https://youtube.com/playlist?list=PLEfydt_NwyraLLUQRM1xCocAqGZizju6I&si=z965SM21iT2LtHn6

Glucose metabolism

youtube playlist
لشرح المواضيع "فيديوهات مرتبة"

أساسيات أتقنها لربط والتحليل

- metabolism
- catabolism
- Regulation of metabolism
- communication between cells
- Regulation of metabolism (Adenylyl cyclase)
- transport of glucose to cells
- Glycolysis
- phosphorylation of glucose
- steps of glycolysis
- Energy gain in aerobic / Anaerobic glycolysis
- Hormonal regulation of glycolysis
- In vitro inhibition of glycolysis
- Fate of pyruvic acid
- Aerobic phase of glucose oxidation

عكس بعض

- A oxidative decarboxylation of pyruvic acid
- Regulation of pyruvate dehydrogenase PDH enzyme
- Tricarboxylic acid cycle (Krebs cycle)
- steps of TCA (Krebs cycle)
- Energy gain in Krebs cycle
- The overall energy gain of glucose oxidation
- Defects in glycolysis
- Gluconeogenesis
- substrates for gluconeogenesis
- Reactions unique to gluconeogenesis
- pyruvate carboxylase PC enzyme
- Regulation of gluconeogenesis

Insulin (eating state)
- Released when blood glucose is high
- Lowers blood glucose
- Moves glucose into cells using GLUT-4 الوحيدة insulin dependent
- Works mainly in muscle and fat (adipose) tissue
- Promotes storage of glucose
- Promotes glycolysis

Glucagon (fasting state)
- Released when blood glucose is low
- Raises blood glucose
- Acts mainly on the liver
- Glucose leaves liver cells through GLUT-2 into the blood
- Stimulates: bidirectional
  - Glycogenolysis (breakdown of glycogen)
  - Gluconeogenesis (formation of new glucose)

Metabolism

- Most pathways can be classified into:

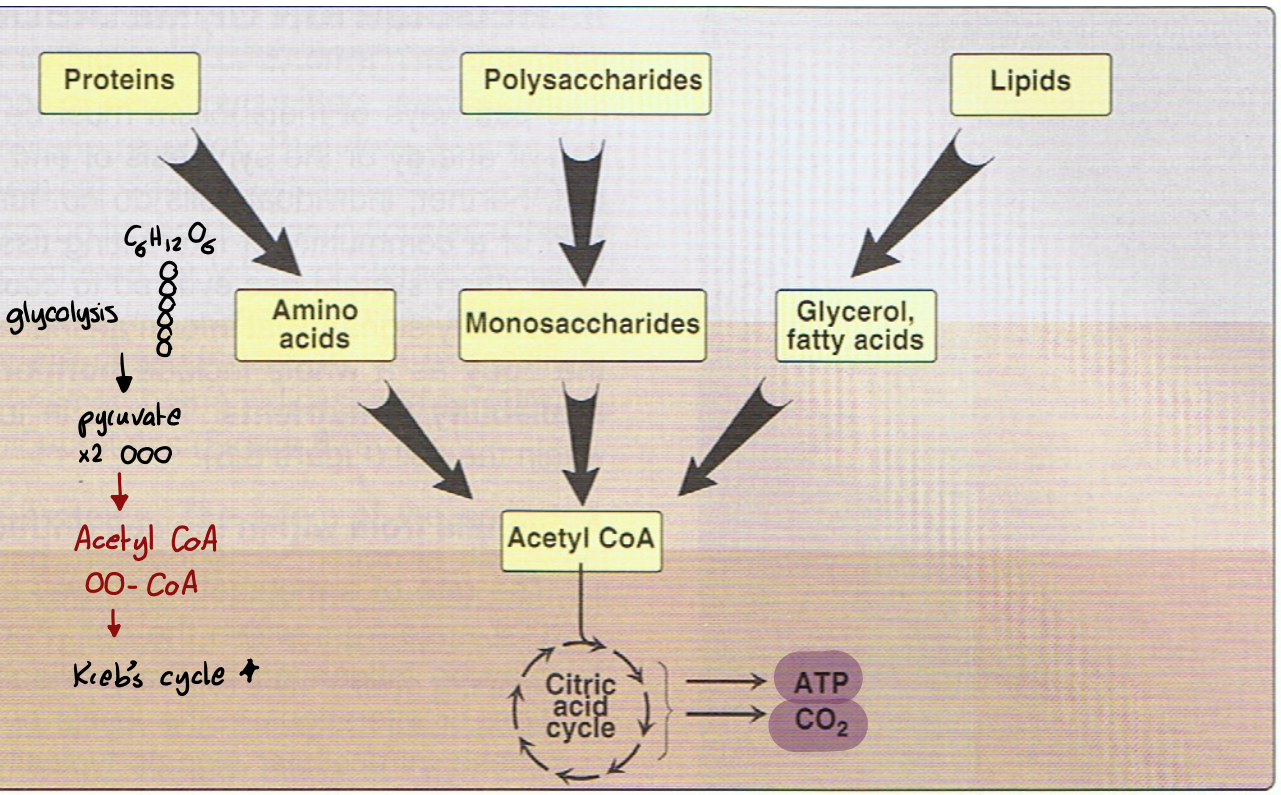
- convergent -

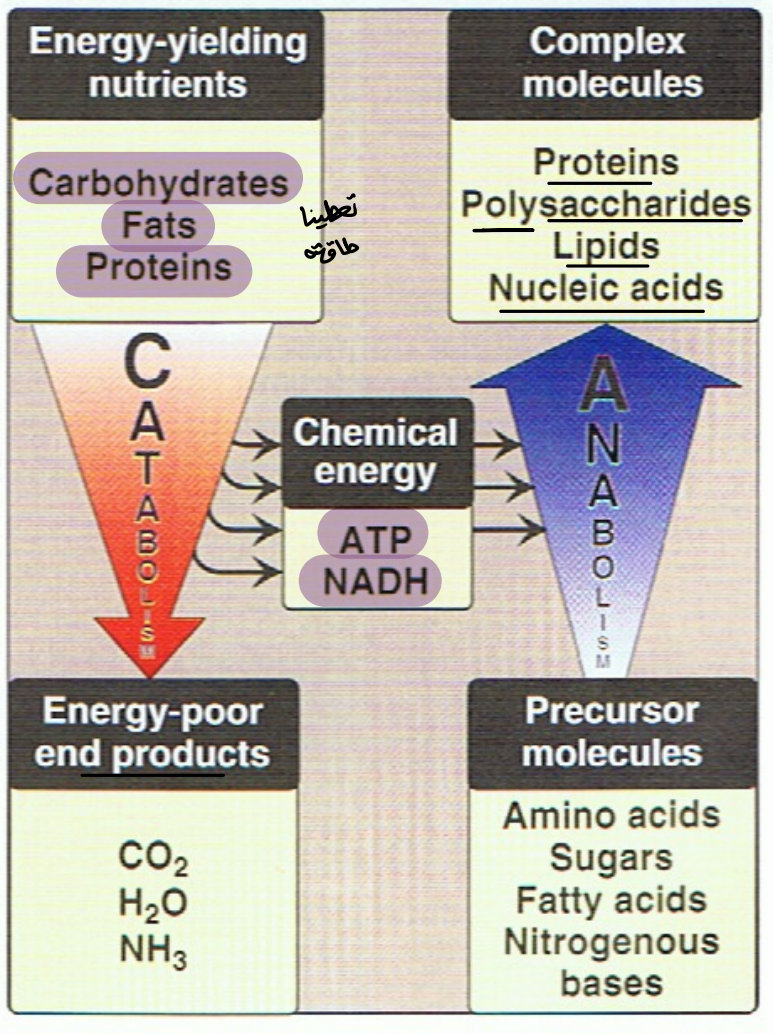
- هدم **Catabolism**: degrade complex molecules (proteins, carbohydrate and triglycerides) to few simple products (CO_2, NH_3 and H_2O). + NADH ATP Capture chemical energy to form ATP. Considered a **convergent** process (large no. of substances are degraded to few common end products). energy poor ending products

- divergent -

- بناء **Anabolism**: synthesize complex end products from simple precursors. Requires energy which is provided by the breakdown of ATP. Considered a **divergent** process (few starting precursors produce wide variety of complex substances)

Catabolism


Proteins
Polysaccharides
Lipids
Amino acids
Monosaccharides
Glycerol, fatty acids
$C_6H_{12}O_6$
glycolysis
pyruvate
x2 ooo
Acetyl CoA
oo- CoA
Kreb's cycle
Acetyl CoA
Citric acid cycle
ATP
CO_2


Energy-yielding nutrients
Carbohydrates
Fats
Proteins
تعطينا طاقة
Complex molecules
Proteins
Polysaccharides
Lipids
Nucleic acids
CATABOLISM
Chemical energy
ATP
NADH
ANABOLISM
Energy-poor end products
CO_2
H_2O
NH_3
Precursor molecules
Amino acids
Sugars
Fatty acids
Nitrogenous bases

https://chatgpt.com/share/69e0b99d-67a4-8330-bd17-6dd48ec65986 (explaining)

1- inside cell
2- between cells
3- second messenger
- Adenylyl cyclase

signals -> messengers -> enzymes

Regulation of metabolism (signaling + signal transduction)

intra جوا الخلية بين بعض
inter بين الخلايا

- Signals from within the cell (intracellular)

The rate of a metabolic pathway may be influenced by the availability of substrates, product inhibition, or alterations in the levels of allosteric activators or inhibitors.

