النادي الطبي

# HEMATOPOIETIC & LYMPHATIC SYSTEM

## -HAYAT BATCH-

SUBJECT : Biochemistry

LEC NO. : 1 /erythrocytes metabolism in blood

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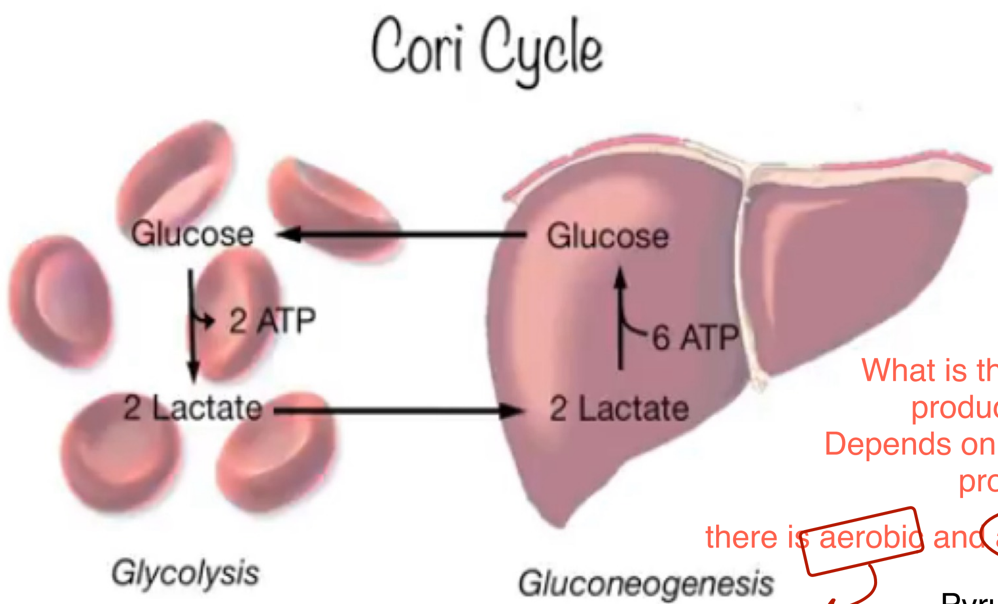
وَقُل رَّبِّ زِدْنِي عِلْمًا

# Hematopoietic & Lymphatic System

Two metabolic pathways for RBC:
1)glycolysis
2)pentose phosphate pathway /HMP(hexose phosphate shunt)

## Glycolysis in red blood cells

## Pentose phosphate pathway




What is the source for ATP production in RBC?
Depends on glycolysis alone for produce ATP

there is aerobic and anaerobic glycolysis

متى بنمشي aerobic إذا كان عندي
O2+mitochondria

كنا بنوصل لعند Pyruvic acid
و إذا ما كان عنا o2 كان بتحول
إلى lactic acid
هاض الحكي كنا نسميه
anaerobic

ATP from aerobic > ATP from anaerobic

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عنا طريقتين للmetabolism في RBC اليوم رام نبدأ بالglycolysis ...بالبداية احنا بنكسر الglucose إلى 2 pyruvate
في حال عدم وجود O2 التفاعل راح يسلك سلوك لا هوائي و يتحول إلى 2 lactate
طب إذا كان في عندي O2+ mitochondria راح اسلك طريق هوائي فبتكمل 2 pyruvate إلى كريبس سايكل....الخ
طيب هل تحتوى الRBCعلى mitochondria ؟لا معناته هتسلك الطريق اللاهوائي

*O2+ mitochondria =aerobic
No mitochondria or mitochondria without O2=anaerobic

كريات الدم الحمراء ما عندها mitochondria فمنطقيا راح تمشي على anaerobic pathway لأنو الaerobic بحتاج o2+mitochondria

# Glycolysis
# (Embden-meyerhof pathway)

- **Definition:**

- It is oxidation of glucose or glycogen to pyruvic acid (in presence of O2) or lactic acid (in absence of O2).

- **Site:**

- It occurs in the cytosol of every cell. Glucose can only give lactic acid in:

- RBCs (no mitochondria).
- Exercising muscles (O2 lack).

