

# Major metabolic pathway of glucose

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*Color index :*





*Main text*

**IMPORTANT**

*Extra Info*

*Drs Notes*

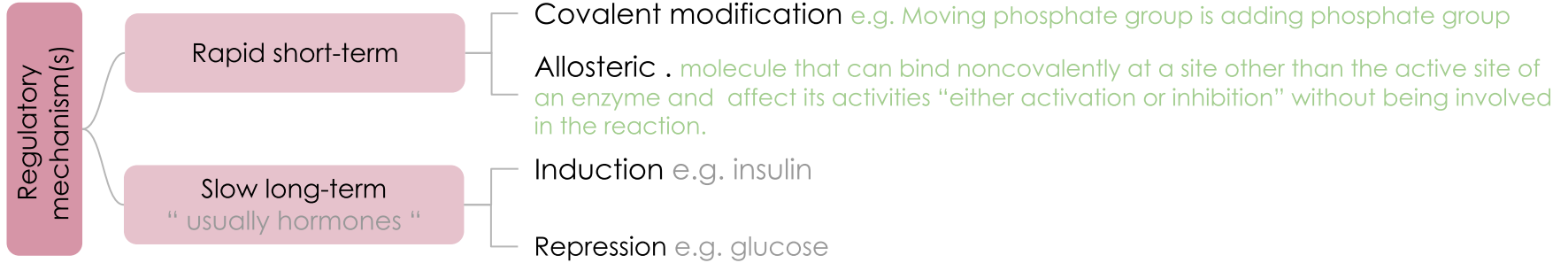
## Objectives:

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

★ This slide is not that important

# Metabolic pathway

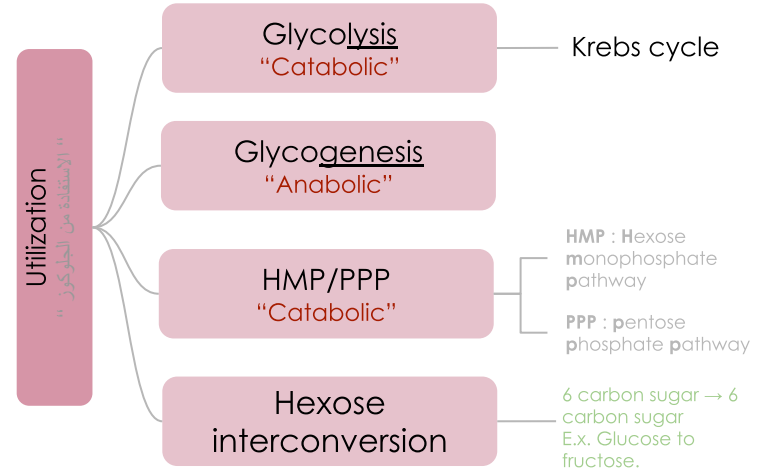
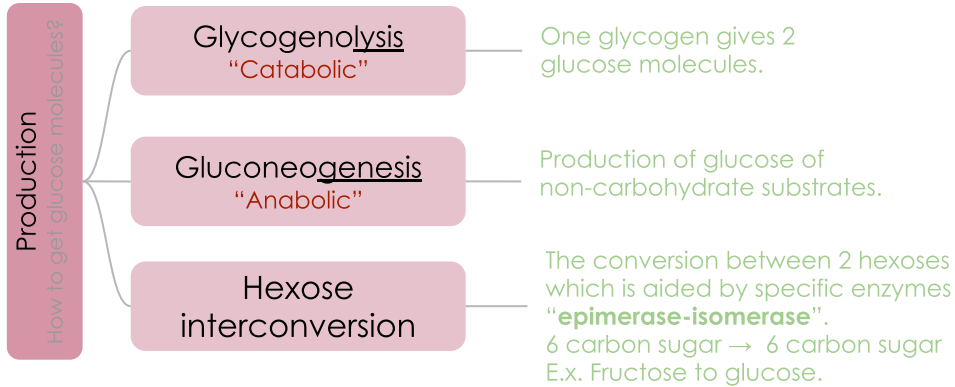
- **Definition :** a sequence or a cascade of chemical reactions which results in a product that will be a substrate for other reaction. “ Usually 1 to 2 pathways “ .
  - Pathway : Series of chemical reactions that have one goal.



