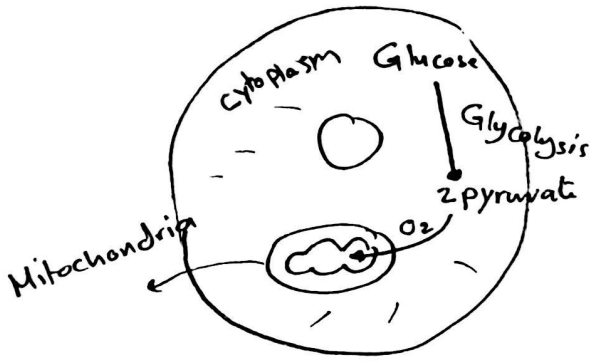
Glycolysis

Glucose تكسير

اول مرحلة في تكسير Glucose (made in cytoplasm) / Carbohydrate, mainly Glucose [$C_6H_{12}O_6$] is the main source of Energy in our bodies



c-c-c-c-c-c

Glucose

Glycolysis

It's Cytoplasm Need No O_2

anaerobic Glycolysis

Alcoholic Fermentation

نوع الخلية يحدد تحول Pyruvate إلى $2CO_2$ + Ethanol أو Lactose

2 Pyruvate

c-c-c

بدون O_2 — أو ممكن تتحول

بدون O_2 ممكن تتحول

2 lactate

- Occurs in RBCs
- highly active muscles
- Bacteria
  " lactobacillus clostridium botulinum"

O_2 بوجود Mitoch تدخل

Pyruvate

CO_2

Acetyl-CoA

Krebs Cycle — Chapter 19

$FADH_2$ / $NADH$

سلسلة نقل الإلكترونات

Electron Transport chain — chapter 20

CO_2 + H_2O

2 Ethanol + $2CO_2$

in some Bacteria and yeast

Glycolysis

Occurs in 10 Steps

(1 - 5) اول خمس خطوات
Preparing phase مرحلة تحضير

Glucose

2 ATP are Consumed تستهلك
Step 1 Step 3

ثاني خمس خطوات
Payoff phase مرحلة التعويض
(6 - 10)

4 ATP and 2 NADH produced تنتج
2 ATP Step 7, 2 ATP Step 10
Step 6

2 Pyruvate

Note

$A \xrightarrow{E_1} B \xrightarrow{E_2} C \xrightarrow{E_3} D \dots$

* Every pathway in our bodies has Control Steps, this mean the pathway can be activated or inhibited by activating or inhibiting Specific enzymes.

Types of control

① Allosteric Control $A \xrightarrow{E} B$

"If Substrate, product, Coenzyme affect the enzyme"

② Covalent Control (phosphorylation)
adding phosphate may activate or inhibit the E

• All enzymes when add (P) Phosphate to them become inactive

Except

active (P)
a. Lipase
b. Fructose 2,6 bisphosphatase / Fructose bisphosphatase II
c. Glycogen phosphorylase

Control Steps in Glycolysis Steps 1, 3, 10
"Irreversible Steps" ②

colysis

Enzyme for Glucose, Fructose, mannose — يحفز ثلاث سكريات

Step 1

"Phosphorylation"

Glucose + ATP $\xrightarrow{\text{Hexokinase, } Mg^{+2}}$ Glucose-6-P + ADP

* Phosphate is added from ATP

* this Step has Control :-

G-6-P can NOT get out the cell so this step traps it inside the cell

↑ Glucose-6-P, HexoKinase will be inhibited

* In Liver the Enzyme doing this Step called GlucoKinase, NOT inhibited by Glucose-6-P — متخصص الجلوكوز

Q:- if Glucose-6-P increase, all your body ↓ Glycolysis Except liver

↑ Km ↓ affinity

* Km GlucoKinase (الكبير) > Km HexoKinase (الصغير)

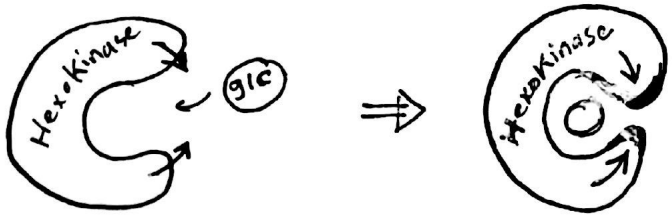
↓ lower affinity to glucose

↓ Higher affinity to glucose

So if Glucose level is low → hexoKinase (الصغير) functioning

if Glucose level is high → Glucokinase functioning (الكبير)