- **Steps:** The steps of glycolysis can be classified into two phases:

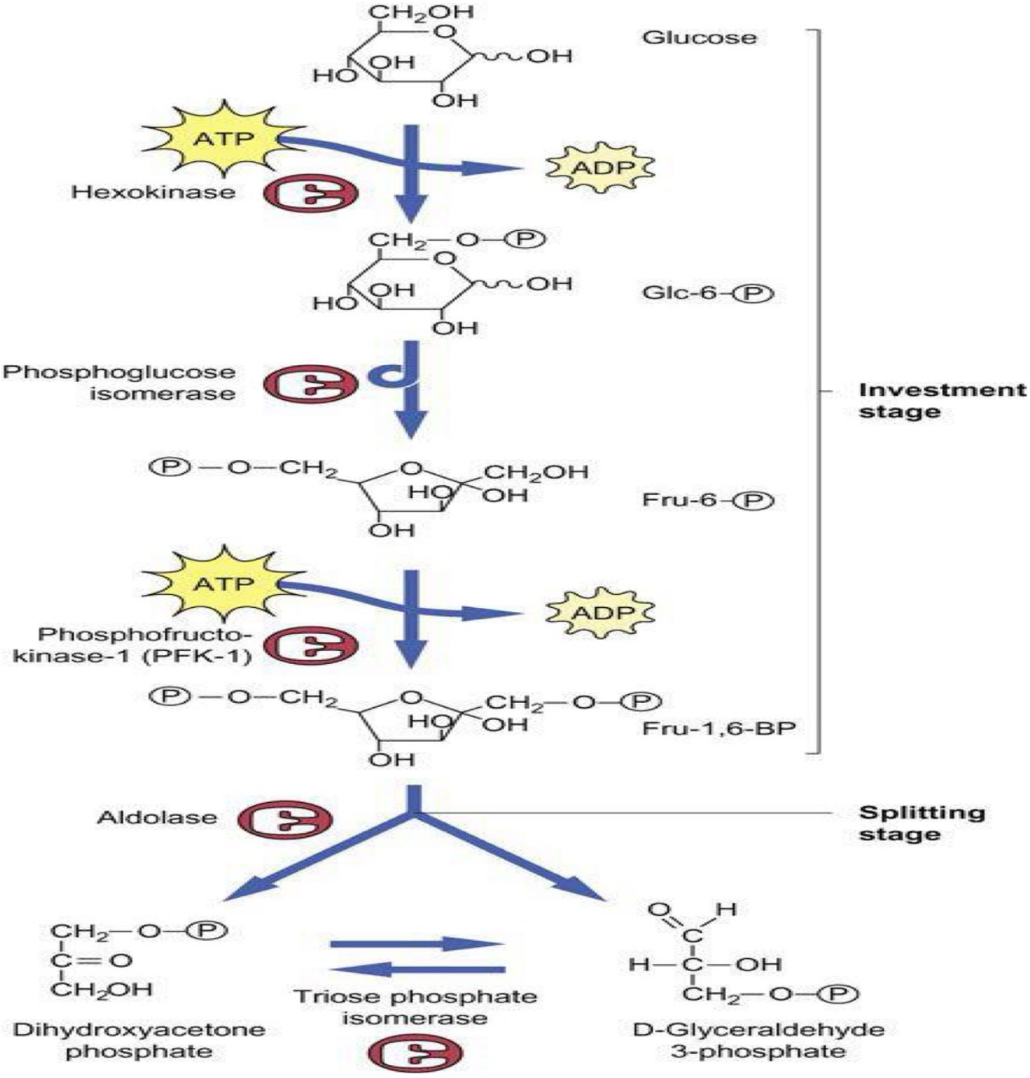
Investment stage

Yield stage

| **PHASE ONE:** | **PHASE TWO:** |
| --- | --- |
| In this phase glucose is converted into two molecules of glyceraldehydes-3-phosphate. | In this phase  the 2 molecules of glyceraldehydes-3-phospshate are converted into two molecules of pyruvate (aerobic) or lactate (anaerobic). |

