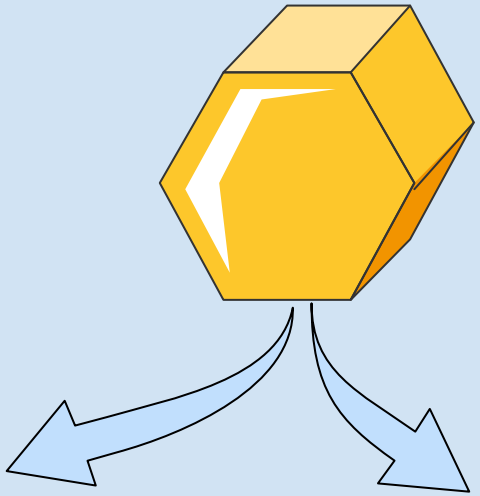
Major Metabolic Pathways of Glucose



MED441
KING SAUD UNIVERSITY

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10
V1

Foundation Block - KSU

Color Index:

- Main text
- Important
- Notes
- Boys slides'
- Girls slides'
- Extra

Editing File

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 Pathway

Definition: Sequence of reactions, which are put together so that the product of any reaction becomes a substrate of the next reaction. Giving you at the end of the reaction a final product, called the final end product of the pathway.

Site:

- Cellular (tissue)
- Subcellular

Reactions: catabolic or anabolic

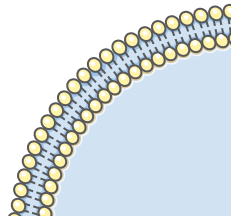
Rate-limiting enzyme(s):

Determine the
rate of that particular reaction
(fast or slow).

Regulatory mechanism(s)

- Rapid, short-term
  - Covalent modification
    e.g. phosphorylation
  - Allosteric
- Slow, long-term
  - Induction
  - Repression

Rapid regulation: mostly by enzymes
Slow regulation: mostly by hormones



Metabolic Pathways of Glucose (production and utilization)

Prefix:
Glyco = glucose
Glycogeno = glycogen (except in glycogenesis)

Suffix:
Genesis = synthesis (thanks to 439 team)
Lysis = breaking down

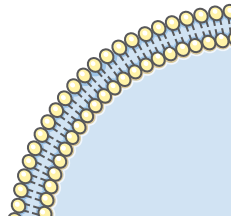
Neo = new

Production of glucose

- Glycogenolysis — Breakage of glycogen.
- Gluconeogenesis — Production of glucose from non-carbohydrate molecules.
- Hexose interconversion — By converting other hexoses into glucose. e.g. fructose to glucose

Utilization of glucose

- Glycogenesis — Synthesis of glycogen.
- Glycolysis — Krebs cycle
- Hexose interconversion — Converting glucose to other hexose. E.g. glucose to fructose
- HMP/PPP (same pathway, dif names)
  - HMP: Hexose Monophosphate Pathway.
  - PPP: Pentose Phosphate Pathway.



Metabolic Pathways of Glucose (catabolic and anabolic)

Catabolic cycles	Anabolic cycles
• Glycolysis (Mainly) • Krebs (Mainly) • Glycogenolysis • HMP	• Gluconeogenesis • Glycogenesis

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- **Glycolysis:**

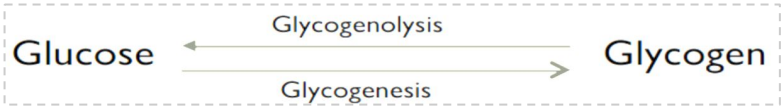
Oxidation of glucose to provide energy. (The main pathway of glucose metabolism)

Aerobic glycolysis		Anaerobic glycolysis
In cells with mitochondria and an adequate supply of oxygen	Occurrence	In absence of oxygen and in cells that lack mitochondria
Pyruvate	End product	Lactate

Metabolic Pathways of Glucose (catabolic and anabolic)

- **Glycogenesis:**

Synthesis of glycogen from glucose Mainly in liver, muscle in Cytosol.



- **Glycogenolysis:**

Degradation (تكسير) of glycogen into glucose Mainly in liver, muscle in 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.
  - Occurs in liver and kidney.

- **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%.

HMP = PPP

HMP Biomedical Importance

It has two main functions:

1

Provides NADPH (only pathway that does) **which is required for:**

- synthesis of fatty acids, steroid and some amino acids.
- Detoxification of drugs by cytochrome p450.
- In scavenging (remove) the free radicals.

The only way in which the cell can make NADPH is through HMP.