* Hexokinase bind to glucose by Induced Fit model



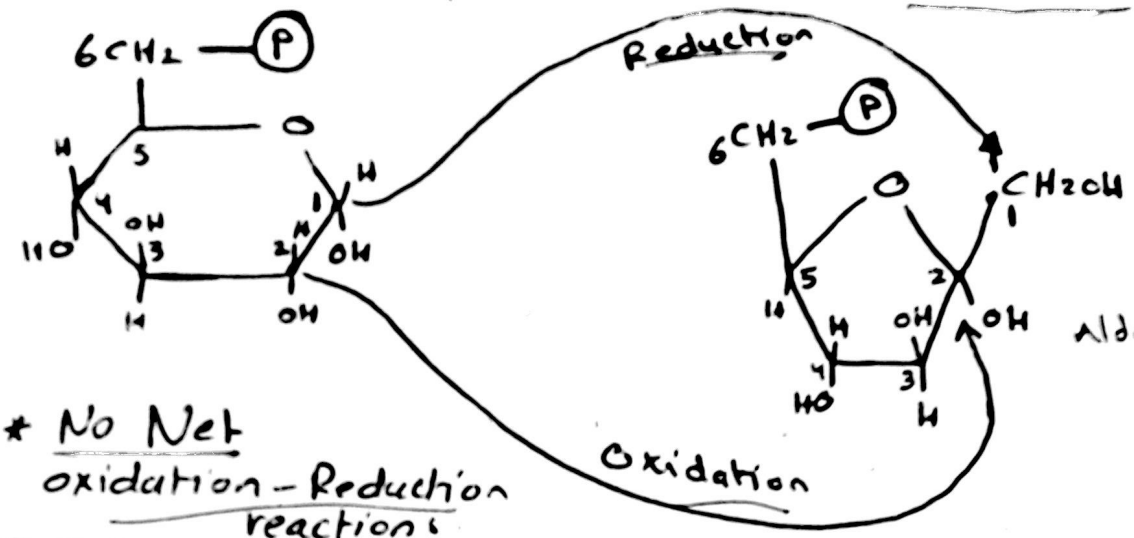
- the 2 loops come closer to each other
" large changes occurs"

all Kinases like this

P2 "Isomeration"

(Aldose) Glucose 6-P ⇌ (Ketose) Fructose-6-P

Glucophosphate Isomerase



Isomerase
Aldose ⇌ Ketose

* No Net oxidation-Reduction reactions

Step 3 "Phosphorylation"

Fructose-6-P —(PFK: Phospho-Fructo-Kinase, Mg+2; ATP → ADP)→ Fructose 1,6 Bisphosphate

"rate limiting step"

* this step is the most important Step in Glycolysis!

طريق واحد لا غير
هذا المركب إذا تكون
هو طريق الـ Glycolysis

this product Committed to glycolysis

Control:-

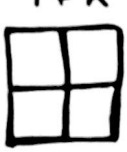
- If ATP ↑ → PFK will be inhibited
- If Fructose 2,6 bisphosphate ↑ → PFK will be activated

* PFK is a Tetramer (4 subunits)

the Subunits can be

M → Muscle
L → liver

PFK



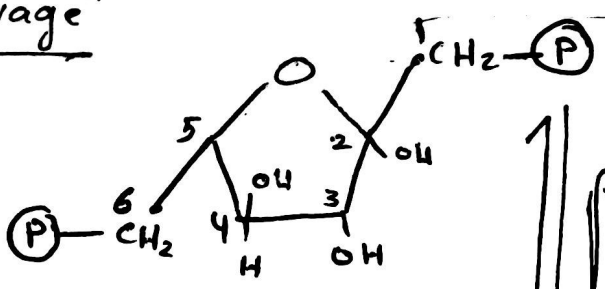
M4 → Muscle
L4 → liver
M2L2
M3L1
M1L3 } RBCs & other tissues

} Isozymes الإنزيمات المختلفة لنفس الإنزيم

differ in some a.a
can be separated by electrophore

Cleavage"

Fructose 1,6 Bisphosphate



Aldolase

lysine and Cystein are important for it's function

* Reverse aldol condensation

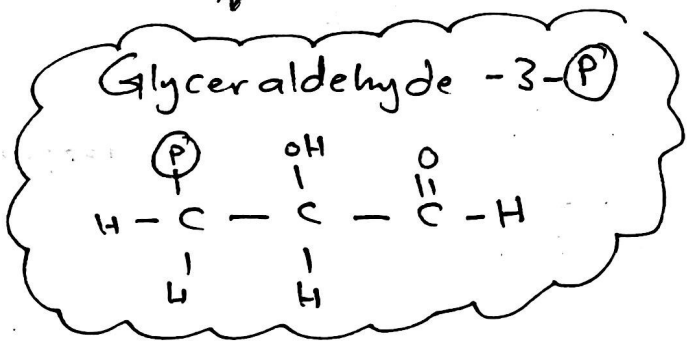
(This step can be reversed to F1,6 Biphosphate)