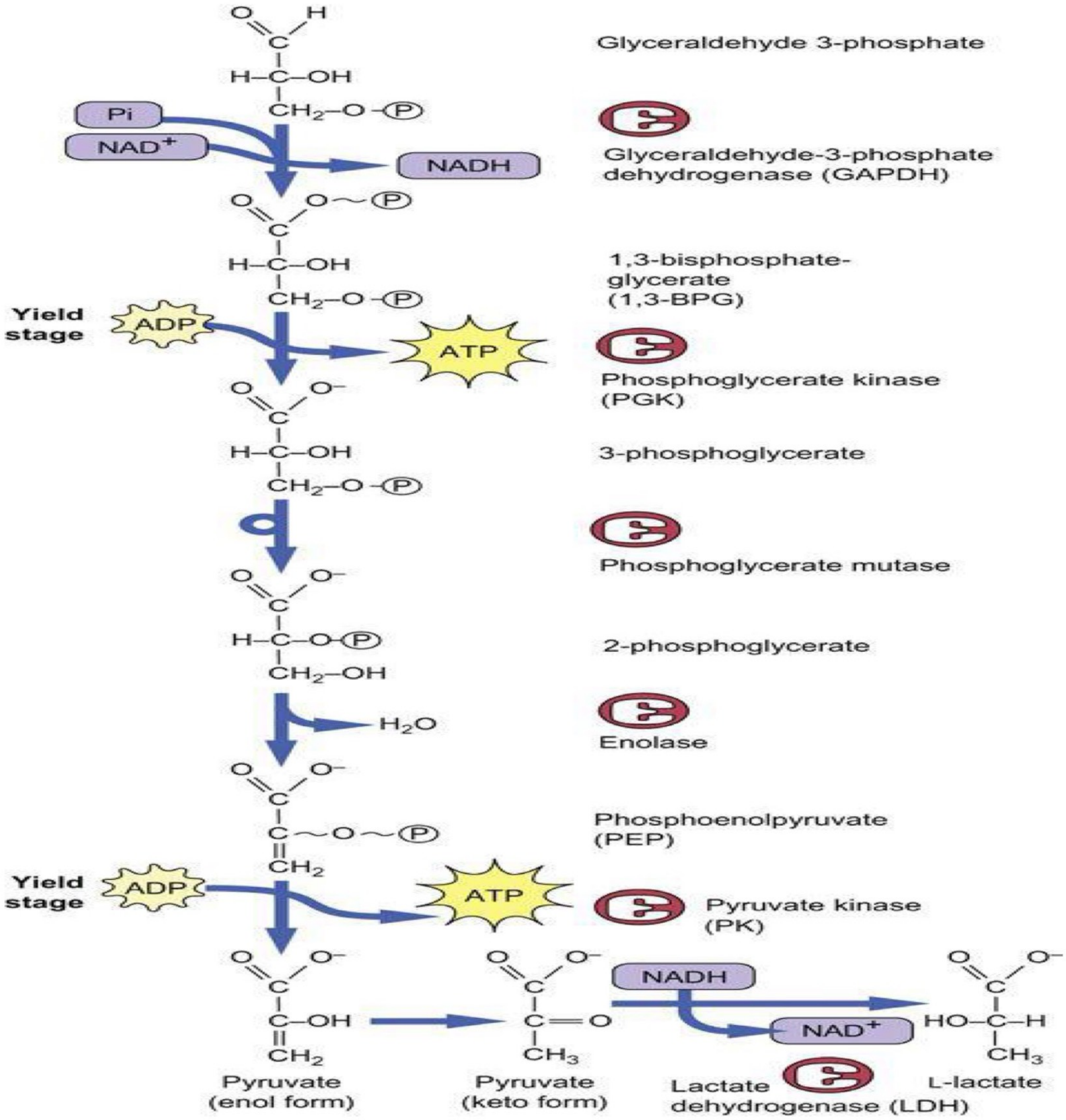
## The investment stage of glycolysis

***2 ATP** are invested to prime the metabolism of glucose by glycolysis*




الدكتوره ما ركزت ع هاي الرسمه و اللي وراها

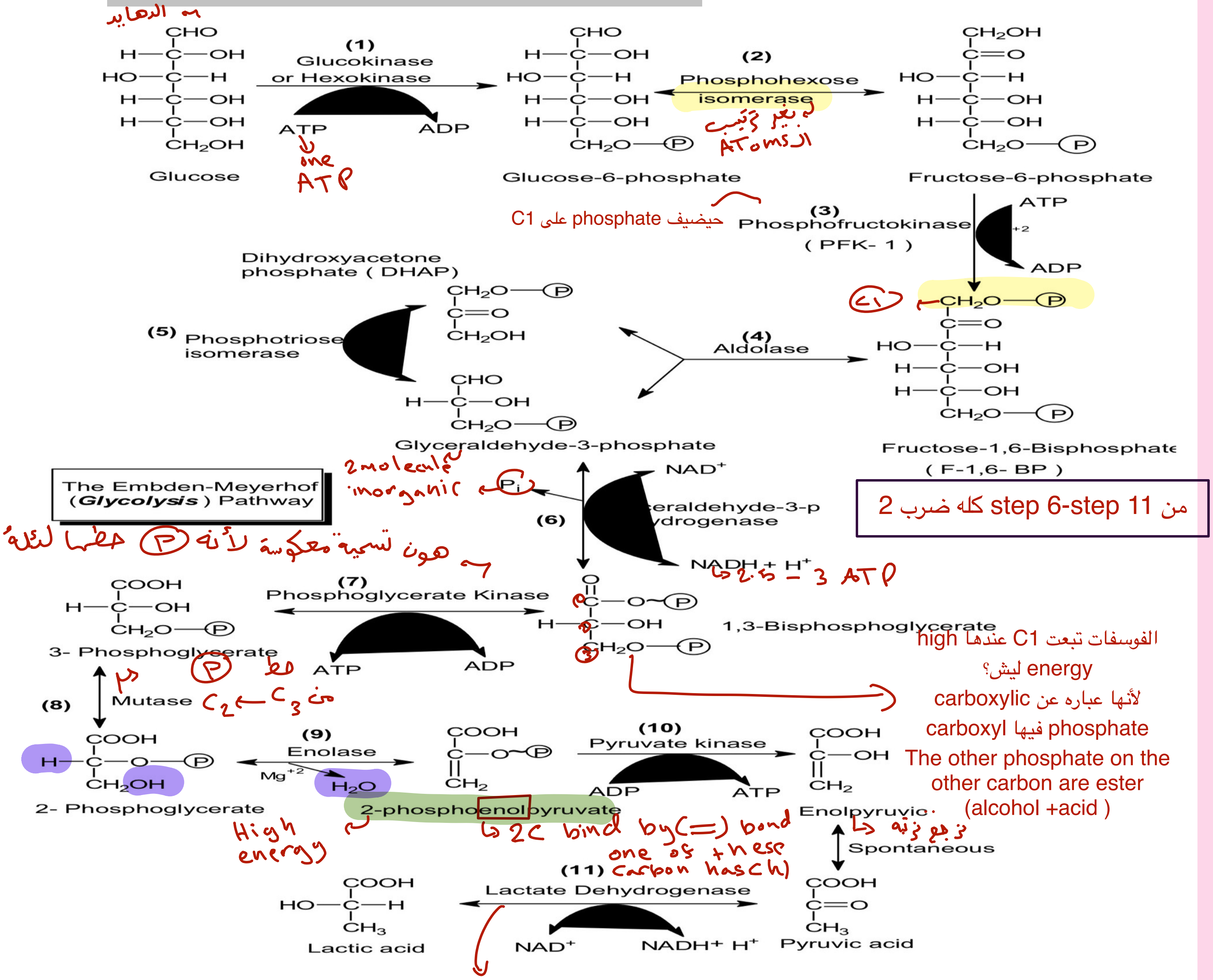
## The yield stage of glycolysis:




وقل رب زدني علماً

# Hematopoietic & Lymphatic System

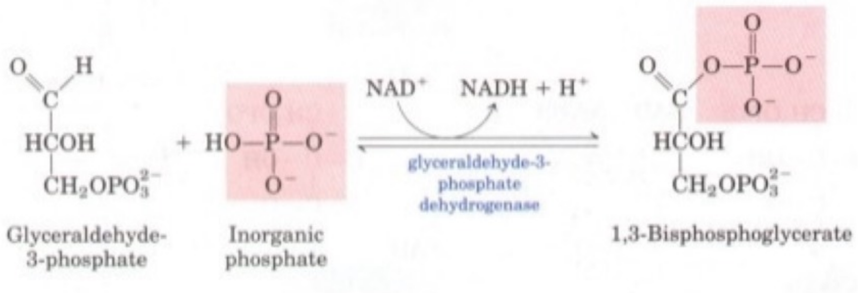
مهم جدا + كل الرسمة حفظ ما عدا الstructure




Reversible

بحط h في الكربونة رقم ٢ فبكسر الرابطة الثنائية

Step 6



## Energy gain of glycolysis:

- **Energy consumed:**

***Step (1) by glucokinase:*** One ATP is lost (spared if we start with glycogen).

***Step (3) by phosphofructokinase:*** One ATP is lost. So, the total lost 2 ATPs

- **Energy gained:**

***Step (6) by glyceraldehyde -3 P dehydrogenase:*** 2 NADH+$H^+$ (6 ATPs) gained only in the presence of $O_2$.

***Step (7) by phosphoglycerokinase:*** 2 ATPs gained.

***Step (10) by pyruvate kinase:*** 2 ATPs gained. So, the total gains 10 ATPs.

So, **Energy gained under anaerobic condition (i.e.) Glucose to 2 molecules of lactic acid is** **2 ATPs** and 3 ATPs if we start with glycogen.