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)

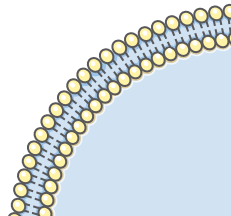
Tissue Distribution

The cytosol of:

- Liver
- Lactating mammary gland
- Adrenal cortex
- Gonads
- Adipose tissue
- Erythrocytes to reduce glutathione

antioxidative molecule
(neutralizes free radicals)

- Lens and cornea



HMP SHUNT

PHASES

Oxidative (irreversible): from Glucose 6-phophate till Ribulose 5-phosphate (end product)

Non-Oxidative (reversible): from Ribulose 5-phosphate till the end of pathway

MAIN OUT-COME

NADPH . synthesis of fatty acids, steroid, amino acid

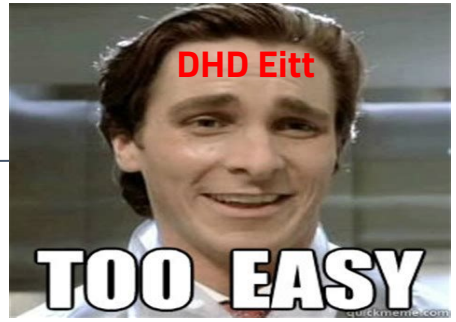
Ribose . synthesis of DNA, RNA, ATP, FAD, NAD

ENZYMES

DHD Eitt . wanna know how?

Dehydrogenase - Hydrolase - Dehydrogenase — oxidative phase

Epimerase - isomerase - transketolase - transaldolase — non-oxidative phase



Recommended video for HMP Shunt pathway
HERE

HMP SHUNT

READ ME

enzymes : Blue
Product : dark purple , Two dark yellow
irreversible "oxidative" : →
reversible"non-oxidative" : ↔
the stranger reaction : dark yellow
Precursor product for non-ox. : Pink

take it easy, step by step

REMEMBER
DHD Eitt

GLUCOSE 6-PHOSPHATE

by?

NADPH , H+ ← NADP+ , H2O — Glucose 6-phosphate Dehydrogenase (G6PD)

6-PHOSPHO-GLUCONOLACTONE

6-phospho-gluconolactone Hydrolase (Lactonase)

6 PHOSPHO-GLUCONATE

NADPH , H+ ← NADP+ , H2O — 6-phospho-gluconate Dehydrogenase (6PGD)

RIBULOSE 5 PHOSPHATE

ribose 5-phosphate isomerase

قلنا في محاضرة الانزيمات ان الأيزو مايغير شي الا ترتيب المركبات .
عشان كذا الإسم تشوفه متشابه مره مع المركب الأساسي

phospho-pentose Epimerase

RIBOSE 5-PHOSPHATE

XYLULOSE 5-PHOSPHATE

Transketolase
and coenzyme called : thiamine pyrophosphate (TPP) (vitamine B1)

SEDOHEPTULOSE 7-PHOSPHATE

GLYCERALDEHYDE 3-PHOSPHATE

Transaldolase

تفاعلهم يتم بالانزيم هذا ويعطي ناتجين

Transketolase + TPP

ERYTHROSE 4-PHOSPHATE

يرجع يتفاعل معه

XYLULOSE 5-PHOSPHATE

FRUCTOSE 6-PHOSPHATE

Glycolytic pathway

GLYCERALDEHYDE 3-PHOSPHATE

Glycolytic pathway

FRUCTOSE 6-PHOSPHATE

Glycolytic pathway

NOTES

Transketolase: needs help from **coenzyme TPP**. this enzyme will take **2 carbon** from Ribose 5-phosphate and put them on Xylulose 5-phosphate to form Sedoheptulose 7-phosphate and the rest 3 carbon from Ribose 5-phosphate will form Glyceraldehyde 3-phosphate.

Transaldolase: this enzyme now will take **3 carbon** from Sedoheptulose 7-phosphate and put them on Glyceraldehyde 3-phosphate to form Fructose 6-phosphate
and also the rest **4 carbon** atoms from Sedo 7-phosphate will form Erythrose 4-phosphate.

Oxidative

- **RATE LIMIT ENZYME FOR ALL THIS PATHWAY IS Glucose 6-phosphate dehydrogenase. how? because without this enzyme, all the pathway won't occur, this enzyme has the ability to switch on/off the pathway**
- **From oxidative phase we will get TWO NADPH . one from reaction 1, another from reaction 3**
- **All oxidative reactions are irreversible**

Non-oxidative

- **The precursor for this phase is Ribulose 5-phosphate**
- **From non-oxidative phase we will get a Ribose 5-phosphate "pentose sugar"**
- **All non-oxidative reactions are reversible**
- **Products with the dark yellow color, are catalyzed by Transketolase to form another new reaction with new products, it is a specific reaction in this phase as you see because none of those compounds are doing like them**
- **Transketolase requires an important co-factor which is thiamine pyrophosphate (TPP) to be activated**

Remember *DHD Eitt* , for enzymes' names according to their reaction order

Clinical Correlation

- Deficiency in Glucose 6-phosphate dehydrogenase (G-6-PD) result in:

  - the only way the body get NADPH is from HMP shunt, so if there is deficiency in the rate-limit enzyme which is G-6-PD, NADPH won't formed, and this lead to stop affect the things that required NADPH "in slide 8" , while the pentoses, body can get them from other resource, so there is no much effect