Glyceraldehyde-3-(P) + Dihydroxyacetone-(P)

Step 5

"Isomerahion"

Triose-(P) Isomerase



* This is the End of phase I

In this phase:-

Glucose ⟶ 2 Glyceraldehyde-3-(P)

and 2 ATP are Consumed in steps 1, 3

: payoff phase مرحلة التعويض

Now on, you should remember that we have 2 Glyceraldehyde-3-P ← لذلك نضرب التفاعل في 2

Step6 (يعطي طاقة) ΔG -ve (يحتاج طاقة) ΔG +ve

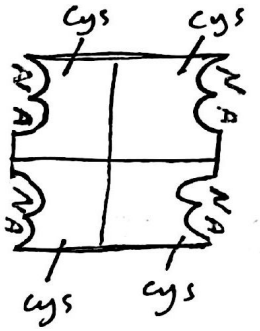
" Oxidation + phosphorylation "

Glyceraldehyde-3-P $\xrightarrow[\text{Dehydrogenase}]{\text{Glyceraldehyde-3-P}}$ 1,3 Bisphosphoglycerate

NAD+ NADH

* So, in this step there are
  - oxidation
  - phosphorylation, but (P) here not from ATP, it's phosphate ion P_i (Mixed acid anhydride)

* this Enzyme - Glyceraldehyde-3-P dehydrogenase - belong to a family of Enzymes Called - NADH-linked-dehydrogenase
  - Tetramer, 4 identical Subunits
  - Each subunit Contain Cyskein
  - Each subunit bind to NAD^+ or NADH
  - there is a specific site for Nicotinamide Ring
  - there is a specific site for Adinine Ring



Step 7 " Transfer of phosphate group to ADP "

1,3 Bisphoosphoglycerate $\xrightarrow[\text{Kinase / } Mg^{+2}]{\text{phosphoglycerate}}$ 3-phosphoglycerate

ADP (P) ATP

* In this step we produce ATP by process called Substrate-level-phosphorylation : (P) group transferred from Substrate "Organic Compound" to ADP producing ATP

UP to this Step, Net ATP produced is Zero

" Isomeration "

3 - phosphoglycerate ⇌ (Phosphoglycerate Mutase / Mg^{+2}) 2 - phosphoglycerate

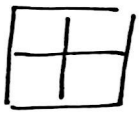
Step 9 : "Dehydration"

2 - phosphoglycerate ⇌ (loss H_2O; Enolase / Mg^{+2}) Phospho enol-pyruvate

Step 10 " Transfer of phosphate group to ADP"

Phosphoenol-pyruvate + ADP —(Pyruvate Kinase, Mg^{+2})→ pyruvate + ATP

* Control : ATP ↑, Alanine ↑ } inhibit Pyruvate Kinase
  Fructose 1,6 Bisphosphate ↑ → activation
* pyruvate Kinase is a Tetramer



M : Muscles
L : liver
A : other tissue

Liver isozyme (L_4) also has Covalent Control
↓ Glucose → Glucagon → L_4-P inactivated ↓ Glycolysis in Liver

Overall Reaction of Glycolysis

Glucose → 2 pyruvate

step 1, step 3 > 2 ~~ATP~~ → 2 ~~ADP~~

step 6 ← 2 NAD^+ → 2 NADH

step 7 − 2 ~~ADP~~ → 2 ~~ATP~~

step 10 − 2 ADP → 2 ATP

Glucose + 2 NAD^+ + 2 ADP → 2 pyruvate + 2 NADH + 2 ATP

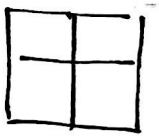
aerobic Glycolysis

خطوة اضافية

Pyruvate + NADH ⇌ (Lactate Dehydrogenase / LDH) ⇌ lactate + NAD+

* The aim of this step is to Regenerate NAD^+, to be used in Step 6

LDH is a Tetramer, belong to NADH-linked-dehydrogen



M: Muscle
H: Heart

M_4 → LDH_5 → in skeletal muscle

H_4 → LDH_1 → in Heart muscle

M_2H_2
M_3H_1
M_1H_3
} in Red blood cells.