- **Site :**
  1. Cellular (Tissue): signaling between cells .
  2. Subcellular : reactions inside the cell .
- **Reactions :** Substrate+Substrate = Product.
  - Rate-limiting enzymes “ Enzymes can slow down the reaction and They are found only in irreversible pathways “

# Metabolic pathway of glucose “ Production and utilization “

- For a better understanding :
  - Prefix :
    1. Glyco = glucose .
    2. Glycogeno = Glycogen “ except in synthesis of glycogen we say Glycogenesis instead of saying glycogeno-genesis  
“ To differentiate : the synthesis of glucose is gluconeogenesis .
  - Suffix :
    1. Genesis = process of producing “ synthesis “ .
    2. Lysis = breaking down .



# Metabolic pathway of glucose “ Catabolic and anabolic “

Catabolic cycles	Anabolic cycles
<ul style="list-style-type: none"><li>• Glycolysis. (Mainly)</li><li>• Krebs cycle. (Mainly)</li><li>• Glycogenolysis.</li><li>• HMP.</li></ul>	<ul style="list-style-type: none"><li>• Gluconeogenesis.</li><li>• Glycogenesis.</li></ul>

## Glycolysis

- Oxidation (breakdown) of glucose to provide energy.

	Anaerobic glycolysis “ Aerobic = with oxygen “	Aerobic glycolysis “ Anaerobic = without oxygen “
Occurs when ?	In absence of oxygen and in cells that lack mitochondria	In adequate supply of oxygen and in cells with mitochondria
End product	the end product is lactate	the end product is Pyruvate

# Glycogenesis and Glycogenolysis

	Glycogenesis	Glycogenolysis
Definition :	Synthesis of <b>glycogen from glucose</b> .	Degradation (breakdown) of <b>glycogen into glucose</b> .
Occurs when ?	Occurs when glucose and ATP are present in relatively high amounts . (This process is: storage). يعني اذا زاد الـ glucose في الجسم وكانت الطاقة موجودة " ATP " يتم تخزين الـ glucose على شكل glycogen عشان يحرقه ويستخدمه بعدين . "More details in MSK block"	Occurs in response to hormonal and neural signals. اذا احتاج الجسم راح يرسل اشارات " هرمونات " لتكسير الـ glycogen وتحويله لـ glucose .
Location	Mainly <b>liver, muscles, and cytosol</b>	

## Gluconeogenesis

- Synthesis of **glucose from non-carbohydrate precursors** .
- precursor : is a chemical that is transformed into another compound.
- The precursors could be lactate (anaerobic), pyruvate (aerobic), glycerol and alpha-keto acids.
  - 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.
- It requires **mitochondria** and **cytosolic enzymes** " cytosolic enzymes = present in cytosol " .
- Occurs in Liver (mainly) and kidney.

# Hexose monophosphate pathway shunt (HMP) / Pentose phosphate pathway (PPP)

- HMP shunt is an **alternative** ( another ) **pathway** of glucose oxidation “ The major pathway is glycolysis “ .
- Oxidation of glucose, also known as glycolysis, is the process which releases energy stored in glucose by combining it with oxygen.
- It has the same regulatory mechanism(s) as glucose (rapid short-term and slow long-term).
- it is **not** involved in the generation of energy unlike glycolysis .
- Around 10% of glucose (that all the body makes) is entered in this pathway.
- In liver and kidney → this percentage is up to 30% .
- Occurs in many places such as the cytosol of the liver, adipose tissue (to produce fatty acids from glucose).
- **Biomedical importance “ it has two main functions “ :**

1

Provide NADPH which is required for :

- Synthesis of fatty acid, steroids, and amino acids.
- Detoxification of drugs, **cytochrome P450**. Cytochrome P450: enzymes also function to metabolize potentially toxic compounds, including drugs and products of endogenous metabolism such as bilirubin.