- Communication between cells (intercellular)

Can be mediated by surface-to-surface contact, hormones and, in some tissues, by formation of gap junctions

- Second messenger systems

for signal transduction

Two of the most widely recognized second messenger systems are:

- The calcium/phosphatidylinositol system ← lipid metabolism (second messenger)
- The adenylyl cyclase system <- المهم جدًا

phosphatidyl + Inositol

phospho PO_4^{-3}

glycerol breakdown + fatty acids

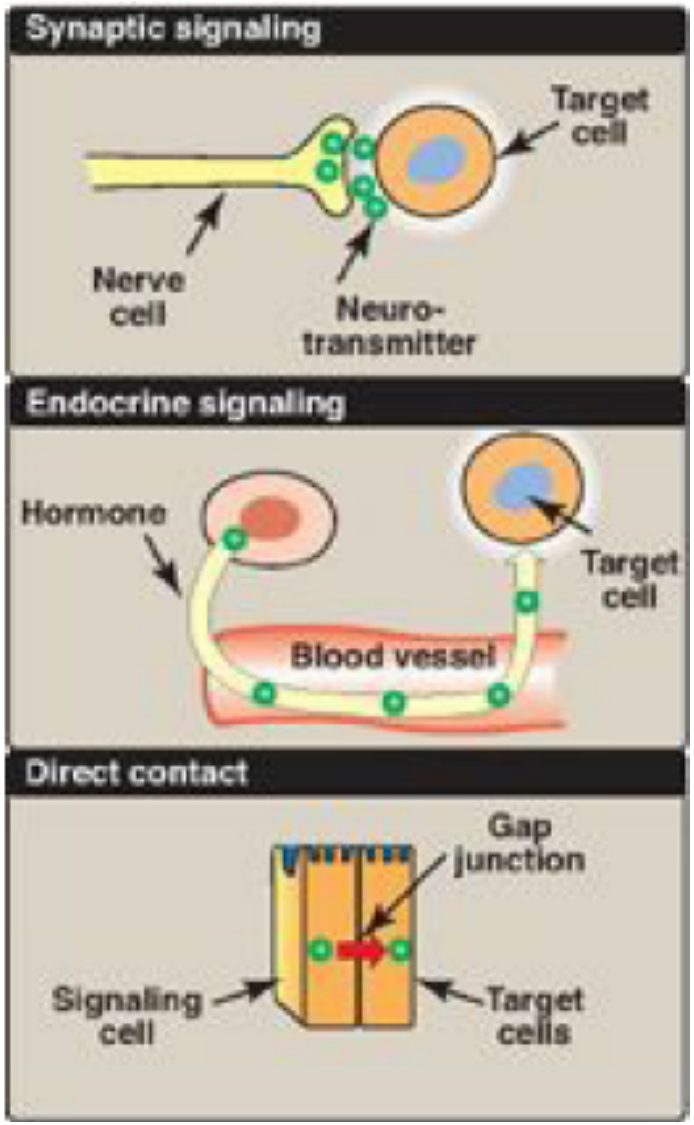
cyclic sugar alcohol

* شو يعني انخفضت طاقة الخلية إذا ratio of ATP : AMP

AMP ↑ ATP ↓

- AMP activates glycolysis (low energy signal)

Communication between cells



surface to surface contact

(neurotransmeter)

Hormones

pancreas → release insulin → Liver cells, Adipose tissues, muscle cells → Action

B-cells

lower blood glucose

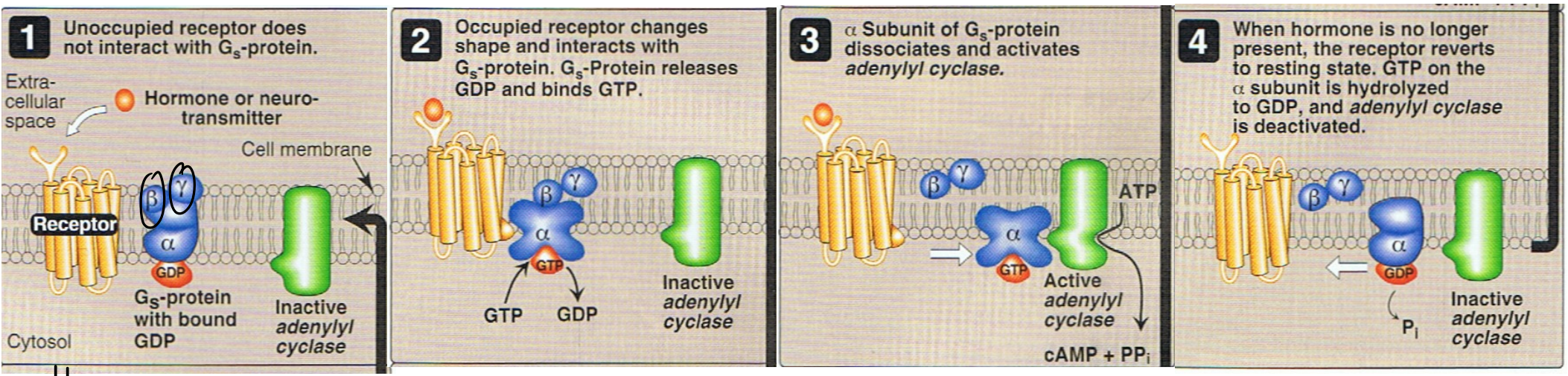
gap junctions

(direct contact)

Regulation of metabolism

Adenylyl cyclase (second messenger system)

(enzyme) ← ATP → (Adenylate cyclase) → cAMP (cyclic)] وظيفتها



- GTP-dependent regulatory proteins (Gs and Gi-proteins) يتكونوا من γ β α subunits
  stimulate inhibit
- Protein kinases: phosphorylates different proteins and enzymes
  Add add PO_4^{-3}
- Dephosphorylation of proteins: Phosphatases reverse the effect of kinases.
  remove PO_4^{-3}

شرح الصورة

ATP + GTP + adenylyl cyclase enzyme → cAMP + cyclic cGMP ★ cyclization

main function

Adenylyl cyclase enzyme mechanism 8

1. hormone release like glucagon or neuro transmeter like EP / NOR EP in blood stream

⇓ receptor ارتبط في Activation

receptor conformation حتى إذا لما يكون occupied مرتبط

ليشان إذا to interact with Gs proteins stimulatory] specifically α subunit

↓

GDP leaves

GTP binds

↓

α subunit GTP ينفصلوا عن β γ subunit-s

⇓

يرتبطوا في adenylyl cyclase

= Activation ويعمل وظيفته

ATP → cAMP + PP_i

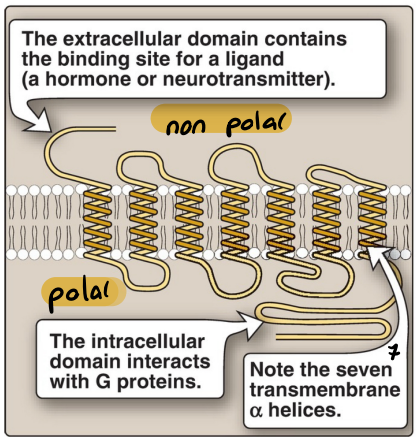
second messenger

↓

Activate protein Kinase = Add PO_4^{-3}

=

metabolism changes

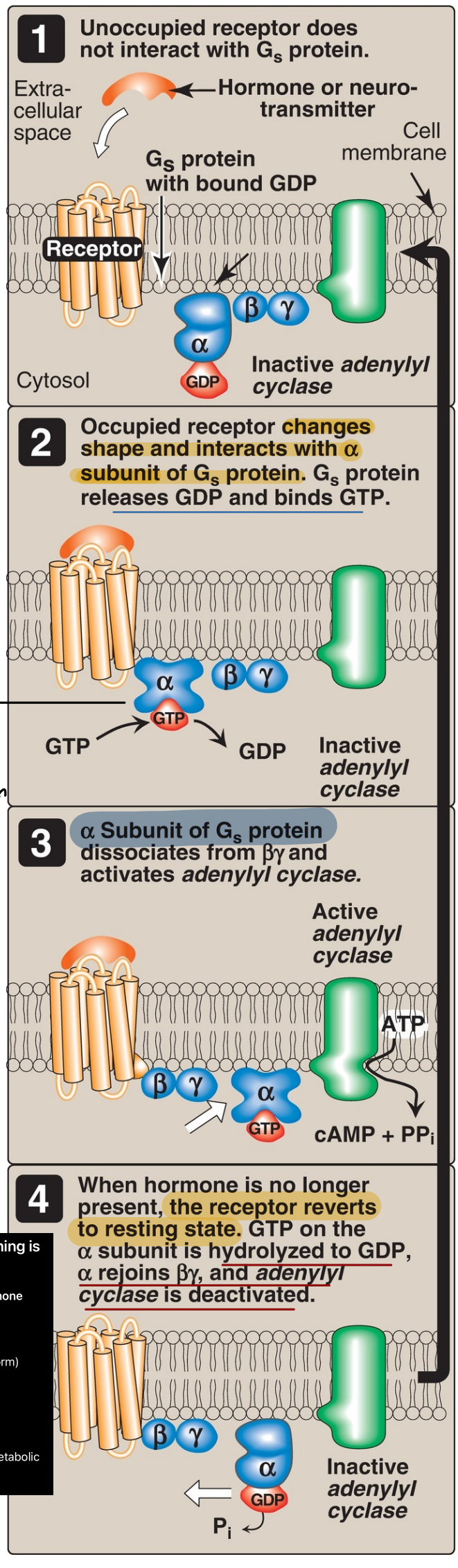


ال receptor لما يتكون من 7 α helices

non polar outside

polar inside

membrane جوا ال non polar بتكون مواجهة lipophilic part



لاحظوا تغير الشكل Conformation

Step 1: Resting state (nothing is happening yet)

- The receptor is **empty (no hormone bound)**
- Gs protein is inactive
- It has **GDP attached** (inactive form)
- Adenylyl Cyclase is OFF

👉 Key idea:

> No hormone = no signal = no metabolic change

⚡ High-yield exam triggers

If you see:

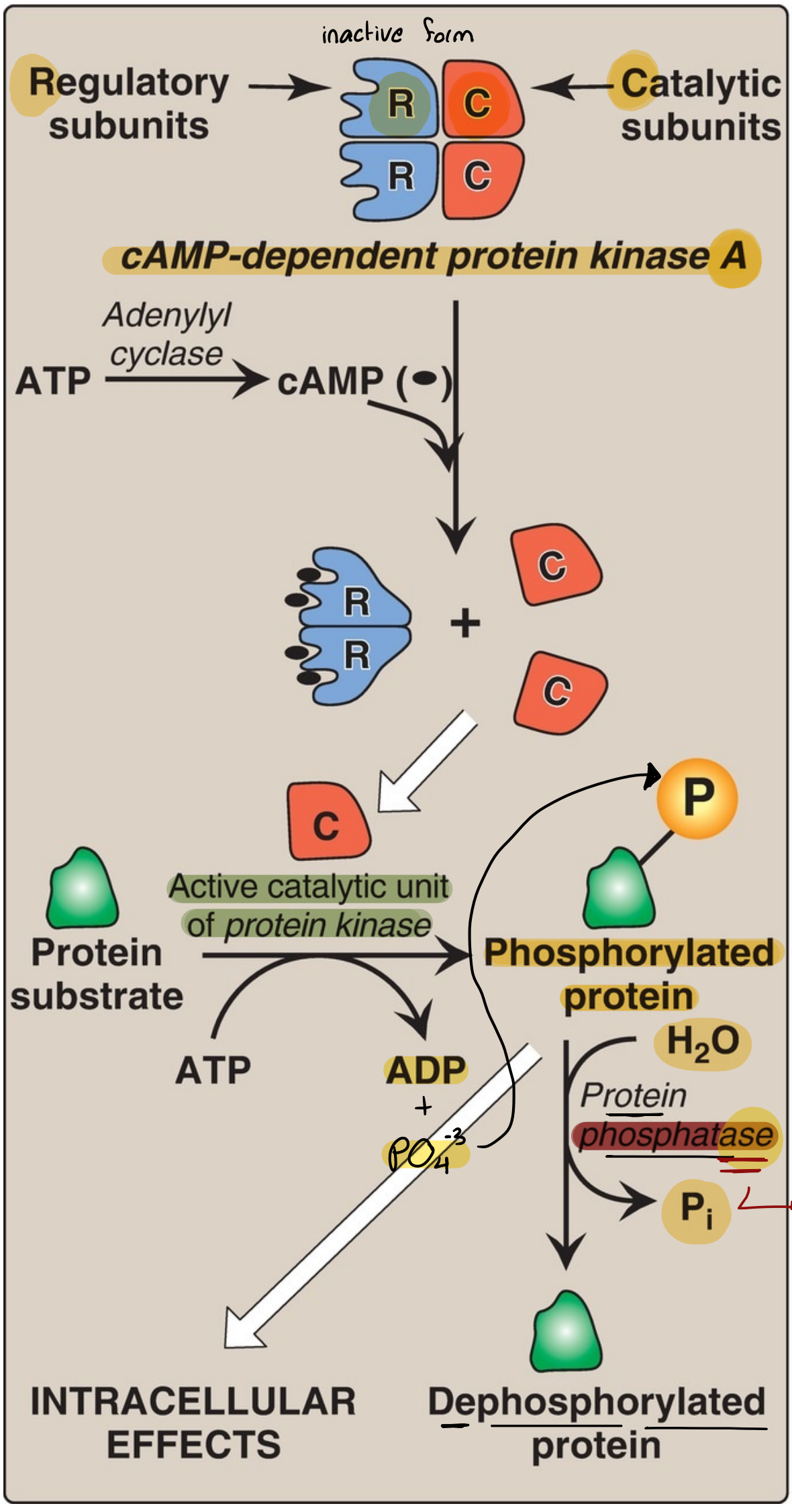
- "Gs protein" → think **increase cAMP**
- "GDP → GTP" → activation step
- "ATP → cAMP" → adenylyl cyclase
- "GTP → GDP" → signal termination