* If person have Heart attack (MI), H_4, M_1H_3 isoenzymes ↑ in Serum

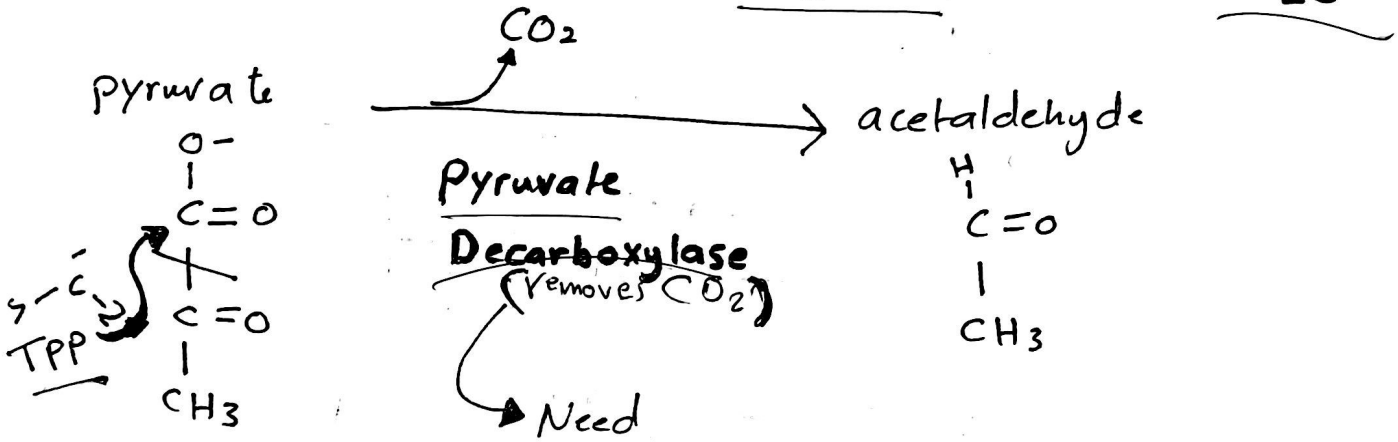
By this we Can diagnose MI

ientation التخمر

Pyruvate (3C) ⟶ Ethanol (2C)

This occurs in 2 steps

① Pyruvate (3C) —decarboxylation→ Acetaldehyde (2C) —Reduction→ Ethanol (2C)



Pyruvate Decarboxylase (removes CO_2)

Need
- Mg^{+2}
- TPP "Thiamine pyrophosphate" B_1

TPP

- Contain Carbon atom between S, N is highly active
- this Carbon form Carbanion ($\bar{C}$)
- $\bar{C}$ attack C=O of pyruvate
- CO_2 split off, ~~TPP bounded to acetaldehyde~~ ~~Ethanol Acetaldehyde~~

② Acetaldehyde + NADH —**alcohol Dehydrogenase**→ Ethanol + NAD^+

NAD^+ → To Recycle NAD^+

alcohol dehydrogenase
- NADH - linked dehydrogenases
- Tetramer

verall Reaction of anaerobic Glycolysis

Glucose ⟶ 2 Lactate

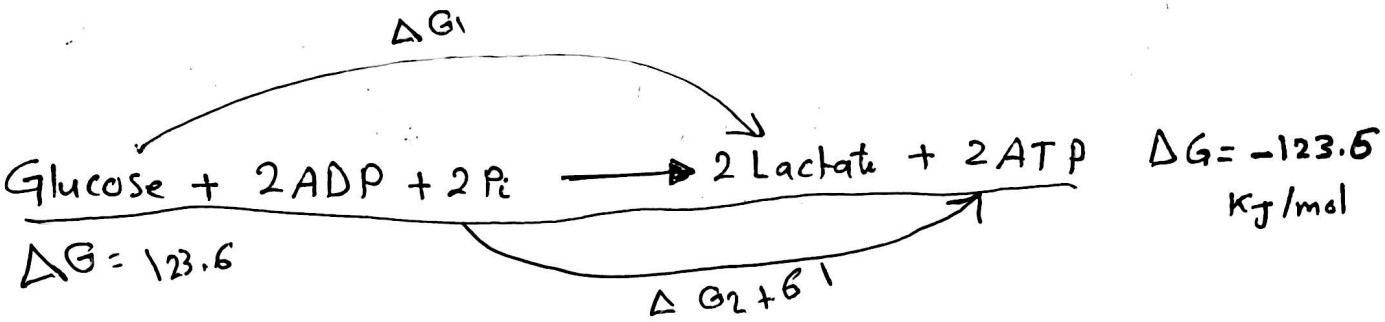
skp 1, skp 3 > 2 ~~ATP~~ ⟶ 2 ADP

skp 6 ← 2 ~~NAD+~~ ⟶ 2 NADH

skp 7 ← 2 ~~ADP~~ ⟶ 2 ATP

skp 10 ← 2 ADP ⟶ 2 ATP

الخطوة الاضافية 2 NADH ⟶ 2 NAD+



Glucose ⟶ 2 lactate ΔG_1 ??