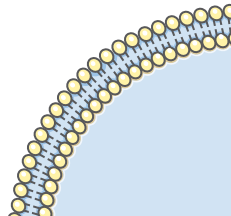
Hemolytic anemia

destruction of red blood cells

Neonatal jaundice

(effects the liver)
neonatal: relating to newborn children

Kidney failure



Glucose Transport

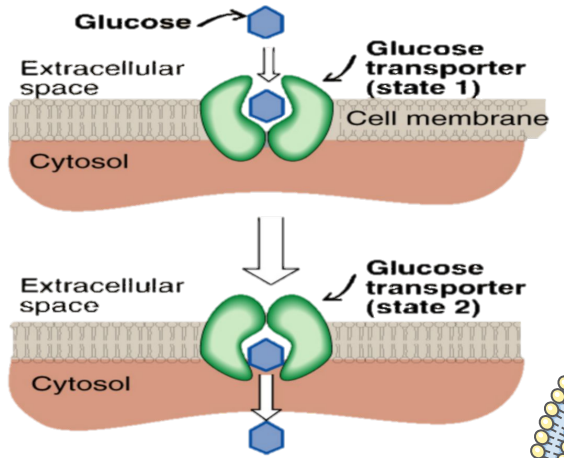
Glucose is hydrophobic molecule that's why it cannot pass easily inside the cell so it needs another way to go inside the cell either by Co-transporter which will take Na+ and glucose together to go inside the cell or by Facilitated diffusion which mean it has a specific carrier to it. (thanks to 439 team)

Na+-Monosaccharide Cotransporter "dependent"

- Against concentration gradient low conc. to high conc.
- Energy dependent why? because it's against conc. (Active transport)
- Carrier-mediated
- Coupled to Na+ transport "لما يطلع لازم يكون في احد يدخل مكانه"
- Small intestine, renal tubules & choroid plexus

Na+-Independent Facilitated Diffusion

- Down the concentration gradient
- Energy Independent (Passive transport)
- Glucose Transporters (GLUT 1-14)

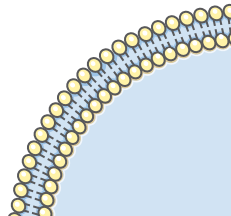


Once you see the word (GLUT) keep in mind this is related to Passive independent Facilitated diffusion.

Glucose Transporter

Tissue-specific expression pattern:

Transporter	Location	Function
GLUT-1	RBCs and brain	Glucose uptake from blood
GLUT-2	Liver, kidney & pancreas	Blood & cells (either direction)
GLUT-3	Neurons	Glucose uptake from blood
GLUT-4	Adipose tissue & skeletal muscle	Glucose uptake from blood Involved in diabetes
GLUT-5	Small intestine & testes	Fructose transport
GLUT-7	Liver (ER-membrane)	-



Take Home Message

- 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 CO_2.
- During non-oxidative phase, pentose phosphate is converted to intermediates of glycolysis.

Quiz

Q1: At which of the following condition, glycolysis end with lactate?							
A	Cells with mitochondria	B	Absence of oxygen	C	Present of oxygen	D	Absence of H+
Q2: The process of degradation of glycogen into glucose is called							
A	Glycogenolysis	B	Gluconeogenesis	C	Glycogenesis	D	Glycolysis
Q3: Which enzyme require an co-factor in order to be activated ?							
A	Dehydrogenase	B	Hydrolase	C	Isomerase	D	Transketolase
Q4: The precursors product for non-oxidative phase is?							
A	G-6-P	B	6-Phospho gluconate	C	Ribose 5-phosphate	D	Ribulose-5 phosphate
Q5: Which of the following transporters (GLUT) is found in small intestine and testes?							
A	GLUT-1	B	GLUT-2	C	GLUT-5	D	GLUT-8

Answer Key: 1) B 2) A 3) D 4) D 5) C

Q6:what can the Deficiency of (G-6-PD) results in our bodies ?

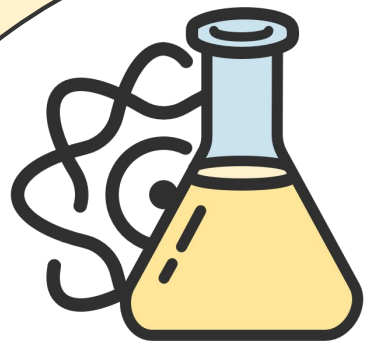
Q7: Enumerate where is GLUT-4 located and what is it responsible for?

Q8: For HMP Shunt, which enzyme is the rate-limit enzyme?

Q6:
Answer: It can cause Hemolytic Anemia, kidney failure and Neonatal jaundice.

Q7:
Answer: It in adipose tissue & skeletal muscle & its function is glucose uptake from blood.

Q8: Answer: Glucose 6-phosphate dehydrogenase (G-6-PD).



Biochemistry 441

Girls

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Fay Alluhaidan
Sarah Alhamlan
Arwa Almobeirek
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Alanoud Alhaider
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Manal Aldhirgham
Raaoum Jabor
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Shahad Helmi
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Ahmed Alayban
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Abdullah Alomran
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