2

Provide pentoses “ The most important pentose is ribose “ :

- Pentose and its derivatives are useful in the synthesis of:
  1. **Nucleic acids (DNA and RNA).**
  2. **Nucleotides (ATP, NAD, FAD, CoA).**



1. NADH : in the electron transport chain as energy molecule .
2. NADPH : cofactor in the glutathione system

# Tissue distribution

The cytosol of:

- 01 Liver.
- 02 Lactating mammary gland.
- 03 Adrenal cortex.
  - The adrenal cortex: the outer part of the adrenal gland.
- 04 Gonads.
  - Gonads: an organ that produces gametes; a testis or ovary.
- 05 Adipose tissue.
- 06 Erythrocytes to reduce glutathione.
  - Glutathione: antioxidant capable of preventing damage caused by reactive oxygen species. (Free Radicals)
- 07 Lens and cornea.
  - Cornea: the transparent layer forming the front of the eye.

# Phases of HMP shunt

It has two phases:

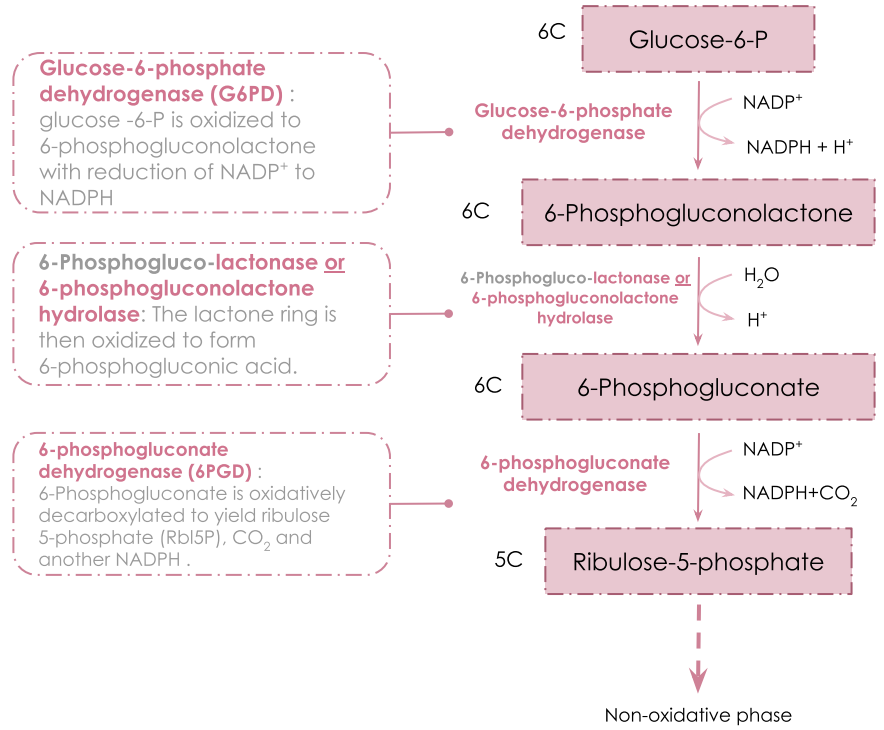
- 1 Oxidative phase .
  - Produce NADPH and it's irreversible.
- 2 Non-oxidative phase .
  - Produce pentose and it's reversible .