+

$2ADP + 2P_i$ ⟶ 2 ATP $\Delta G_2 = +61$ Kj/mol

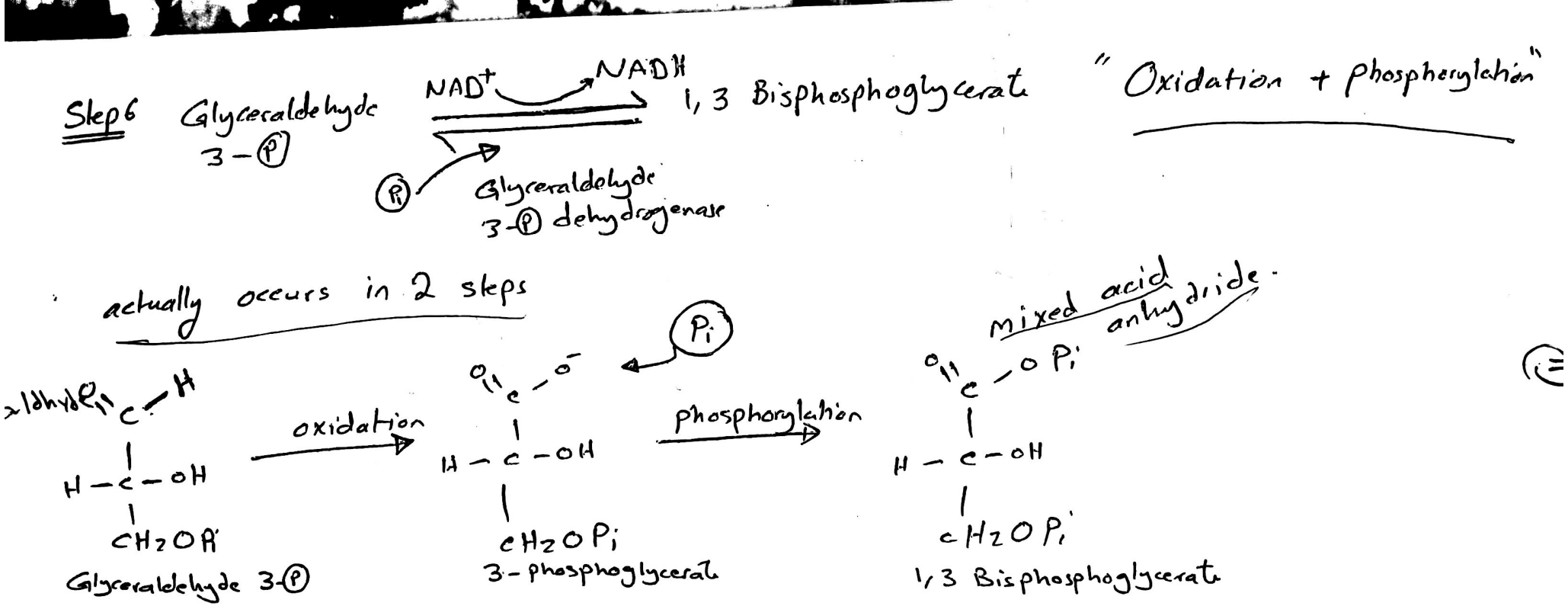
$\Delta G_{overall} = -123.6$ Kj/mol

So $\Delta G_1 + \Delta G_2 = -123.6$

$\Delta G_1 = -123.6 - 61 = -184.6$ Kj/mol

Efficiency of Coupling $= \frac{61}{184.6} \times 100\% \simeq$ **33%**

Dr. Tariq Jibril
07909799188
wish you the Best



The amino acid cysteine is important in adding a second phosphate to glyceraldehyde phosph in glyceraldehyde-3-phosphate dehydrogenase reaction.