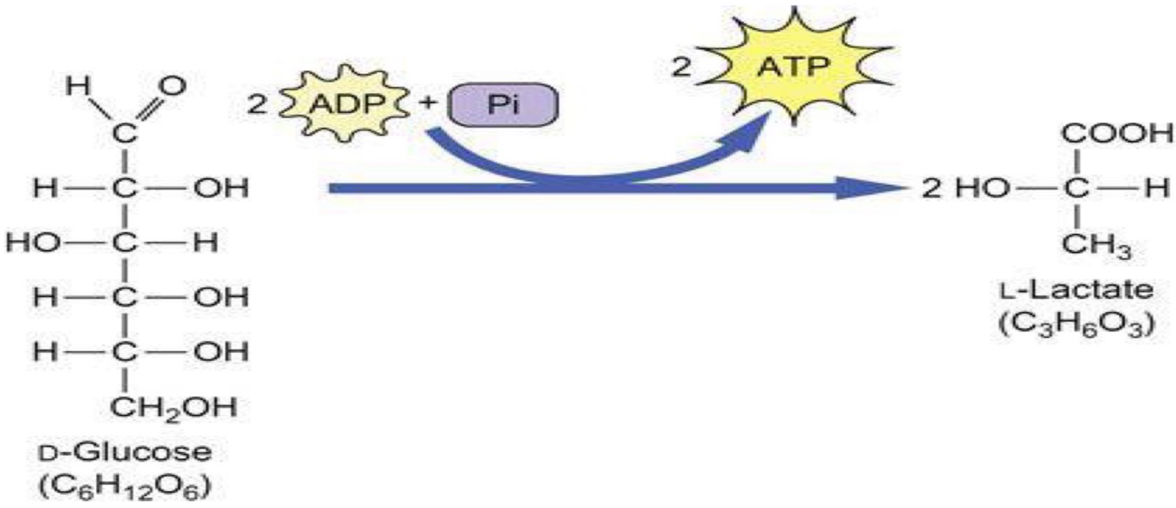
**Energy gained under aerobic condition (i.e.) Glucose to 2 molecules of pyruvic acid and 2 NADH +H+**

= 2 ATPs + 6 ATPs (from 2 NADH+$H^+$) = **8 ATPs** and 9 ATPs if we start with glycogen.

Summary:
2NADH =6 ATP from step 6
2 ATP from step 7
2 ATP from step 10
Total until now =6+2+2=10
We lose 2 NADH in step 11(6 ATP)
10-6=4
And then we loss 2 ATP one from step 1
And the other from step 3
Soo 4-2=2
We have 2 ATP

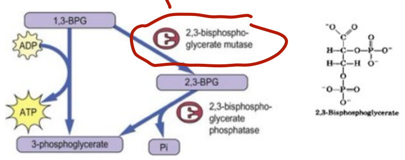
# Glycolysis in red blood cells

- RBCs have no mitochondria so, glucose oxidation by Glycolysis gives **2 lactic acids** and only **2 ATPs.**



Sometimes Glycolysis in RBCs gives NO ATP !!!!!!!!!!!!!!!!!!!!!!!!!!!

Pathway for biosynthesis and degradation of 2,3-bisphosphoglycerate.




- This pathway discovered by Rapoport-Lubring and called Rapoport-Lubring cycle.
- About 15 to 25% of the glucose utilized in red cells is utilized through BPG shunt.

**Remember**

- The 2,3-bisphosphoglycerate (BPG) molecule carries 5 negative charges and is derived from oxidation of glucose (glycolysis) in red cells.
- It binds to a positively charged pocket in Hb between the 2 β chains (small cavity in the center of the four Hb subunits)
- Binding favors the T- form of Hb, reducing affinity for oxygen and helping delivery of oxygen to tissues.
- BPG increases in red blood cells in cases of chronic anemia and in hypoxia. This helps delivery of oxygen to tissues.