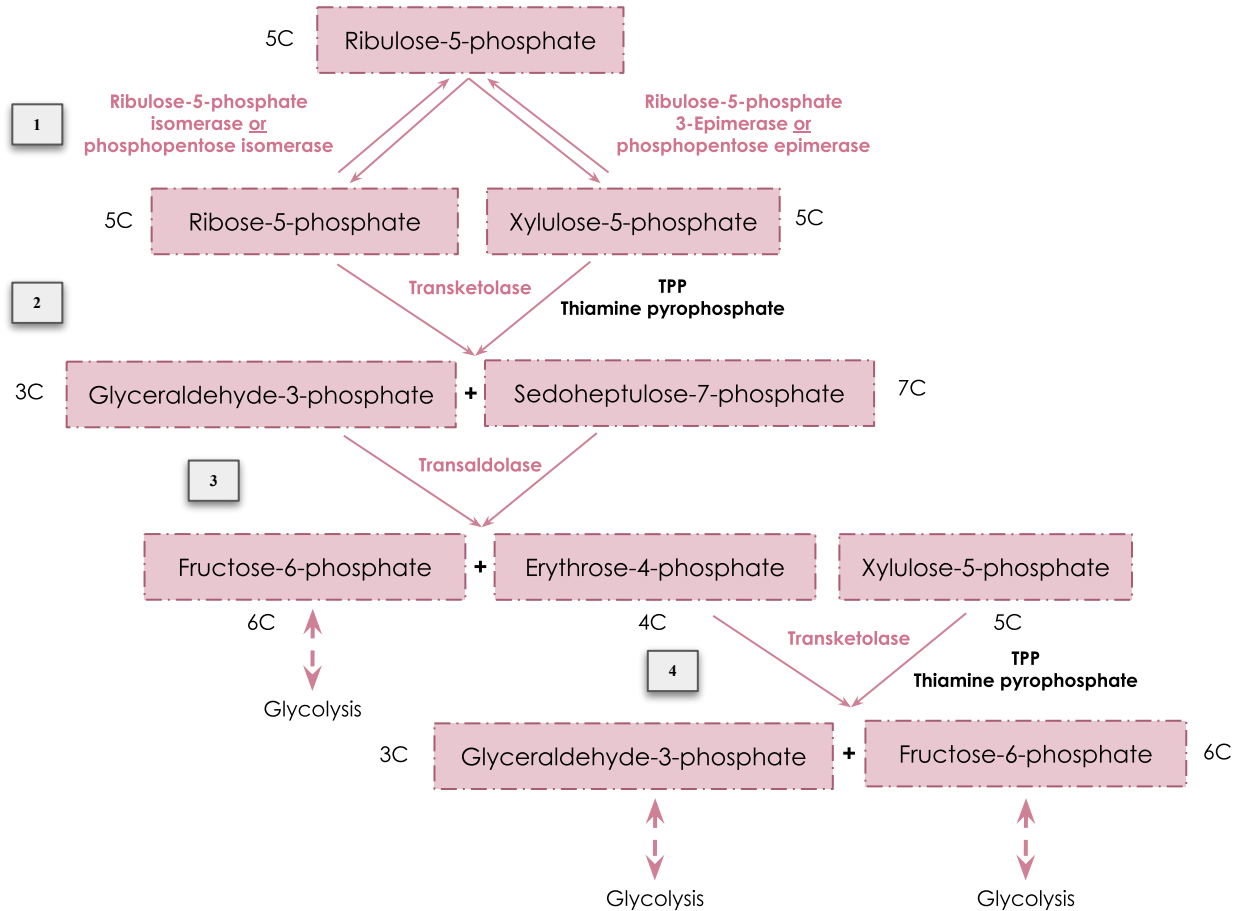


# Phase 1 : oxidative phase “ irreversible “

- 1 We start with **glucose-6-phosphate** which will be oxidized “ loss of electron “ to 6-Phosphogluconolactone with the help of **Glucose-6-phosphate dehydrogenase (G6PD) enzyme** and the electron that being lost will be added to **NADP<sup>+</sup>** to produce **NADPH** .
- 2 Now we have 6-Phosphogluconolactone and it has a ring structure so we have to open this ring by hydrolysis reaction that catalyzed by **lactonase enzyme** or you can say **6-phosphogluconolactone hydrolase** that will produce 6-Phosphogluconate and we release **H<sup>+</sup>** .
- 3 We have 6-Phosphogluconate which doesn't have a ring structure and ready to undergo decarboxylation and oxidation reaction that catalyzed by **6-phosphogluconate dehydrogenase enzyme** which means we will remove a carbon and oxidize it “ loss of electron “ to **Ribulose-5-phosphate** which will release **CO<sub>2</sub>** and add an elctron to **NADP<sup>+</sup>** to produce **NADPH** .