True

False

ANS: A

Which of the following enzymes forms a thioester using a cysteine residue as a key intermediate?

a. hexokinase

b. triose phosphate isomerase

c. glyceraldehyde-3-phosphate dehydrogenase

e. enolase

ANS: C

Step	Kcal ΔG^{o1} at standard state	Kcal ΔG inside the Body
1	-16.7	-33.9
2	+1.67	-2.92
3	-14.2	-18.8
4	+23.9	-0.23
5	+7.56	+2.41
6	2(+6.2)	2(-1.29)
7	2(-18.8)	2(+0.1)
8	2(+4.4)	2(0.83)
9	2(+1.8)	2(+1.1)
10	2(-31.4)	2(-23.0)
overall	-123.5	-127.6

* Some steps in glycolysis have + ΔG^{o1} at standard state but have - ΔG at physiological condition (Step 4)

* The most Excergonic reaction in glycolysis is step 1 then 10 then 3

* Some steps (5, 7, 8, 9) in glycolysis have + ΔG inside the body but the reaction continue because the product consumed rapidly in the next steps shifting the equilibrium forward

Q: which of the following is NOT true ?

a. Every reaction in a metabolic Pathway must have - ΔG or the pathway Cannot run

b. Largest - ΔG is the hexokinase reaction

c. the overall pathway of glycolysis has -ve ΔG

Q: The ΔG values for glycolytic reactions at physiological condition may be excergonic, even though the ΔG^{o1} may be Endergonic

True False

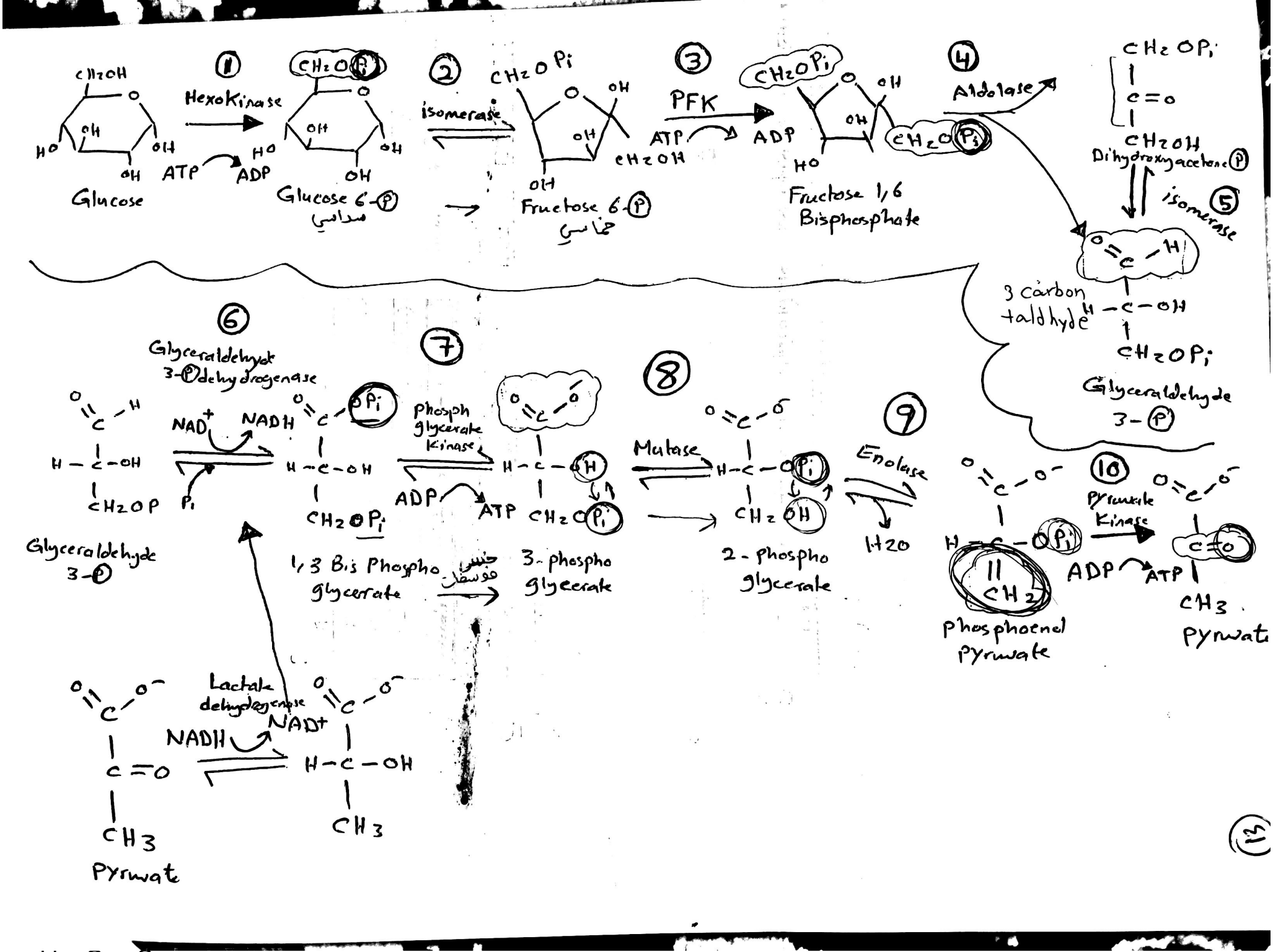
Q: The equilibrium for isomeration of dihydroxyacetone (P) to glyceraldehyde 3-P is favord because