very very important 8

PO_4^{-3} group منفنا = protein Kinase فعلنا ← cAMP انتجنا ٥ نكمل إلي بلشنا

رح يصير Activation لـ cAMP dependent protein Kinase A

← من اسمها معتمدة على cAMP



1 cAMP bind to R regulatory subunits → shape changes

↳ catalytic subunits are released

Active

وظيفتها إنزيم PKA

protein phosphorylate

ATP → ADP صار عندي PO_4^{-3} منوين نجيب؟

When cAMP → PKA is activated... what does the body want? Fasting state

👉 It usually means:

- "I need energy NOW" (stress, fasting, exercise)

= glycogen breakdown = gives energy

(glycogenlysis)

glycogen إلي تكسر enzymes الـ تفعل Activated

inhibited طيب الإنزيمات إلي تصنع إذا

⇒ dephosphorylation of proteins

remove PO_4^{-3}

Transport of glucose to cells

RBCs ✓ Blood ✓ Fetus ✓ BBB > glut 1 > Placenta, Neurons, Kidneys > glut 3

✓ Kidneys ✓ S small intestine ✓ Liver ✓ Pancreas > glut 2 > Muscle, Fats (Adipose tissues) > glut 4

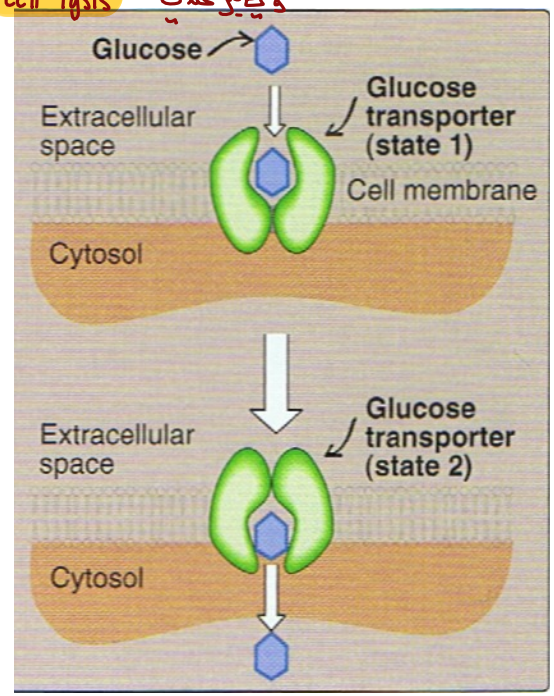
glucose أكثر organs تستهلك — الأهم — insulin dependent

- Glucose cannot diffuse directly into cells, but enters by one of two transport mechanisms:
  - [1] Na-independent, facilitated diffusion
  - [2] Na-monosachacide cotransporter system — ATP energy يحتاج
- Na-independent, facilitated diffusion transport system
  - In facilitated diffusion, glucose movement follows a concentration gradient
  - Tissue specificity of GLUT gene expression:
    - GLUT-3 is the primary glucose transporter in neurons
    - GLUT-1 is abundant in erythrocytes and brain, but is low in adult muscle — RBC in blood
    - insulin dependent ← GLUT-4 (in adipose tissue and skeletal muscle). Their number is increased by insulin
    - bidirictional ← GLUT-2 (in the liver, kidney, and β cells of the pancreas) can either transport glucose into these cells or from it depending on blood glucose levels

glucose ينقل
galactose
fructose

transpolt from cells يدخل

insulin independen- الباقي كلهم
يعني مريضنا السكري لما يرتفع عنده السكر بصير يدخل
from high conc → low conc الخلايا
water تسحب ← osmotically active تصير
cell lysis وبصير عندي



Transport of glucose to cells

only fructose entry ★

- GLUT-5 is the primary transporter for fructose in the small intestine and the testes
- ★ مهمة تنزل تجيب عليها اسئلة GLUT-7 (in the liver and other gluconeogenic tissues) mediates glucose تدفق flux across the endoplasmic reticular membrane.
- **Na-monosaccharide cotransporter system:** is an energy-requiring process that transports glucose against a conc. gradient
  - This system is a carrier-mediated process in which the movement of glucose is coupled to the conc. gradient of Na, which is trasported into the cell at the same time.
  - It occurs in the epithelial cells of the intestine, renal tubules, and Choroid plexus.
  - This system is mediated by a family of fourteen glucose transporters in cell membranes (GLUT-1 to GLUT-14)
  - They exist in the membrane in two conformational states. Extracellular glucose binds to the transporter, which then alters its conformation, transporting glucose across the cell membrane.

🧠 GLUT-7 (simple summary)

تلخيص لمحكي الدكتورة عن glut 7

- **Location:** Endoplasmic reticulum (ER) in liver and kidney cells
- **Role:** Moves glucose **out of the ER into the cytosol**

🔄 Why it exists (in one pathway)

During **gluconeogenesis**:

1. Glucose-6-phosphate enters the ER
2. Inside ER: it is converted to glucose by glucose-6-phosphatase
3. Glucose cannot stay in the ER
4. **GLUT-7 transports glucose out of the ER**

🎯 One-line meaning

👉 GLUT-7 = "ER exit transporter for glucose after it is formed"

.4. Glucose uptake by:

A. brain cells is through energy-requiring (active) transport.

B. intestinal mucosal cells requires insulin.

C. liver cells is through facilitated diffusion involving a glucose transporter.

D. most cells is through simple diffusion up a concentration gradient.

Correct answer = C. Glucose uptake in the liver, brain, muscle, and adipose tissue is down a concentration gradient, and the diffusion is facilitated by tissue-specific glucose transporters (GLUT). In adipose and muscle tissues, insulin is required for glucose uptake. Moving glucose against a concentration gradient requires energy and is seen with the sodium-dependent glucose cotransporter 1 (SGLT1) of intestinal mucosal cells.

Glycolysis

- Glycolysis occurs in the cytosol of all tissues and cells
- Defined as oxidation of glucose to pyruvic acid (in the presence of O2, Aerobic) and to lactic acid (in the absence of O2, anaerobic)
- The catabolism of 1 mol of glucose (6 C) produces 2 moles of pyruvate or lactate (3 C)

1 glucose → 2 pyruvate

(anaerobic)

- Lactate is produced only in:
- RBC: as there is no mitochondria
- Exercising muscles: lack of O2

Phosphorylation of glucose

Feature	Glucokinase (Liver/Pancreas)	Hexokinase (Most Tissues)
K_m (Affinity)	High (Low affinity)	Low (High affinity)
V_{max} (Capacity)	High (Can process a lot)	Low (Saturates quickly)
Function	Acts as a sensor; stores excess.	Ensures cell gets energy first.
Hypoglycemia	Inactive (Saves sugar for brain)	Active (Uses sugar for survival)

Key Takeaway: If Glucokinase had a low K_m (like Hexokinase), it would be "on" all the time, causing the pancreas to release insulin even when blood sugar is low, which would lead to dangerous hypoglycemia. Its "inefficiency" at low glucose levels is actually a vital safety feature.

- Phosphorylated sugar molecules do not readily penetrate cell membranes (no carriers, too polar to cross)

تخترق

- low Km low V max Hexokinase has broad substrate specificity and it is inhibited by the reaction product, glucose 6-phosphate

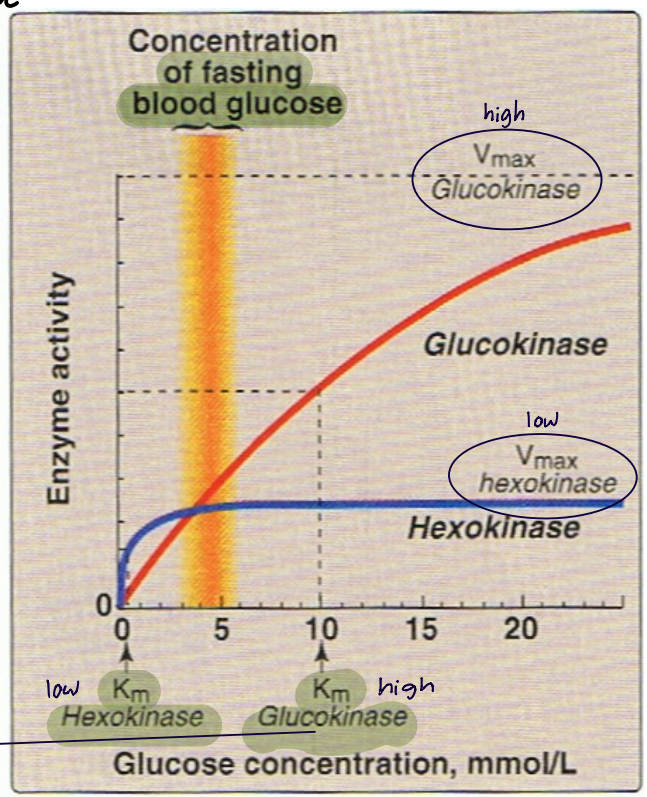
- It has a low Km (high affinity) for glucose and low Vmax

uncompetitive enzyme

- high Km (low affinity) high Vmax Glucokinase (similar broad specificity): In liver parenchymal cells and islet cells of the pancreas

- In β cells (pancreas), glucokinase functions as the glucose sensor (signaling), determining the threshold for insulin secretion. In the liver, the enzyme facilitates glucose phosphorylation during hyperglycemia.