# Phase 2 : Non-oxidative phase " reversible "



## Phase 2 : Non-oxidative phase “ reversible “

- 1 We will take Ribulose-5-phosphate and convert it to Ribose-5-phosphate by **Ribulose-5-phosphate isomerase** or you can say **phosphopentose isomerase** “نسوي هالخطوة مرتين عشان يصير الناتج اثنین مو واحد” and also we will reverse the reaction from 2 Ribose-5-phosphate to 2 Ribulose-5-phosphate by **Ribulose-5-phosphate isomerase** or **phosphopentose isomerase** فہمتوا لفة جحا ؟ كل ذا عشان نوصل لناتج اخر  
 Now we have 2 Ribulose-5-phosphate will be converted to 2 Xylulose-5-phosphate by **Ribulose-5-phosphate 3-Epimerase** or you can say **phosphopentose epimerase** .  
 يعني بكل بساطة راح نستخدم الـ Ribulose-5-phosphate ونحوه لـ Ribose-5-phosphate واعيد الرياكشن مره ثانيه عشان يصير عندي الناتج اثنین من الـ Ribose-5-phosphate حلو ؟ الحين راح نعكس الرياكشن عشان نوصل لناتج اخر فراح نعكسه ويكوّن عندنا اثنین من الـ Ribulose-5-phosphate وهالناتج راح يكون مُتفاعل لتفاعل ثاني وراح نحوله ويعطينا اثنین من Xylulose-5-phosphate ليش كل هاللفة ؟ لان بالكيمستري الـ Ribulose اقرب كشكل ويتحول بسرعه لـ Xylulose وليش عندنا اثنین من الـ Xylulose ؟ لان واحد بنستعمله الحين وواحد بنستعمله بعدين فالفكره نبي نكوّن اثنین من الـ Xylulose بفيديونا بالتفاعل
- 2 - Xylulose-5-P: an intermediate in the pentose phosphate pathway. It is a ketose sugar formed from ribulose-5- phosphate.  
 Now we will take Xylulose-5-phosphate and another Ribose-5-phosphate with the help of **Transketolase enzyme** .  
 يعني اخذنا واحد من الـ Xylulose-5-phosphate اللي طلع عندنا من الخطوة اللي راحت ونجيب Ribose-5-phosphate جديده من ريباكشن الـ oxidative phase اللي مافهم يشوف الفيديو .  
**Transketolase enzyme** requires a cofactor which is **Thiamine pyrophosphate (TPP)** to be activated, now this enzyme will take 2 carbons from Xylulose-5-phosphate and put them on Ribose-5-phosphate to form Sedoheptulose-7-phosphate and the rest 3 carbons from Xylulose-5-phosphate will form Glyceraldehyde-3-phosphate .
- 3 Here we will take Glyceraldehyde-3-phosphate and Sedoheptulose-7-phosphate with the help of **Transaldolase enzyme** and this enzyme requires a cofactor which is **Thiamine pyrophosphate (TPP)** to be activated, now this enzyme will take 3 carbons from Sedoheptulose-7-phosphate and put them on one carbon from Glyceraldehyde-3-phosphate to form Erythrose-4-phosphate and also it will take the rest 4 carbons from Sedoheptulose-7-phosphate and put them on the rest 2 carbons from Glyceraldehyde-3-phosphate to form Fructose-6-phosphate .
- 4 Remember Xylulose-5-phosphate in step 1 ? We used one of them in the previous reaction and the other one we will use it here so we will take Xylulose-5-phosphate and Erythrose-4-phosphate with the help of **Transketolase enzyme** that will take 2 carbons from Xylulose-5-phosphate and put them on Erythrose-4-phosphate to form Fructose-6-phosphate and the 3 carbons from Xylulose-5-phosphate will form Glyceraldehyde-3-phosphate “ both Glyceraldehyde and fructose are intermediates of glycolysis “ .

