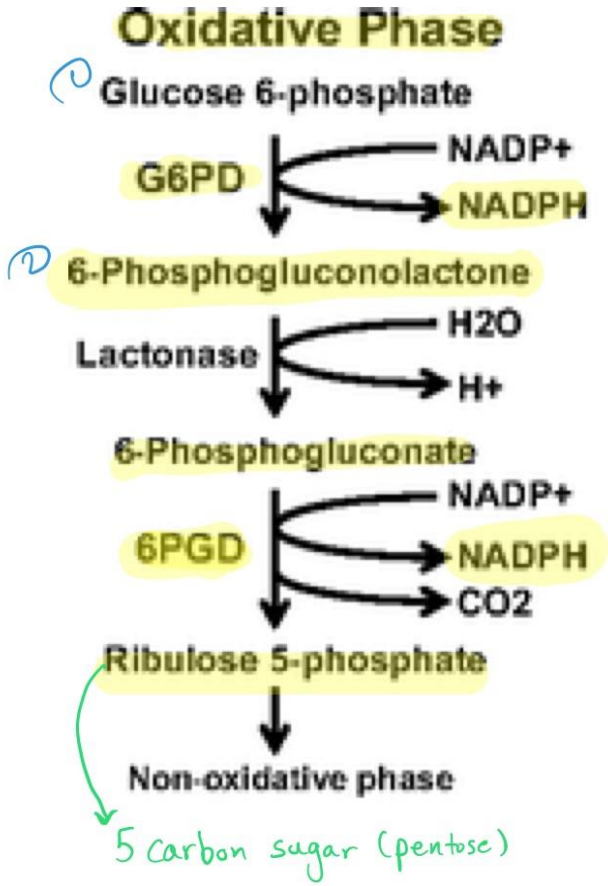
important : Enzymes numbered above are: 1, 2) *glucose 6-phosphate dehydrogenase* and 6-*phosphogluconolactone hydrolase*, 3) *6-phosphogluconate dehydrogenase*, 4) *ribose 5-phosphate isomerase*, 5) *phosphopentose epimerase*, 6 and 8) *transketolase* (coenzyme: thiamine pyrophosphate), and 7) *transaldolase*.