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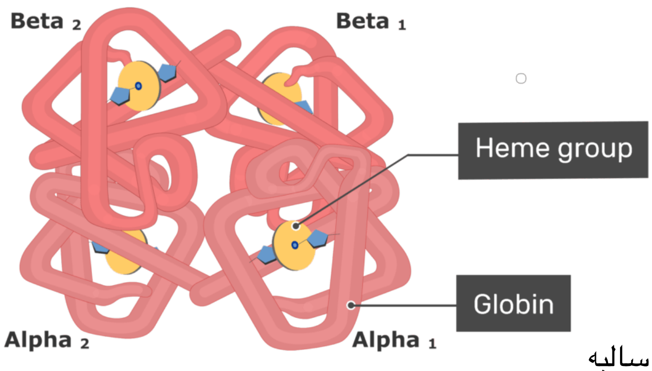
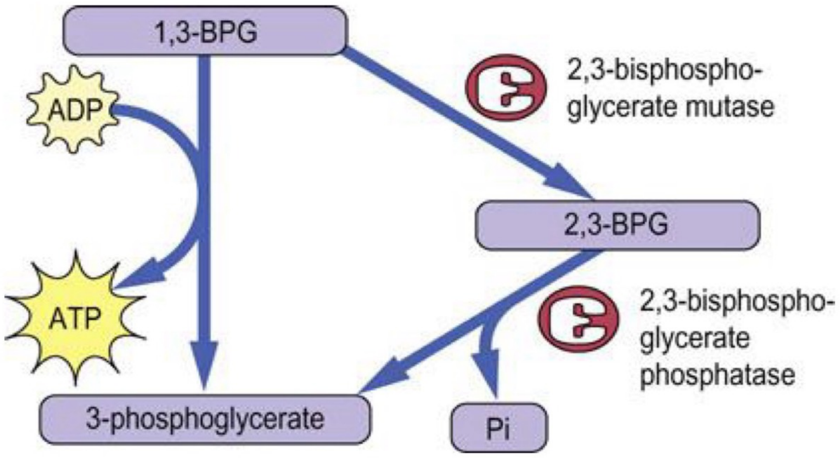
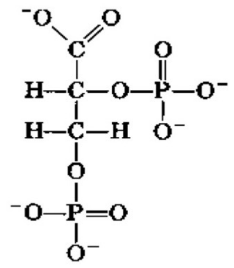
بكل بساطة مرات RBC ما بتعطيني ATPو هاض بكون بسبب إنزيم اسمه 2،3 bisphospho-glycerrate phosphatase  حيث بحول BPG-1,3 إلى BPG-2,3 ثم إلى phosphoglycerate-3
فهيك أنا عملت skip لخطوه انتاج الATP
لكن هل هاض الاشئ بفيدني ؟
الجواب نعم
هسا عنا المركب 2,3 Bisphosphoglycerate هاض مركب عنده 5 negative charge بمعنى عنده high negativity




طيب بشو بفيدني هاض الاشي؟
ذاكرين تركيب الهيموغلوبين؟
عنا رابطتين بيتا و رابطتين الفا
كل وحده فيها heme جواه iron لازم يكون في Ferrous state
على شان الهيموغلوبين يمسك بالO2 و يسلمها
هسا 2beta chain يكونوا positively charge
أو الأصح في بالنص بوكيت بكون شحنته موجبة
طب احنا شو حكينا عن 2,3BPG؟حكينا انو شحنته سالبه
فبروح بزنق نفسه بالبوكيت اللي شحنته موجبه(هو سالب برتبط بالموجب)
طيب و إذا ارتبط شو بصير؟
بحوله الهيموغلوبين لفورم اسمه T form
طيب شو بميز هاض الفورم؟
انو بقفل ع نفسه فبترك الo2بسهوله للtissue
بنستفيد منه في حاله chronic anemia/hypoxia
في فورم ثاني اسمه R Forn بمسك o2 فمنطق نلاقيه بالlung  و بوخذ الo2

**Pathway for biosynthesis and degradation of 2,3-bisphosphoglycerate.**





2,3-Bisphosphoglycerate

(اسم)

•This pathway discovered by Rapoport-Lubring and called Rapoport-Lubring cycle.

•About 15 to 25% of the glucose utilized in red cells is utilized through BPG shunt.

- So RBCs need 2, 3 bisphosphoglycerate as its increase will decrease the oxygen affinity for hemoglobin to oxygen and helping oxygen delivery to tissues.
- RBCs 1, 3 diphosphoglycerate is changed by mutase to 2, 3 diphosphoglycerate which by phosphatase is changed to 3-phosphoglycerate to continue glycolysis till pyruvic acid.