# To summarize

HMP shunt			
Phases	<p>Oxidative <math>\text{NADP}^+ \rightarrow \text{NADPH}</math> 1 glucose <math>\rightarrow</math> 2 NADPH</p> <p>Non-Oxidative</p>		
Mains outcomes	<ol style="list-style-type: none"><li>1. NADPH</li><li>2. Ribose ( for DNA , <math>\text{NAD}^+</math> ..etc )</li></ol>		
Main enzymes	<table border="1"><tbody><tr><td><ol style="list-style-type: none"><li>1. Glucose-6-phosphate <b>dehydrogenase</b> .</li><li>2. 6-Phosphogluco-<b>lactonase</b> or 6-phosphogluconolactone <b>hydrolase</b> .</li><li>3. 6-phosphogluconate <b>dehydrogenase</b> .</li></ol></td><td><ol style="list-style-type: none"><li>1. Ribulose-5-phosphate <b>isomerase</b> or phosphopentose <b>isomerase</b> .</li><li>2. Ribulose-5-phosphate 3-<b>Epimerase</b> or phosphopentose <b>epimerase</b> .</li><li>3. <b>Transketolase</b> " Transfers 2 carbons " .</li><li>4. <b>Transaldolase</b> " transfers 3 carbons " .</li></ol></td></tr></tbody></table>	<ol style="list-style-type: none"><li>1. Glucose-6-phosphate <b>dehydrogenase</b> .</li><li>2. 6-Phosphogluco-<b>lactonase</b> or 6-phosphogluconolactone <b>hydrolase</b> .</li><li>3. 6-phosphogluconate <b>dehydrogenase</b> .</li></ol>	<ol style="list-style-type: none"><li>1. Ribulose-5-phosphate <b>isomerase</b> or phosphopentose <b>isomerase</b> .</li><li>2. Ribulose-5-phosphate 3-<b>Epimerase</b> or phosphopentose <b>epimerase</b> .</li><li>3. <b>Transketolase</b> " Transfers 2 carbons " .</li><li>4. <b>Transaldolase</b> " transfers 3 carbons " .</li></ol>
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# Clinical correlation

## “ G6PD deficiency “

- Deficiency in **Glucose-6-phosphate dehydrogenase** enzyme results in :
  - 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.

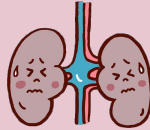
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### Neonatal jaundice

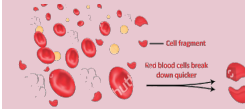
Neonatal : relating to newborn children

2



### Kidney failure

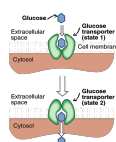
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### Hemolytic anemia

Hemolytic anemia: relating to or involving the rupture or destruction of red blood cells.

# Glucoses transport

	Na <sup>+</sup> Monosaccharide Co-transporter	Na <sup>+</sup> - Independent Facilitated diffusion
About	<p>Glucose is hydrophobic molecule that's why it cannot pass easily inside the cell so it needs another way to go inside the cell either by <b>Co-transporter</b> which will take Na<sup>+</sup> and glucose together to go inside the cell or by <b>Facilitated diffusion</b> which mean it has a specific carrier to it as you see in the right pic</p>	
		
Movement of glucose	<p>Against concentration gradient                      " From low concentration to high concentration "</p>	<p>Down the concentration gradient                      " From high concentration to low concentration "</p>
Energy need	<p>Energy <b>dependent</b>                      " requires energy "</p>	<p>Energy <b>Independent</b>                      " doesn't require energy "</p>
-	<p>It's Carrier-mediated and Coupled to Na<sup>+</sup> transport</p>	<p>Glucose Transporters (GLUT 1-14)</p>
Location	-	<p>Small intestine, renal tubules &amp; choroid plexus</p>

# Glucoses transporters

BBB kids lips are pink mother father " mnemonic "  
 بالنسبة للـ function نحفظ المتشابهه عشان تسهل علينا