- Glucokinase functions only when the intracellular concentration of glucose in the hepatocyte is elevated, such as during the brief period following consumption of a carbohydrate- rich meal



hyperglycemia تكون كتير عالية blood glucose level الي ما يعمل بشكل كامل

Steps of glycolysis

- Energy investing phase:
  - Step 1: glucose is phosphorylated to glucose-6-phosphate. The reaction is irreversible and is catalyzed by either glucokinase (GK) in liver cells and hexokinase (HK) in other tissues.
  - Step 2: glucose-6-phosphate is isomerized to fructose-6-phosphate by isomerase enzyme (reversible)
  - Step 3: fructose-6-phosphate is phosphorylated to F-1,6-diphosphate. The reaction is catalyzed by phosphofructo-kinase (PFK).
  - Step 4: F-1,6-bP is split by aldolase (reversible) into two trioses (Glyceraldehyde-3-P and dihydroxyacetone phosphate)

G-3-P DHAP

Steps of glycolysis

- Step 5: DHAP is isomerized to G-3-P which is catalyzed by isomerase

II- Energy generating phase:

- G-3-P is oxidized phosphorylated forming 1,3-biphosphoglycerate (1,3-BPG) and NADH which is catalyzed by glyceraldehyde 3-P dehydrogenase. NADH produces 2.5 ATP in ETC.
- Step7: 1,3-BPG gives its high energy phosphate to ADP to form ATP converting to 3-PG. This is catalyzed by phosphoglycerate kinase.
- Step 8: 3-PG is converted to 2-phosphoglycerate by mutase

Just moves PO_4^{-3} group from one carbon to another

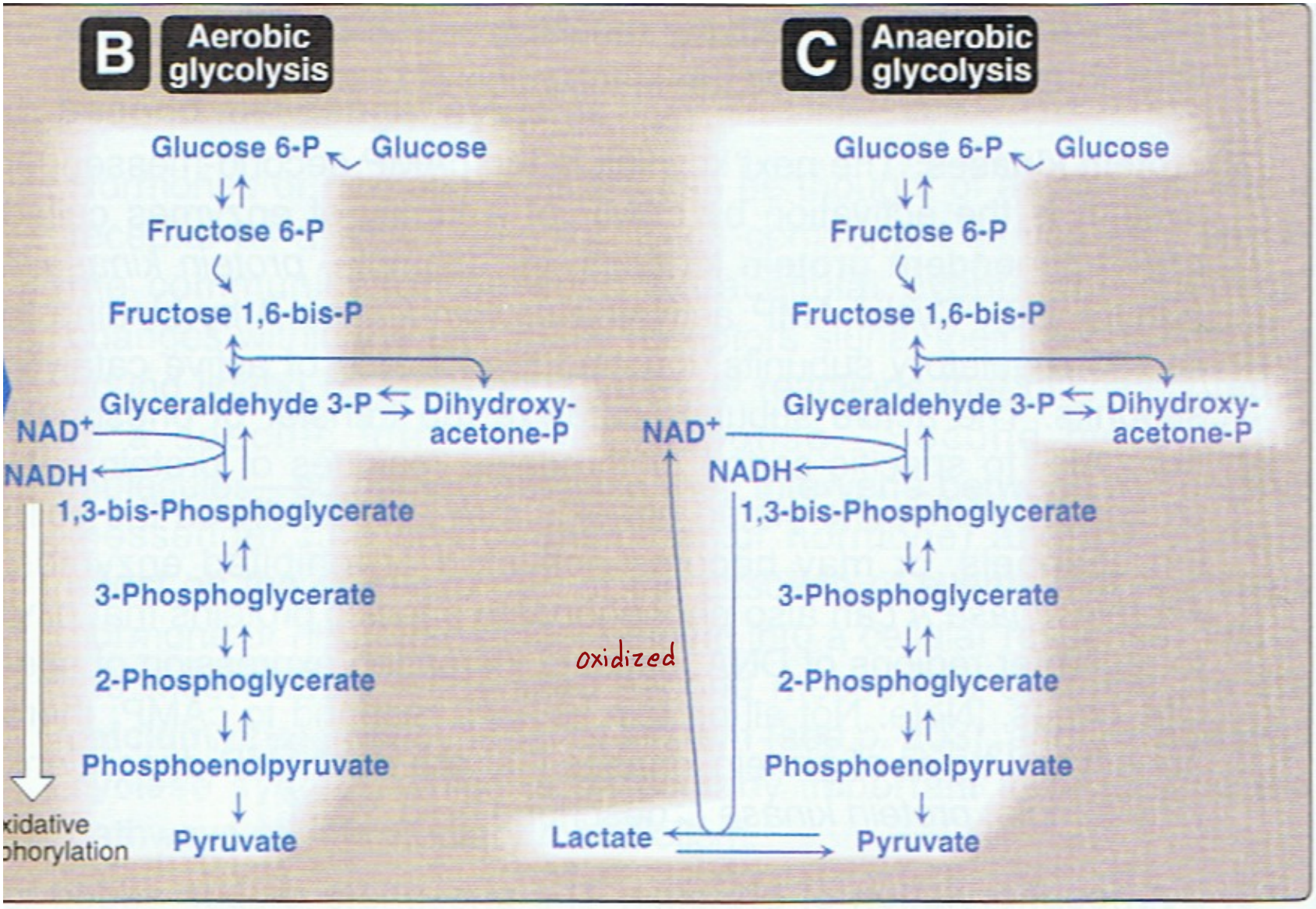
Steps of glycolysis

- Step 9: Enolase enzyme dehydrates 2-PG forming 2-phosphoenol pyruvate (PEP)
- Step 10:PEP is dephosphorylated giving its P to ADP to form ATP and converted to pyruvate. Rxn is irreversible and catalyzed by pyruvate kinase.
- Step 11: in RBC's and under anaerobic conditions NADH formed in step 6 is oxidized to give hydrogen and pyruvate which converts into lactate by lactate dehydrogenase

$2NADH \rightarrow 2NAD^{+} + 2H^{+}$

- **The Logic:** 7 out of 10 steps are reversible. The 3 irreversible "checkpoints" are:
  1. Hexokinase (Step 1)
  2. PFK-1 (Step 3)
  3. Pyruvate Kinase (Step 10)

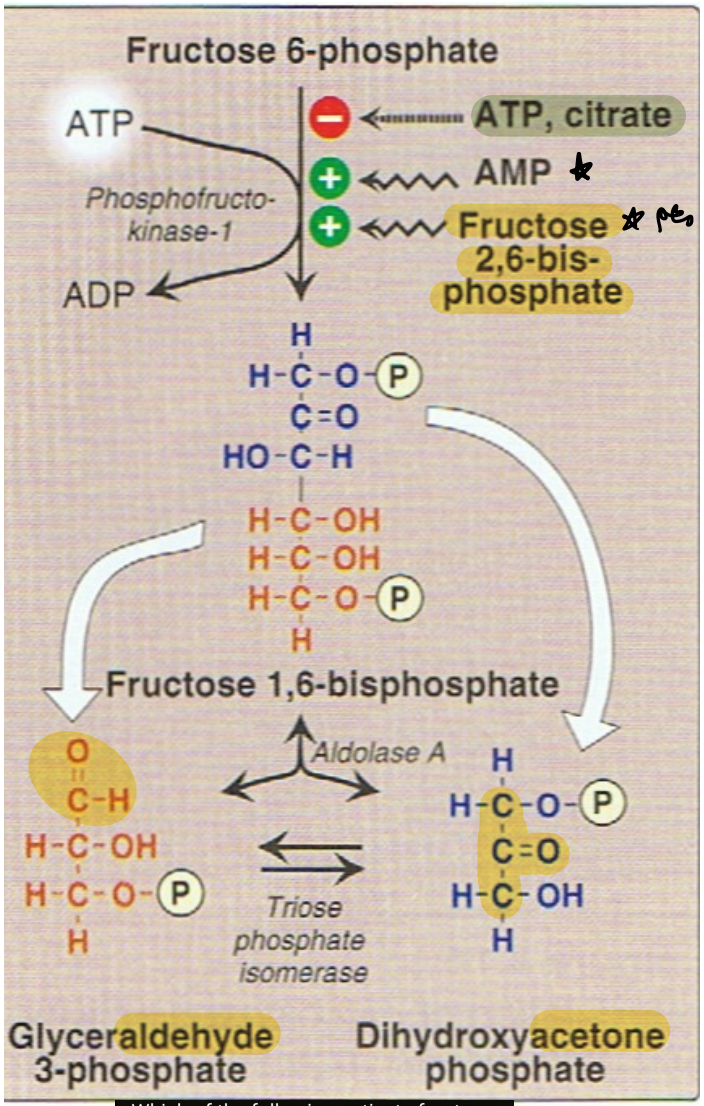
Schematic representation

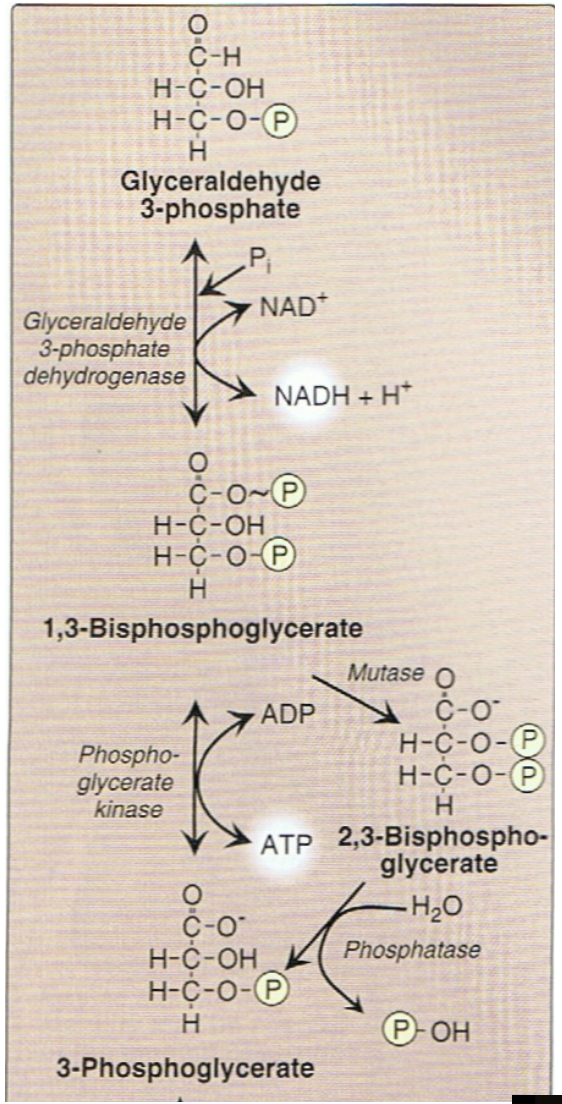


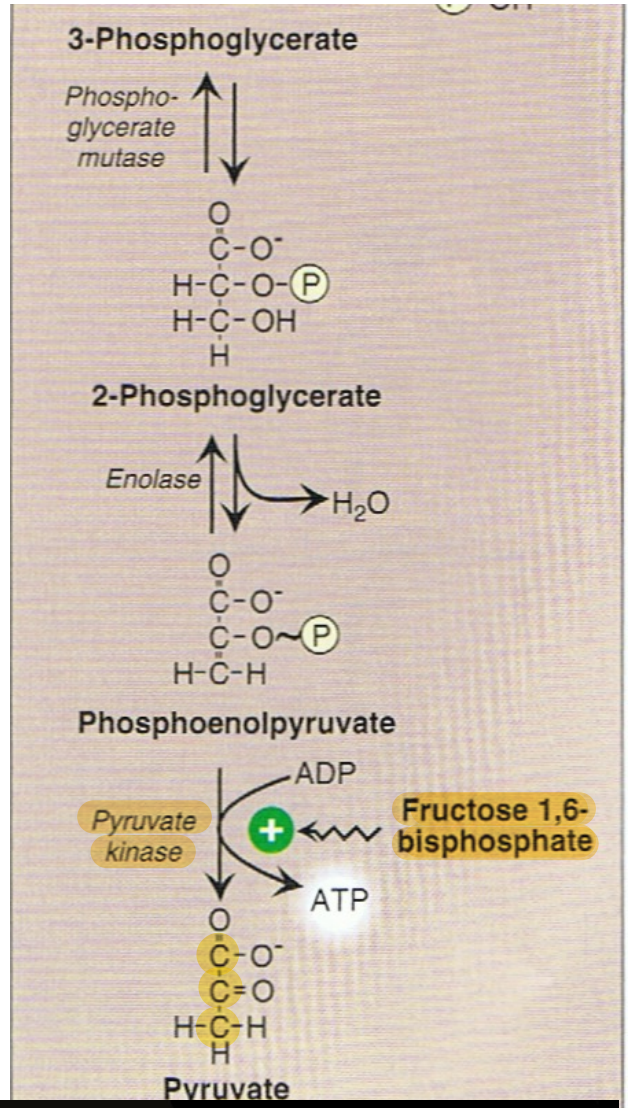
ATP + citrate inhibits PKA-1 → there is too much energy / TCL is full stop glycolysis