a. the ΔG^{o1} is -ve

b. glyceraldehyde 3-(P) being contineously drained off for subsequent reactions

c. driven by ATP hydrolysis

d. the value of the equilibrium constant favor the reaction



Q=1 In aerobic metabolism, what is the fate of pyruvate produced by glycolysis?

a. Pyruvate loses carbon dioxide, and the remaining two carbon atoms become linked to coenzyme A.
b. Pyruvate loses carbon dioxide, producing acetaldehyde, which, in turn, is reduced to ethanol.
c. Pyruvate is reduced to lactate.
d. None of these

ANS: A

Q=2 Which of the following is not an end product of glucose metabolism via either aerobic or anaerobic means?

a. ethanol
b. carbon dioxide
c. lactate
d. fructose
e. all of these are end products of glucose metabolism

ANS: D

Q=3 In the conversion of glucose to pyruvate, how many of the actual steps involve electron transfer?

a. none
b. 1
c. 2
d. 3
e. 4

ANS: B

Q=4 The phosphorylation of glucose to glucose 6-phosphate

a. is so strongly exergonic that it does not require a catalyst.
b. is an exergonic reaction not coupled to any other reaction.
c. is an endergonic reaction that takes place because it is coupled to the exergonic hydrolysis of ATP.
d. is an exergonic reaction that is coupled to the endergonic hydrolysis of ATP.

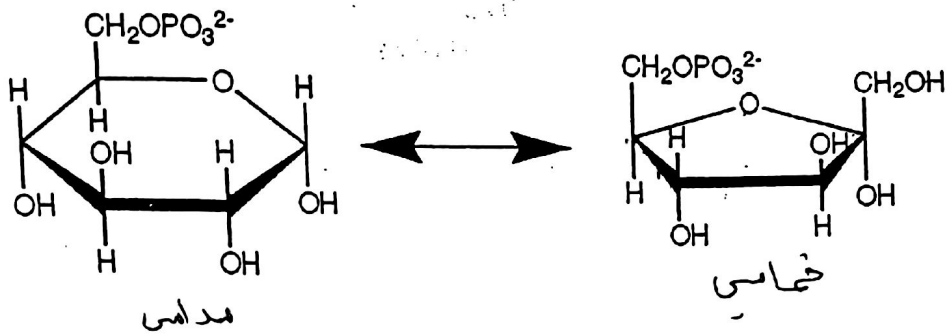
ANS: C

Q=5 The enzyme glucokinase

a. phosphorylates a number of different sugars, including glucose, fructose, and mannose.
b. specifically phosphorylates glucose rather than other sugars.
c. is the only kinase involved in glycolysis.
d. none of the above.

ANS: B

Q=6 Which enzyme catalyzes the reaction shown?



Q=7 Which of the following sugars can be a substrate for hexokinase?

a. glucose
b. fructose
c. mannose
d. all of these
e. none of these

ANS: D

Q=8 Which enzyme is the key regulatory enzyme in glycolysis?

a. Glyceraldehyde-3-phosphate dehydrogenase
b. Enolase
c. Phosphofructokinase
d. Aldolase

ANS: C

Q=9 Which of the following exercise(s) allosteric control in the reaction of phosphofructokinase?

a. ATP
b. fructose 2,6-*bis*phosphate
c. both of these
d. neither of these

ANS: C

Q=10 The reaction of fructose 1,6-*bis*phosphate to give glyceraldehyde-3-phosphate and dihydroxyacetone phosphate is an example of

a. a reverse aldol condensation.
b. hydrolysis.
c. oxidation.
d. dehydration.

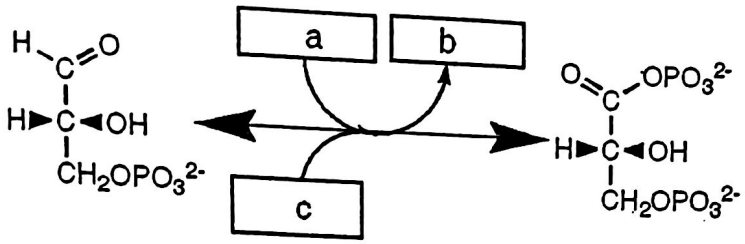
ANS: A

Q=11 In glycolysis, ATP is synthesized by

a. substrate-level phosphorylation.
b. oxidative phosphorylation.
c. photophosphorylation.
d. both substrate-level and oxidative phosphorylation.
e. all three of the above methods.