	Transporter	Location	Function
<b>BBB</b>	GLUT-1	<b>B</b> lood (RBCs ), <b>B</b> rain and ( <b>b</b> aby = fetus )	Glucose uptake from blood
<b>Kids Lips</b>	GLUT-2 (Gluconeogenesis for maintain Homeostasis)	<b>L</b> iver , <b>K</b> idney & <b>P</b> ancreas	Blood & cells (either direction )
<b>Pink</b>	GLUT-3	<b>N</b> eurons , <b>P</b> lacentas and <b>k</b> idney	Glucose uptake from blood
<b>Mother Father</b>	GLUT-4 (Insulin dependent)	Adipose tissues ( <b>F</b> at ) and skeletal <b>m</b> uscles	Glucose uptake from blood
	GLUT-5	Small intestine and testes	Fructose transport
	GLUT-7	Liver ( ER – membrane )	-

## 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  $\text{CO}_2$ .



During non-oxidative phase, pentose phosphate is converted to intermediates of glycolysis .



# Quiz

Q1 : The metabolic pathway of HMP shunt is :

- |               |                  |                     |              |
|---------------|------------------|---------------------|--------------|
| A ) Catabolic | B ) Glycogenesis | C ) Gluconeogenesis | D ) Anabolic |
|---------------|------------------|---------------------|--------------|

Q2 : The end product of aerobic glycolysis is :

- |              |                         |              |             |
|--------------|-------------------------|--------------|-------------|
| A ) Glycerol | B ) Glucose-6-phosphate | C ) Pyruvate | D ) Lactate |
|--------------|-------------------------|--------------|-------------|

Q3 : The conversion of ribulose-5-phosphate into ribose-5-phosphate is aided by :

- |                                      |                                       |                   |               |
|--------------------------------------|---------------------------------------|-------------------|---------------|
| A ) Ribose-5-phosphate dehydrogenase | B ) Glucose-6-phosphate dehydrogenase | C ) Transketolase | D ) Isomerase |
|--------------------------------------|---------------------------------------|-------------------|---------------|

Q4 : The end product of the oxidative phase of HMP pathway is :

- |                                |                          |                          |             |
|--------------------------------|--------------------------|--------------------------|-------------|
| A ) Glyceraldehyde-3-phosphate | B ) Ribulose-5-phosphate | C ) Xylulose-5-phosphate | D ) Glucose |
|--------------------------------|--------------------------|--------------------------|-------------|

Q5 : GLUT-2 is found in:

- |          |           |             |                     |
|----------|-----------|-------------|---------------------|
| A ) RBCs | B ) liver | C ) Neurons | D ) Adipose tissues |
|----------|-----------|-------------|---------------------|

Q6 : Which of the following enzymes is found in the oxidative phase ?

- |          |               |               |                   |
|----------|---------------|---------------|-------------------|
| A ) G6PD | B ) Isomerase | C ) Epimerase | D ) Transketolase |
|----------|---------------|---------------|-------------------|

## SAQs :

Q1: enumerate which molecule responsible for Fructose transportation and in what organ is it located ? ?

Q2: What is the final product of the oxidative phase of HMP shunt ?

★ MCQs Answer key:

1) A 2) C 3) D 4) B 5) B 6) A

★ SAQs Answer key:

- 1) GLUT-5 & it's in small intestine and testes
- 2) Ribulose-5-phosphate



## Girls team:

Alia Zawawi  
Nada Babilli  
Rania Aqil  
Reem alamri

📍 Reema Alomar  
📍 Reem Alqahtani

Renad Alhumaidi  
Shaden Alobaid  
Noura Alsalem  
Lama Alahmadi

Sadem Alhazmi  
Somow Abdulrahman  
Budoor Almubarak  
Samar Almohammedi

Nuha Alkudsi  
Norah Alsheikh  
Muneerah Alssdhan  
Mayasem Alhazmi  
Noura alshathri  
Duaa Alhumoudi



## Boys team:

Mansour albawardi  
Hassan alshuraf  
Abdulrahman almbki  
Mohammed alsayari  
Abdullaziz alomar  
Abdulaziz alrabiah  
Saud alrasheed  
Abdullah almazro  
Hamad almousa  
Ahmad alkhayat



We can either walk  
towards Growth, or  
stand in Safety.

📍 Shatha Aldhohair

Mishal Althunayan

Made by 📍



Bio Chem 439



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