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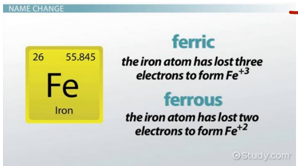
# •Importance of glycolysis in Red cells:

Source of ATP

- **Energy production**: the only pathway that supplies the red cells with ATP.
- **Bisphosphoglycerate shunt** (BPG shunt).
- **Reduction of methemoglobin**: glycolysis provides NADH for reduction of met-Hb in red cells by the **NADH-cyt.b5-methemoglobin reductase system.**




هسا الهيموجلوبين تعامله مع o2 فهو عرضة للاكسده يعني
وارد جدا انو الferrous يتحول إلى
Ferric
هيك بصير اسمه methemoglobin مشكلته ما بنقل o2
يعني مالوش أي لازمة فلازم أرجعه هيموجلوبين عن طريق
احول ال ferric إلى ferrous عن طريق cyst.b5

- The **ferrous iron of hemoglobin** is susceptible to oxidation by superoxide and other oxidizing agents, forming **methemoglobin**, **which cannot transport oxygen.**
- Only a very small amount of methemoglobin is present in normal blood, as the red blood cell possesses an effective system **(the NADH-cytochrome b5 methemoglobin reductase system)** for reducing heme Fe3+ back to the Fe2+ state.

Cyt b5:electron transport hemoprotein

Flavoprotein : FAD دا حل في ذ كيبه

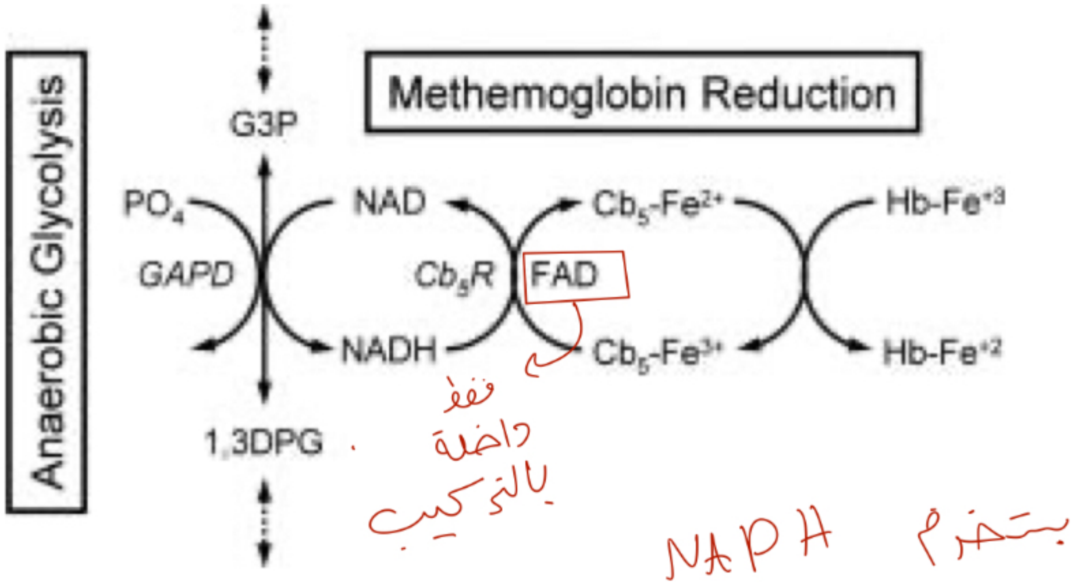
- This system consists of **NADH (generated by glycolysis)**, a **flavoprotein named cytochrome b5 reductase** (also known as methemoglobin reductase), and **cytochrome $b_5$** (electron transport hemoprotein).
- The $Fe^{3+}$ of methemoglobin is reduced back to the $Fe^{2+}$ state by the action of **reduced cytochrome $b_5$**:

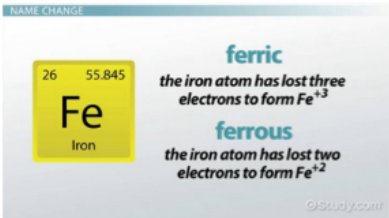
$$Hb\text{-}Fe^{3+} + \text{cyt } b_{5\ red} \longrightarrow Hb\text{-}Fe^{2+} + \text{cyt } b_{5\ ox}$$

- Reduced cytochrome $b_5$ is then regenerated by the action of cytochrome $b_5$ reductase (NADH-dependent enzyme ):