AMP
+
Fructose-2,6-bisphosphate
] stimulate PKA-1

we need energy
we want glycolysis







Which of the following activate fructose 6 phosphate :

1.ATP
2. Citrate
3.fructose 2,6 bisphosphate
4. Fructose 1,6 bisphosphate

Which of the following is activator of pyruvate kinase :
Fructose 1,6 bisphosphate

Energy gain in aerobic glcolysis

Net (aerobic glycolysis):

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

Step 1	Glucokinase (GK) irreversible	- 1 ATP
Step 3	Phosphofructokinase (PFK) irreversible	- 1 ATP
Step 7	Phosphoglycerate kinase	+ 2 ATP
Step 10	Pyruvate kinase (PK) irreversible	+ 2 ATP
☆ Step 6	2 NADH 1 NADH → 2.5 ATP 2 NADH → 5 ATP	+ 5 ATP
Net gain		+ 7 ATP

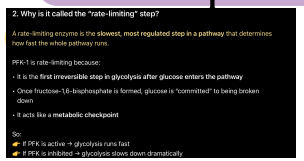
Anaerobic glycolysis

Step 1	Glucokinase (GK)	- 1 ATP
Step 3	Phosphofructokinase (PFK)	- 1 ATP
Step 7	Phosphoglycerate kinase	+ 2 ATP
Step 10	Pyruvate kinase (PK)	+ 2 ATP
Net gain		+ 2 ATP

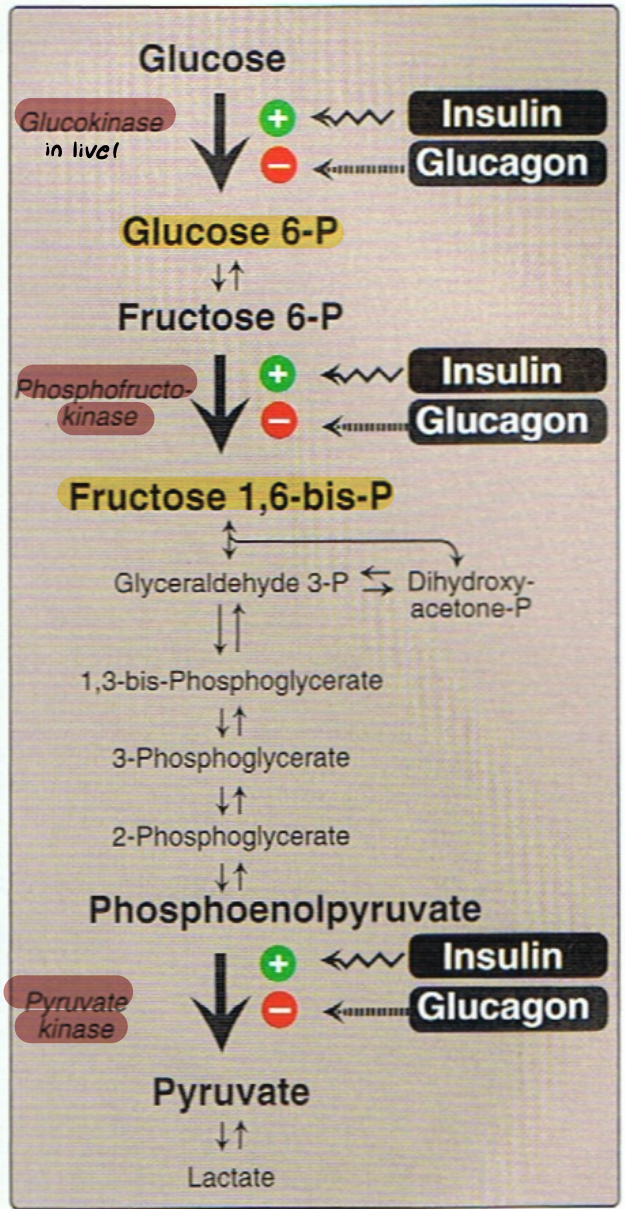
Hormonal regulation of Glycolysis

- GK (or HK), PFK and PK are the key enzymes of glycolysis. (irreversible)

- PFK is the most important and considered the rate limiting enzyme.

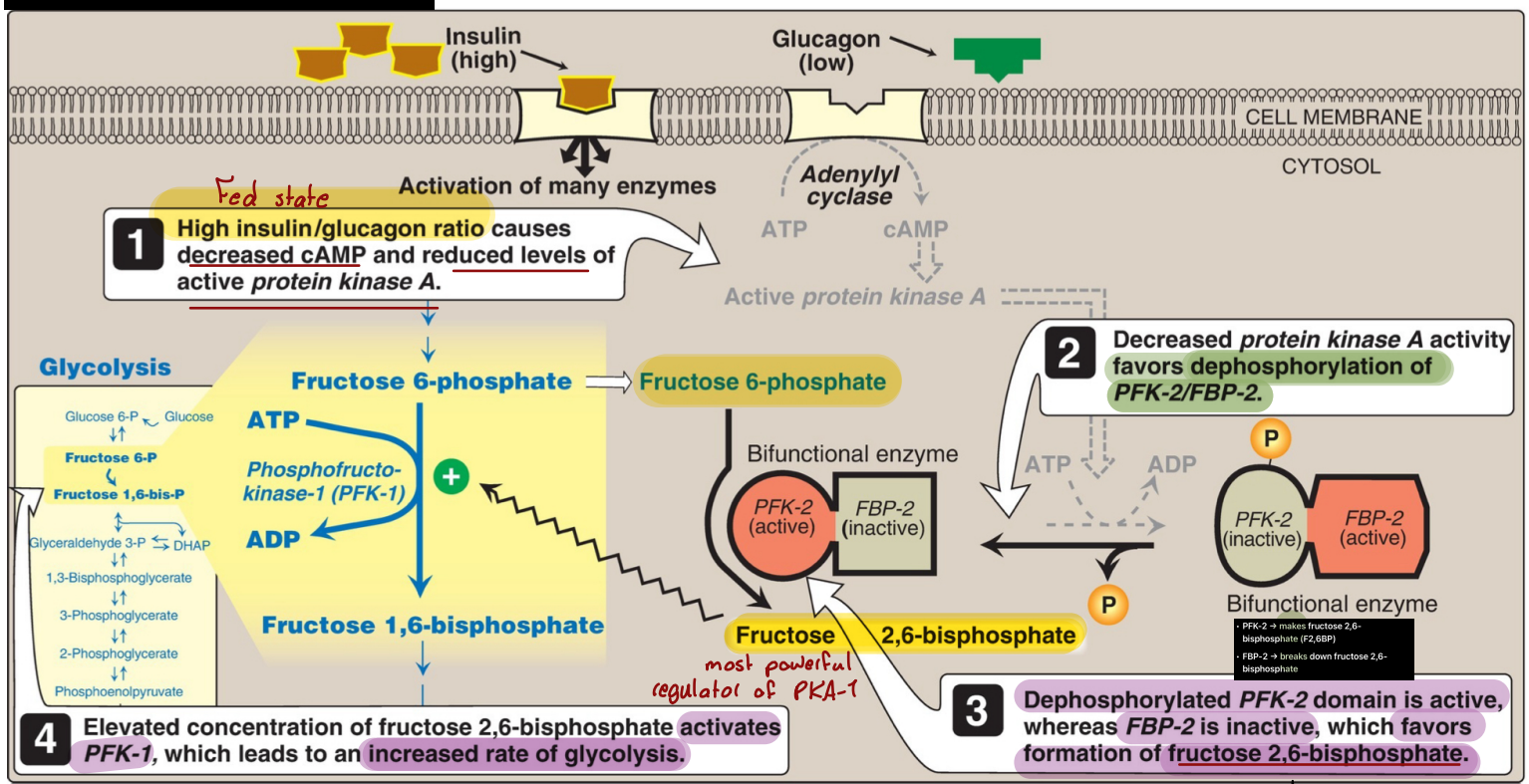


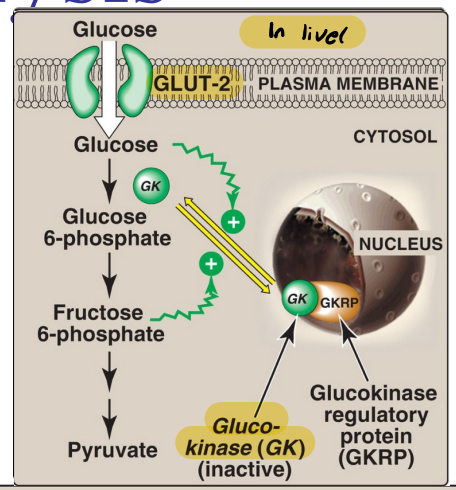
- Hormones regulate glycolysis according to blood glucose level:
  - After CHO feeding (carbohydrates): blood glucose increases, this stimulates insulin secretion, insulin stimulates glycolysis by increasing the synthesis of the three key enzymes: GK, PFK and PK.
  - During fasting: blood glucose level decreases, which inhibits insulin secretion and stimulates glucagon, adrenaline and corticosteroid which inhibit the synthesi of and activity of GK, PFK and PK.