PHASE 1- OXIDATIVE PATHWAY

Phase 1- Oxidative pathway

* you have to know the enzymes

• enzyme



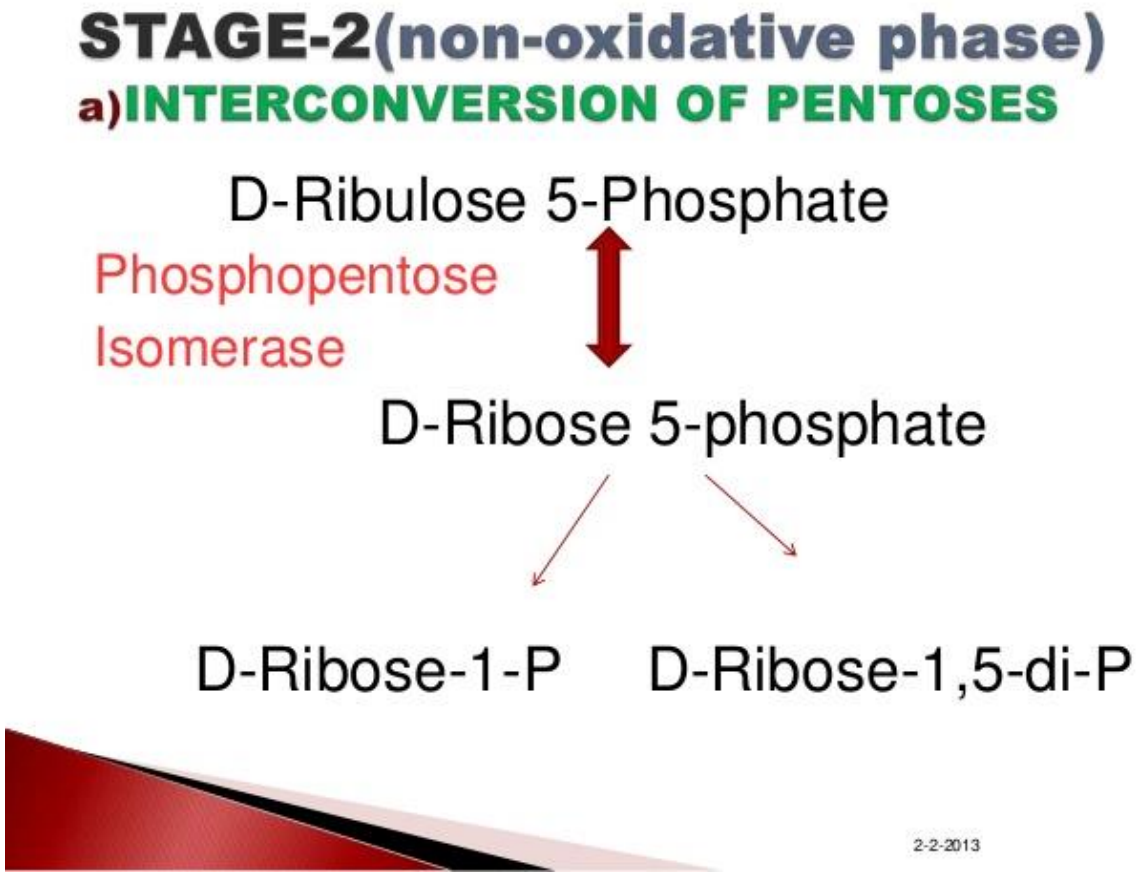
G6PD- Glucose 6-Phosphate Dehydrogenase

Lactonase- 6 phosphogluconolactone hydrolase

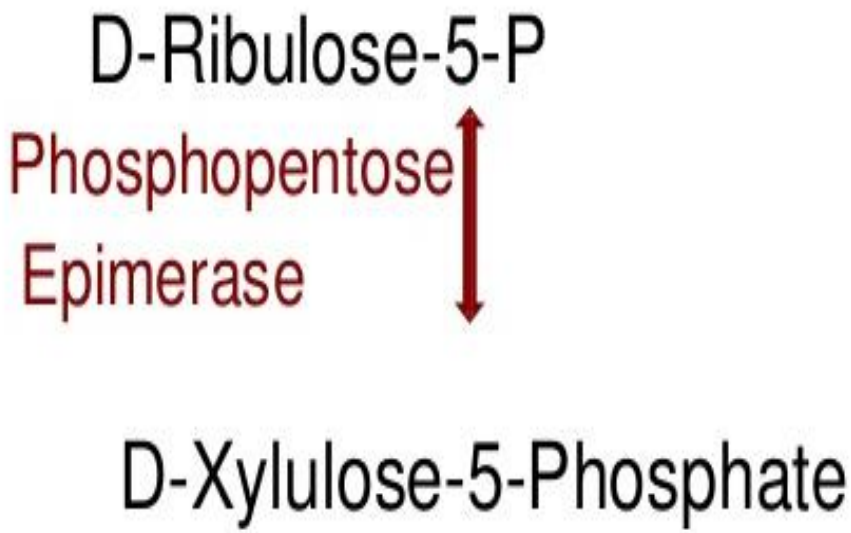
6PGD- 6 phosphogluconate dehydrogenase

results ⟹
- 2 NadPH
- 1 molecule of Ribulose 5-phosphate "pentose sugar"