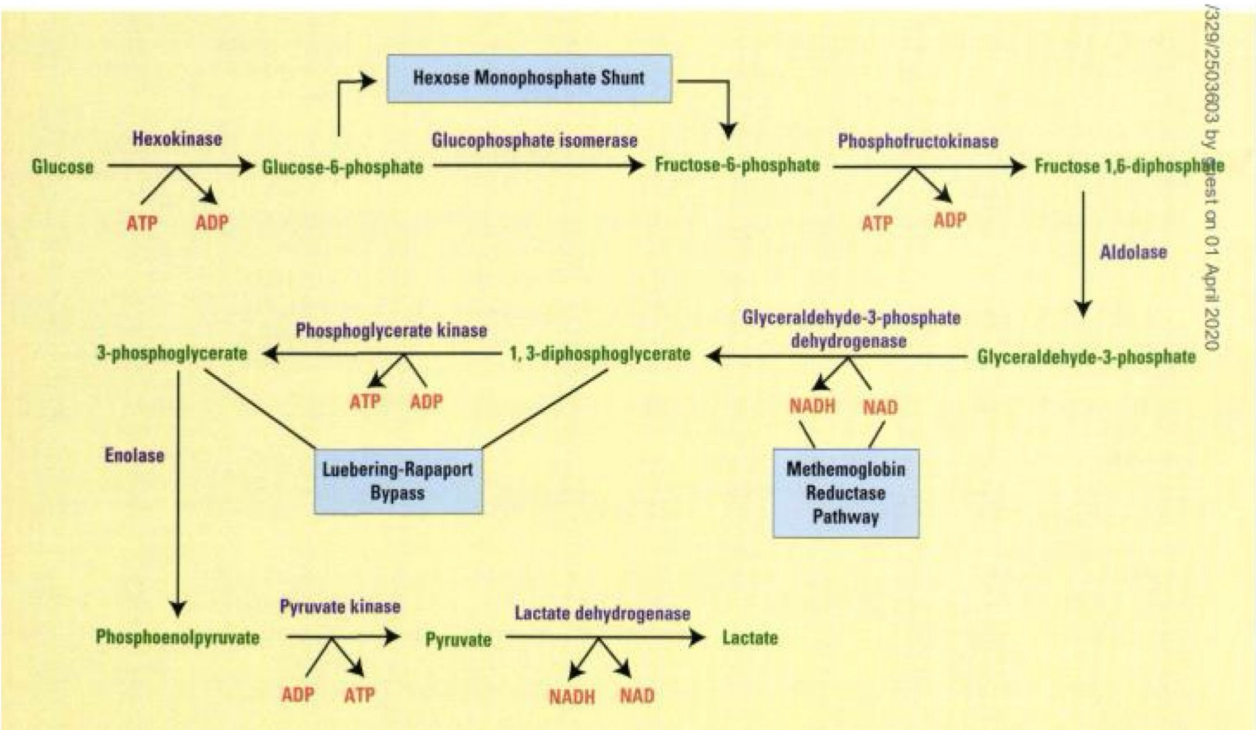
$$\text{cyt } b_{5\ ox} + NADH \longrightarrow \text{cyt b5 red} + NAD$$

Summary




Summary



## Quiz time

1) Which of the following is a FALSE statement about the fate of the glycolytic pathway in erythrocytes?
   a) Glycolysis is the sole source of ATP (adenosine triphosphate) in erythrocytes.
   b) Deficiency of pyruvate kinase leads to hemolytic anemia.
   c) Pyruvate generated during glycolysis is converted to lactate.
   d) Pyruvate generated during glycolysis is converted to acetyl CoA and enters the TCA cycle (tricarboxylic acid cycle) in mitochondria

2) What would happen to red blood cells if the haem group were removed from haemoglobin?
   a) Red blood cells would not be able to bind oxygen.
   b) Red blood cells would not be able to reproduce.
   c) White blood cells would not be able to reproduce.
   d) Blood clot formation would be inhibited.

3. What is the fate of pyruvate generated during glycolysis in red blood cells?
a) Converted to acetyl CoA for the TCA cycle
b) Converted to lactate
c) Utilized for gluconeogenesis
d) Excreted unchanged

4. Which molecule serves as the final electron acceptor in the glycolytic pathway in red blood cells?
a) Oxygen
b) NAD+
c) FAD
d) Pyruvate

Ans:
1)d
2)a
3)b
4)b

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