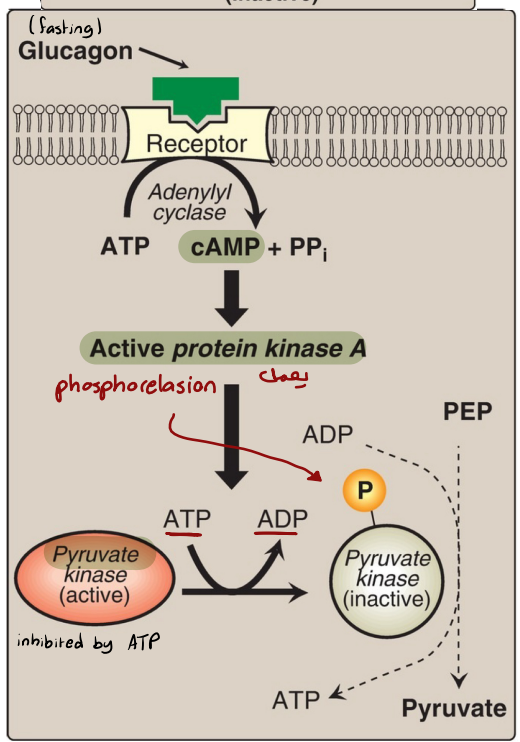


Hormonal regulation of Glycolysis

- Glucagon = increases cAMP
- Insulin = decreases cAMP effects







fructose 2,6-bisphosphate stimulate(+) PKA-1

↳ It's produced from F-6-P by [PKA-2/FBP-2] enzyme

I need them to promote glycolysis

good for glycolysis

outside the body

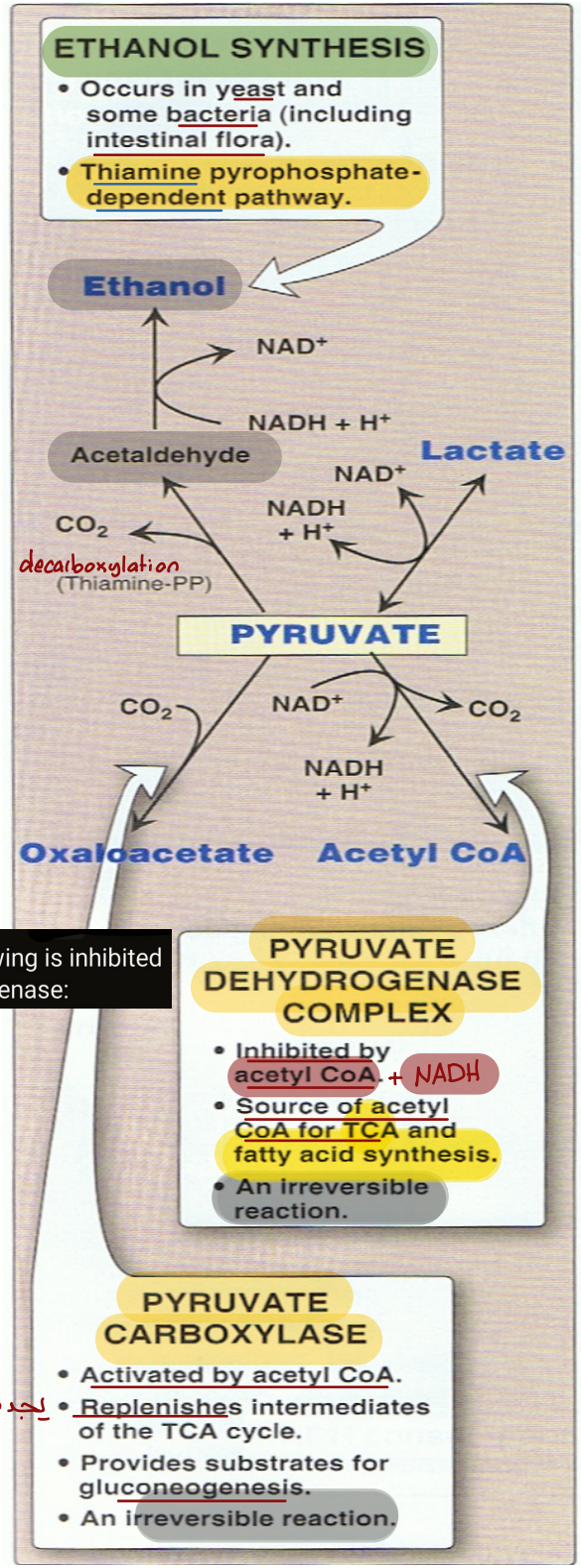
In-vitro inhibition of glycolysis

- Flouride inhibits enolase enzyme (step 8)

- It is used in toothpastes as it inhibits glycolysis in mouth bacterial flora.
- It is also used as anticoagulant for blood samples to estimate its glucose content.

Fate of pyruvic acid

- Formation of acetyl CoA irreversible
  oxidative decarboxylation By pyruvate dehydrogenase complex PDHC
  $-CO_2$
- Formation of oxaloacetic acid irreversible
  carboxylation $+CO_2$ by pyruvate carboxylase
- Formation of lactate (In anerobic glycolysis)
  No NADH
  لأنه يتأكسد إلى NAD^+
- Formation of ethanol (in yeast and some M.O)
  microorganisms



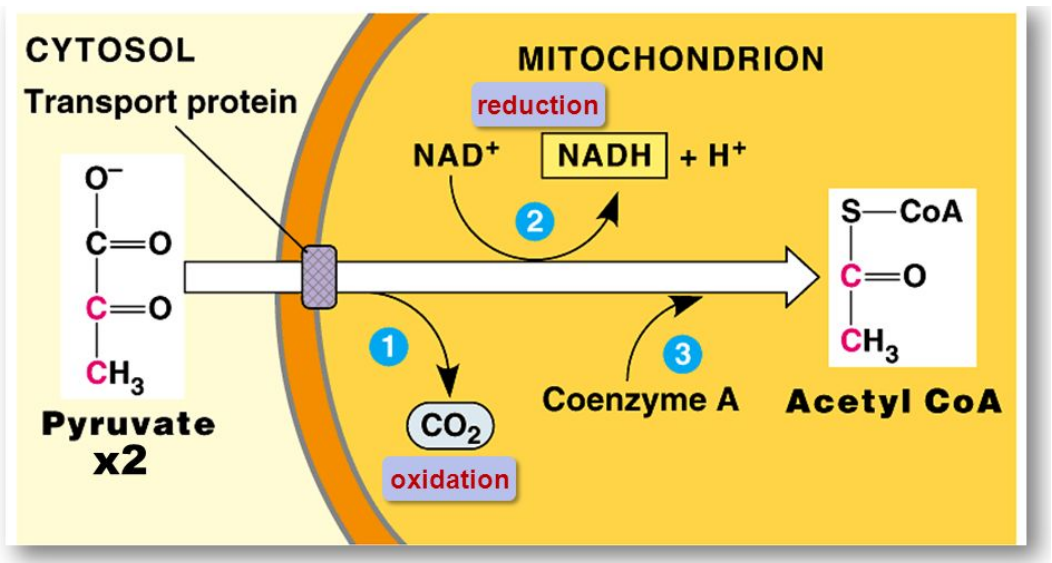
Which of the following is inhibited pyruvate dehydrogenase:

يجدد

Aerobic phase of glucose oxidation

- Pyruvic acid formed by glycolysis enters the mitochondria where:
  - it will be metabolized to acetyl-CoA by oxidative decarboxylation and
  - then Acetyl-CoA is oxidized in Kreb's cycle

- pyruvate oxidized to Acetyl-CoA
  NAD^+ is reduced to $NADH + H^+$



Yield = 2C compound + CO_2 + NADH x2

Kreb's cycle → 2 CO2 + 10 ATP

7 ATP aerobic
2 NADH → 5 AT
2 pyruvate → 20 ATP
} 32 ATP

* رح يجي سؤال على irreversible enzymes

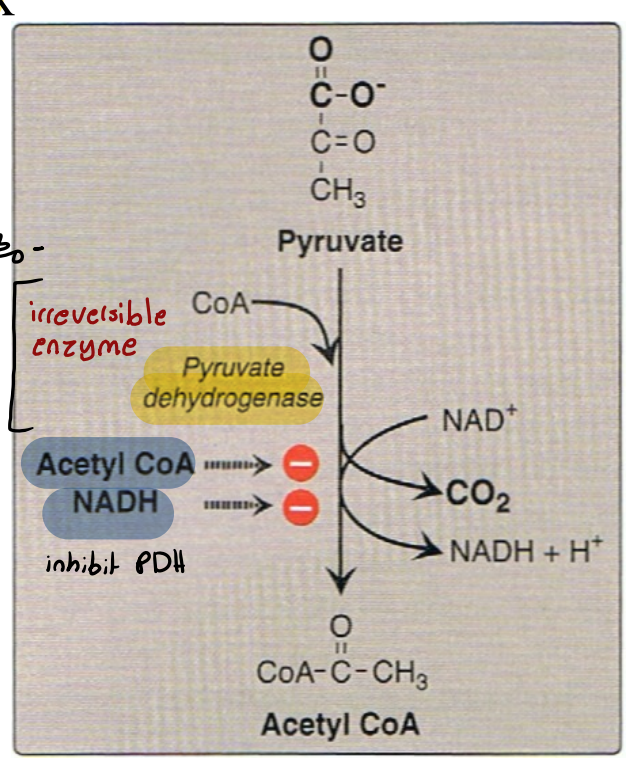
A-Oxidative decarboxylation of pyruvic acid

produce Acetyl-CoA

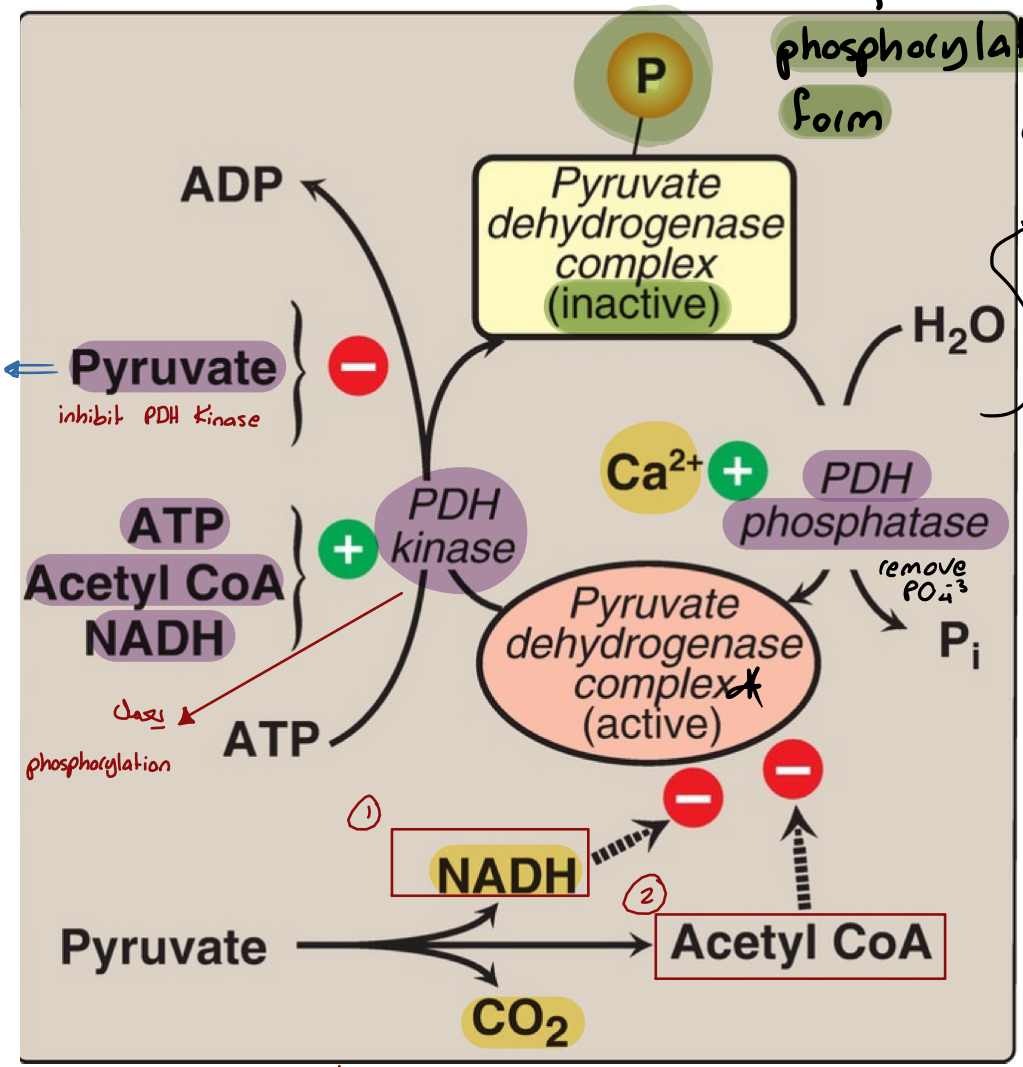
- Occurs in mitochondria
- Irreversible
- Needs pyruvate dehydrogenase (PDH) complex