Phase 2- Non-oxidative
a) Interconversion of pentoses



Phase 2- Non-oxidative



Phase 2- Non-oxidative

a) Conversion of pentose phosphate to hexose phosphates

2 Particular Enzymes are required:

1)TRANSKETOLASE

2)TRANSALDOLASE

Transketolation

1) Xylulose-5-P+Ribose-5-P

Transketolase ↕ TPP

Sedoheptolose 7-Phosphate +

Glyceraldehyde-3-Phosphate

Transaldolation

هي عملية reversible أي ذو اتجاهين يقوم بها انزيم transaldolase لتعطي التالي :

fructose 6-phosphate + erythrose 4-phosphate → (add 3 carbon to sedoheptulose)

7th Reaction

Sedoheptolose 7-P+G3P

Transaldolase

Fructose 6-Phosphate

+

Erythrose 4-Phosphate

Transketolation

- انزيم Transketolase يلعب دور مهم في التفاعلين السادس والثامن .

- يضيف كاربونين ، عكس transaldolase الذي يعطي ٣ كربونات .

-لا بد من وجود العامل المحفز coenzyme: thiamine pyrophosphate .

2)Xylulose 5-P+Erythrose 4-P

Transketolase TPP

Fructose 6-Phosphate +G3P

Dihydroxy-acetone-P+G3P

Recycles the Pathway

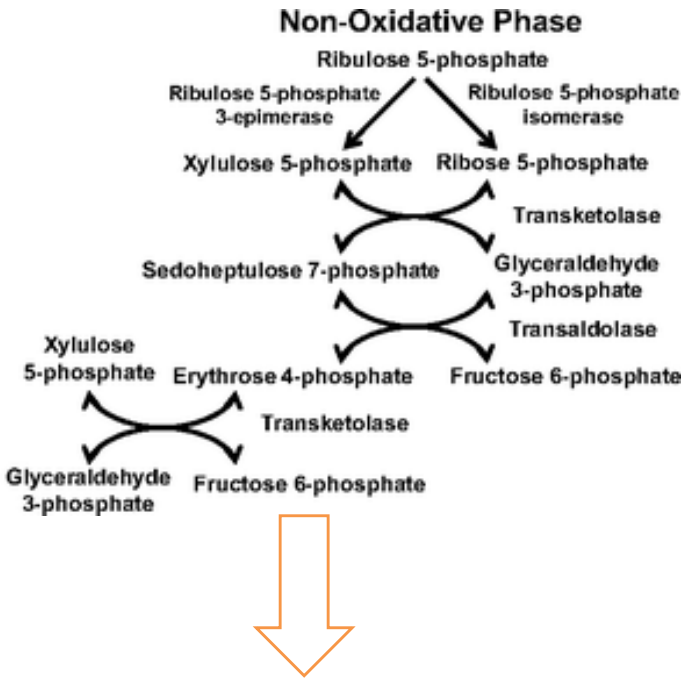
Fructose-1,6-bi-P

Glucose-6-P ⬅ Fructose-6-P

6- Ribose + xylulose (this reaction is catalyzed by Transketolase with TPP). And will give us 2 new sugar molecules :
Sedoheptolose (7C) AND glyceraldehyde (3C)

التفاعل الأخير

8- Xylulose5-P+Erythrose4-P (this reaction is catalyzed by Transketolase with TPP. And will give us 2 sugar molecules :
Fructose 6-P AND
Glyceraldehyde 3-P .



4) ***ribose 5-phosphate isomerase,***
5) ***phosphopentose epimerase,***
6 and 8) ***transketolase*** (coenzyme: thiamine pyrophosphate),
7) ***transaldolase***.
يفضل فهمها من خريطة Glycolysis

Clinical Correlations

G-6-PD deficiency results in:

- Heamolytic Aneamia
- Neonatal Jaundice
- Kidney failure

Med4 36

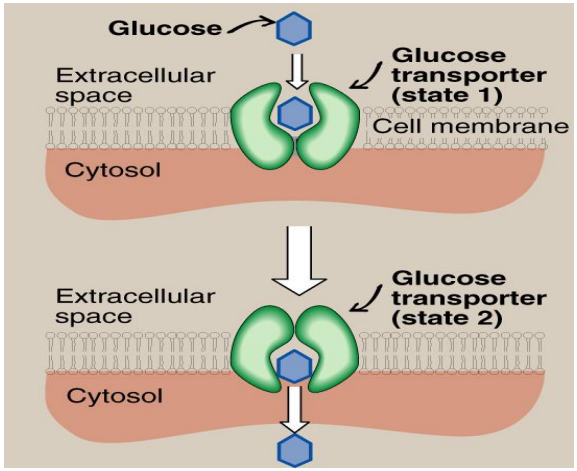
Glucose-6-phosphate dehydrogenase deficiency The condition is characterized by abnormally low levels of glucose-6-phosphate dehydrogenase, an enzyme involved in the pentose phosphate pathway that is especially important in the red blood cell. G6PD deficiency is the most common human enzyme defect
Hemolytic anemia: relating to or involving the rupture or destruction of red blood cells.
Neonata: relating to newborn children

Source – wordpress.com

Glucose Transport

Na+-Monosaccharide Cotransporter: active transport	Na+-Independent Facilitated Diffusion:
➢ Against concentration gradient (SGLT-1.2) ➢ Energy dependent ➢ Carrier-mediated ➢ Coupled to Na+ transport ➢ Small intestine, renal tubules & choroid plexus(blood brain barrir).	➢ Down the concentration gradient ➢ Energy Independent ➢ Glucose Transporters (GLUT 1-14)

Glucose Transport: Facilitated Diffusion



Glucose Transporters

- Tissue-specific expression pattern

GLUT-1	RBCs and brain
GLUT-2	Liver, kidney & pancreas
GLUT-3	Neurons
GLUT-4	Adipose tissue & skeletal muscle
GLUT-5	Small intestine & testes
GLUT-7	Liver (ER-membrane)

- Functions:

GLUT-1, 3 & 4	Glucose uptake from blood
GLUT-2	Blood & cells (either direction)
GLUT-5	Fructose transport

Take home messages

- There are multiple pathways for glucose that can be grouped in to catabolic (utilizing glucose) or anabolic (producing glucose)
- Glycolysis is the major metabolic pathway of glucose breakdown to provide energy
- Alternative pathway for glucose oxidation but not meant for producing energy
- Has two phases- oxidative and non-oxidative
- During oxidative phase, glucose-6-P is oxidized with generation of 2 moles of NADPH, and one mole of pentose phosphate, with liberation of CO2
- During non-oxidative phase, pentose phosphate is converted to intermediates of glycolysis

1- Phases of HMP Shunt

A-Oxidative phase and substrate-Level

B-Non-Oxidative phase and substrate-Level

C-Oxidative phase and Non-Oxidative

D-None

2- What is the main function of HMP ?

A- produce energy

B- Provides NADPH

C- Provides Pentoses

D- B & C

3- NADPH is required synthesis of

A- synthesis of fattyacids, steroid and some amino acids

B- In scavenging the free radicals

C- synthesis of Nucleic acids

D- A & B

4- what is the function of GLUT-5

A- Fructose transport

B- Uptake of glucose from the blood

C- Allowing glucose to flow in 2 directions

D- All of above

GIRLS TEAM:

- الهنوف الجلعود
- رهف الشنيبر
- شهد الجبرين
- لينا الرحمة
- منيرة المسعد
- ليلى الصّباغ
- العنود المنصور
- أرجوانة العقيل
- ريناد الغريبي
- مجد البراك
- روان مشعل

BOYS TEAM:

١- محمد صالح القسومي
٢ -نواف عبدالعزيز
٣ -عبدالملك الشرهان
٤ -صالح المعيقل

Team leaders:

١-محمد حسن حكيم
٢- رهام الحلبي

Contact us:
teambiochem437@gmail.com

For editing file:

https://docs.google.com/presentation/d/16yNcm2Y08Cr0Am83lDRfH5NB4F1ng3tdHiB3O1AqMc8