ANS: A

Q! =12 Which group of small molecules best fit the boxes associated with the reaction shown?

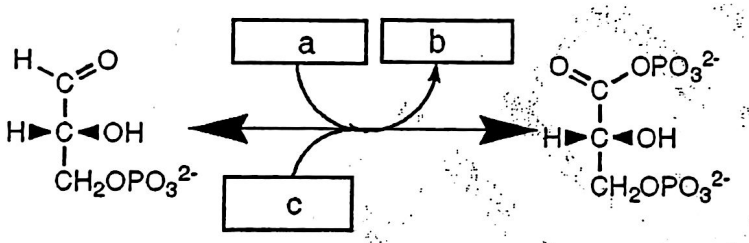


	a	b	c
I.	ATP	ADP	H_2O
II.	NADH	NAD^+	P_i
III.	NAD^+	NADH	H_2O
IV.	NAD^+	NADH	P_i

a. I
b. II
c. III
d. IV

ANS: D

Q! =13 What kind of enzyme catalyzes the reaction shown?



a. an epimerase
b. an isomerase
c. a mutase
d. a dehydrogenase

ANS: D

Q! =14 During glycolysis, ATP is synthesized from ADP and a phosphate group transferred from an acid anhydride.

True
False

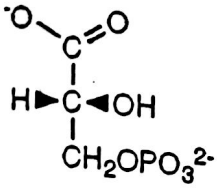
Q! =15 The fate of NADH from glycolysis depends on whether conditions are anaerobic or aerobic.

True
False

ANS: A

Q: 16

What is the name of the pictured glycolytic intermediate?



a. 1-phosphoglycerate
b. glyceraldehyde-3-phosphate
c. dihydroxyacetone phosphate
d. 3-phosphoglycerate

ANS: D

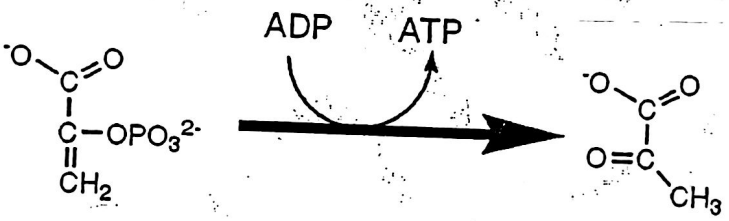
Q: 17

Which of the following is required for substrate-level phosphorylation?
a. The substrate must contain multiple phosphate groups.
b. Molecular oxygen must present.
c. The standard free energy of the hydrolysis reaction is more negative than that for hydrolysis of the new phosphate compound being formed.
d. All of the above are necessary for substrate-level phosphorylation.

ANS: C

Q: 18

Which enzyme catalyzes reaction the reaction shown?



a. enolase
b. pyruvate dehydrogenase
c. pyruvate kinase
d. phosphoglycerate mutase

ANS: C

Q: 19

During anaerobic metabolism in yeast, the carbons of glucose end up in
a. CO_2.
b. ethanol.
c. lactic acid.
d. both CO_2 and ethanol.
e. all of these

ANS: D

Q 20 Which of the following glycolytic enzymes forms a mixed anhydride from phosphoric acid?

a. hexokinase.
b. phosphofructokinase.
c. glyceraldehyde-3-phosphate dehydrogenase.
d. phosphoglycerate kinase.
e. pyruvate kinase.

ANS: C

Q = 21 In the conversion of glyceraldehyde 3-phosphate to 1,3-*bis*phosphoglycerate

a. an alcohol group is phosphorylated.
b. an alcohol is oxidized to an aldehyde.
c. an alcohol is oxidized to a carboxylic acid.
d. an aldehyde is oxidized to a carboxylic acid.

ANS: D

Q = 22 How many different reactions involve substrate-level phosphorylation during glycolysis?

a. 1
b. 2
c. 3
d. 4
e. 6

ANS: B

Q = 23 Anaerobic metabolism can occur in all these organisms or cells, except:

a. Yeast
b. Red blood cells
c. Muscle tissue that is working very fast
d. Lactobacillus in milk
e. Anaerobic metabolism can occur in all of these.

ANS: E

Q = 24 Which of the following enzymes of anaerobic metabolism is not tetrameric?

a. Hexokinase
b. Phosphofructokinase
c. Pyruvate kinase
d. Lactate Dehydrogenase

ANS: A