irreversible enzyme

- Requires 5 coenzymes
  - Thiamine pyrophosphate PP
  - 2-lipoic acid
  - CoA-SH
  - FAD
  - NAD+



Regulation of pyruvate dehydrogenase PDH



phosphorylated is the inactive form

so اي اللي يعطله

→ dephosphorylation activates it

- Ca^{+2} activate PDH phosphatase

NADH
Acetyl CoA
inhibit PDH

يتحول إلى Acetyl CoA

Active PDH تنشط

dephosphorylated

Signal	Effect on PDH Activity	Why?
ADP	Increase	Signals low energy; needs more ATP.
Pyruvate	Increase	High substrate availability; needs processing.
Ca^{2+}	Increase	Signals muscle contraction/ demand for work.
ATP	Decrease	Signals "energy tank is full."
Acetyl CoA	Decrease	Product buildup; slows down production.
NADH	Decrease	Product buildup; signals high electron supply.

stimulate PDH

No PO_4^{-3}

inhibit it

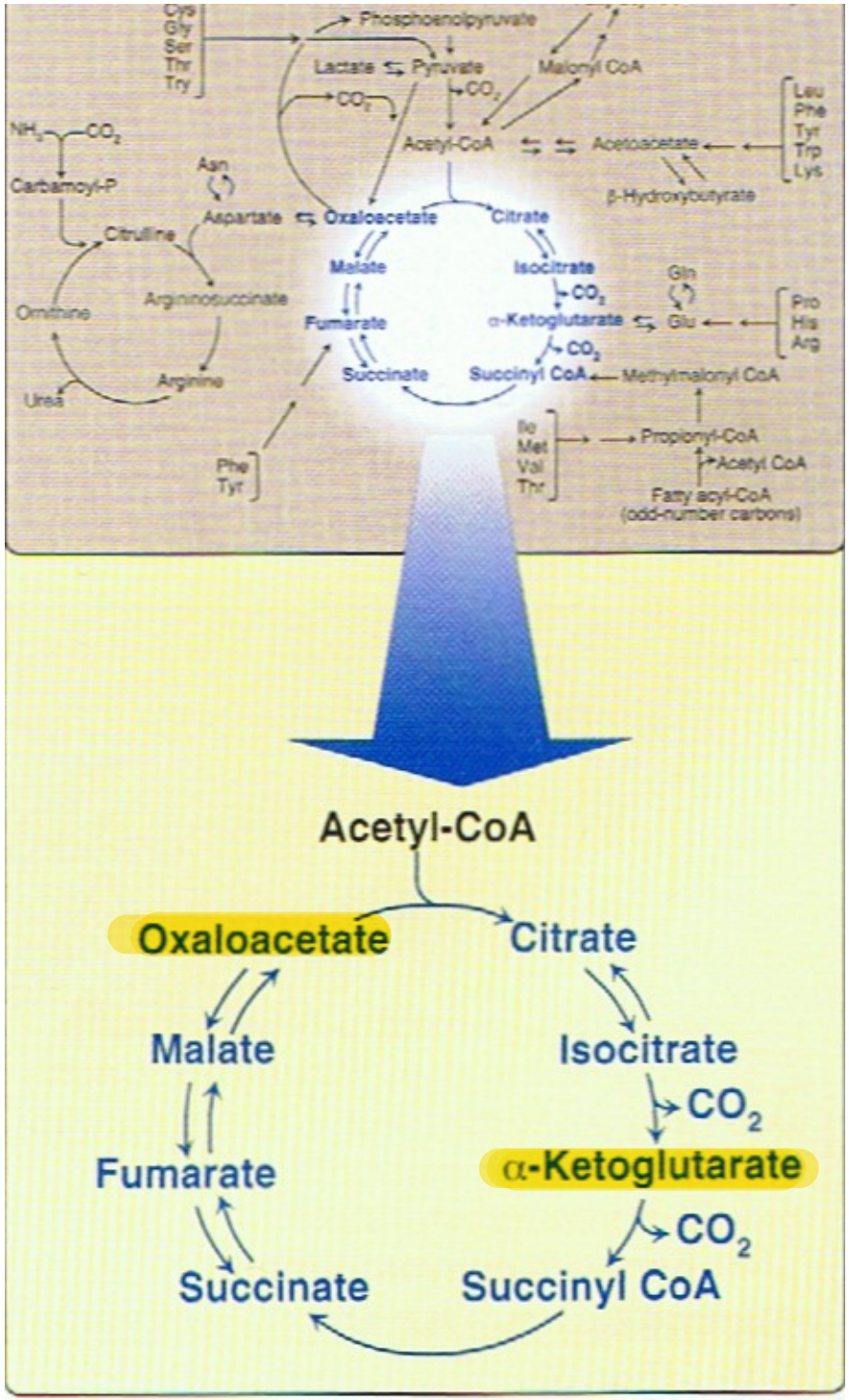
dephosphorylation = Active = stimulate PDH

phosphorylated = inactive = inhibit PDH

https://youtu.be/JOncWQUpMzc?si=5Ev5mOGm_H9Vg4ie

Tricarboxylic acid cycle

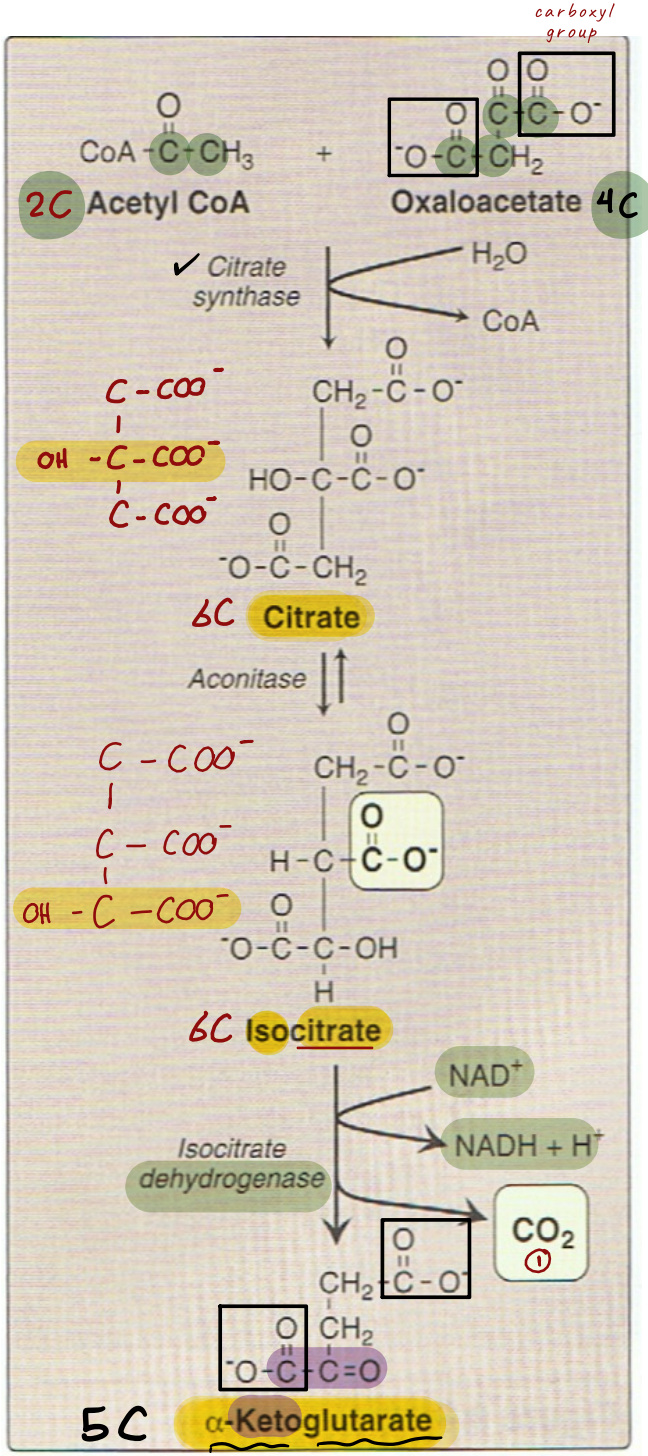
- Occurs in the mitochondria of each cell
- Does not occur in RBCs (no mitochondria)
- Considered the final common pathway for the complete oxidation of acetyl-CoA obtained from partial oxidation of CHO, lipids and proteins.



Tricarboxylic Acid cycle

Steps of TCA (Krebs cycle)

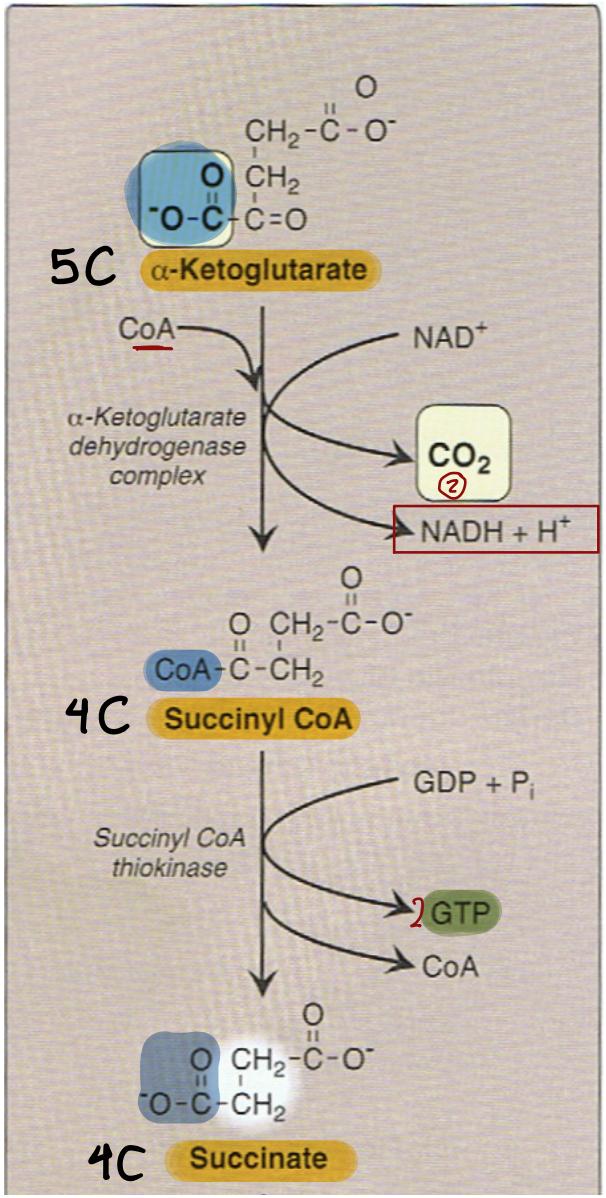
- Step 1: condensation of acetyl-CoA and oxaloacetic acid to form citric acid. Catalyzed by citrate synthase.
- Step 2: Citric acid is converted to isocitrate by aconitase.
- Step 3: Isocitrate is oxidized to α-ketoglutarate by isocitrate dehydrogenase. NADH is produced and CO2 is released.



Steps of TCA

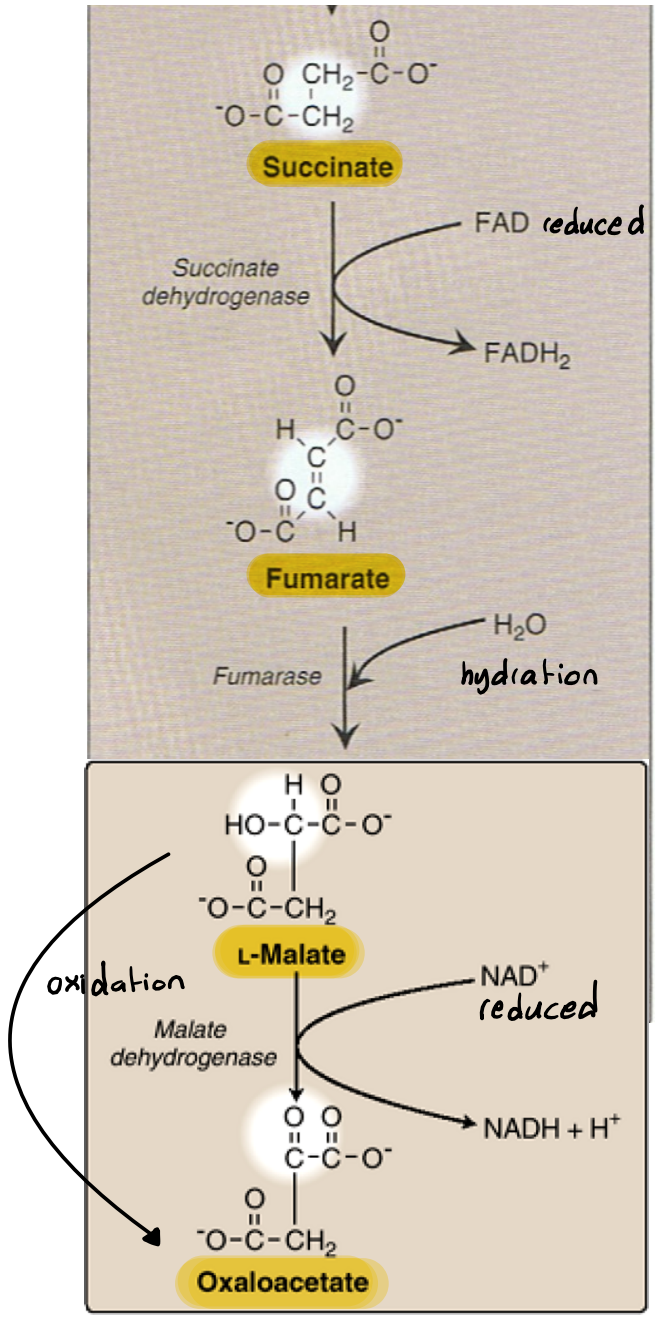
- Step 4: α-ketoglutarate is converted to succinyl CoA. CO2 is released and NADH is produced. The reaction is catalyzed by α-ketoglutarate dehydrogenase complex. It also requires 5 coenzymes (thiamine pyrophosphate, lipoic acids, CoA-SH, FAD and NAD)

- Step 5: the high-energy, thioester bond of succinyl-CoA is cleaved providing energy for the synthesis of GTP fro GDP and Pi. Succinate is formed and the reaction is catalyzed succinate thiokinase.



Steps of TCA

- Step 6: succinate is oxidized to fumarate by succinate dehydrogenase. FAD is reduced to FADH2.
- Step 7: fumarate is hydrated to form malate by fumarase.
- Malate is oxidized to oxaloacetate by malate dehydrogenase. NAD is reduced to NADH.
- Oxaloacetate will reinitiate the cycle again.



1 glucose → 2 pyruvate → $4CO_2$, 6 NADH, $2FADH_2$, 2 GDP (in Kreb's cycle (2 turns))

one turn: 3 NADH, 1 FADH, 1 GTP, 2 CO_2

Energy gain in Kreb's cycle

(1cycle)

Isocitrate DH	1 NADH	2.5 ATP
α-ketoglutarate	1 NADH	2.5 ATP
Succinate thiokinase	1 GTP	1 ATP
Succinate DH	1 FADH2	1.5 ATP
Malate DH	1 NADH	2.5 ATP
Net gain		**10** ATP → one turn

2 turns = 20 ATP

The overall energy gain of glucose oxidation

- Glycolysis --------- 7 ATP + 2 pyruvate (Aerobic)
- 2 pyruvate -------- 2 acetyl-coA + 2 NADH ----- 5 ATP
- 2 acetyl CoA --------- 20 ATP (Krebs cycle)
- The net ATP produced by the oxidation of 1 mol of glucose = 32 ATP

- **Pyruvate (3C) → Acetyl CoA (2C):** This releases **1** CO_2 (via PDH). Since one glucose makes two pyruvates, this is **2** CO_2.
- **TCA Cycle:** Releases **2** CO_2 per turn.
- **Total Oxidation:** $2(\text{from PDH}) + 4(\text{from TCA}) = \mathbf{6\ CO_2}$.
- **Exam Logic:** She might link this to the "Bypass" reactions in gluconeogenesis. For example: "Pyruvate carboxylase adds a CO_2 to pyruvate to make oxaloacetate, which is later released by PEP carboxykinase."

Defects in Glycolysis

convert pyruvate → Acetyl CoA

- **Pyruvate dehydrogenase deficiency:** leads to congenital lactic acidosis.

- This enzyme deficiency results in an inability to convert pyruvate to acetyl CoA, causing pyruvate to be shunted to lactic acid via lactate dehydrogenase.

- This causes particular problems for the brain, which relies on the TCA cycle for most of its energy, and is particularly sensitive to acidosis.

https://youtu.be/cProcjVNvtU?si=m3qmwXWt9m9-AVtP

= make new glucose from non carbohydrate sources

Gluconeogenesis

When and where does it occur

Fasting state
I need energy!!

↳ liver / kidneys

1. **Immediate:** Use what you just ate. glycolysis
2. **Short-term:** Break down stored sugar (Glycogen). glycogenolysis
3. **Long-term:** Manufacture sugar from scratch (Gluconeogenesis).

- During prolonged fast and depletion of hepatic glycogen

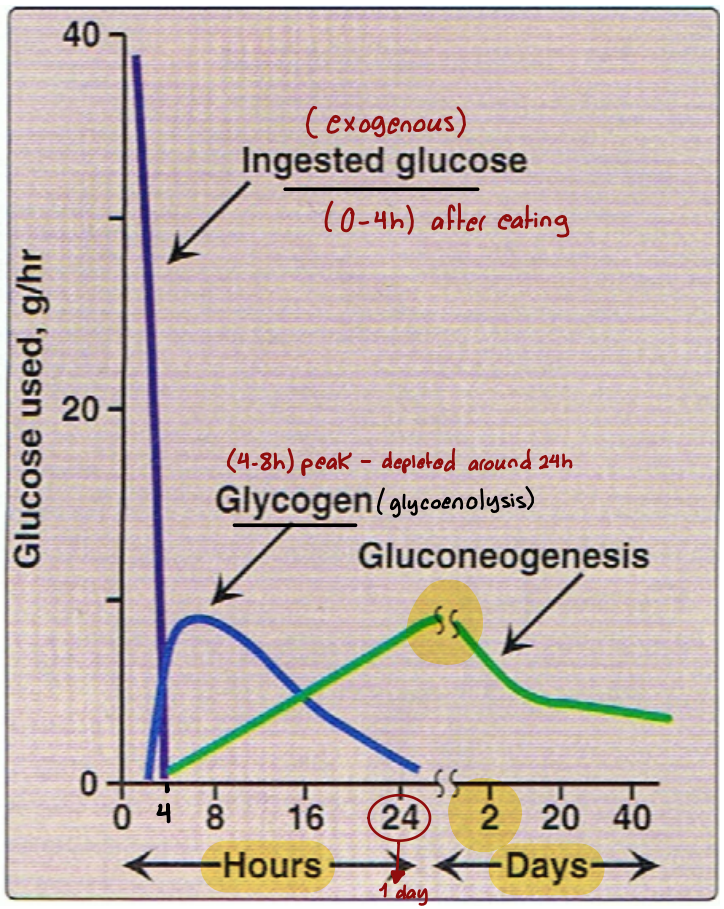
نفاد

- During overnight fast, liver is responsible for the majority of gluconeogenesis (90%) and the rest in the kidney

10 %

- During prolonged fast, kidney produces about 40% of glucose production.

- Glucose is formed from precursors as lactate, pyruvate, glycerol and ketoacids



Substrates for gluconeogenesis

Those include all the intermediates of glycolysis and the citric acid cycle.

Glycerol: released during the hydrolysis of triglycerols in adipose tissue and delivered to the liver. Glycerol is phosphorylated by glycerol kinase to glycerol 3-phosphate, which is oxidized by glycerol 3-phosphate dehydrogenase to dihydroxyacetone phosphate which is an intermediate of glycolysis.

Lactate: released by exercising muscles and RBC's. This is transferred to the liver and reconverted to glucose.

Amino acids: hydrolysis of tissue proteins are the major source of glucose. α-ketoacids (oxaloacetate and α-ketoglutarate are derived from the metabolism of glucogenic aa which can enter the TCA

Substrates for gluconeogenesis

Glycerol

released during - Hydrolysis of triglycerols in Adipose tissue

By **glycerol kinase** Add PO_4^{-3}

Glycerol-3-phosphate

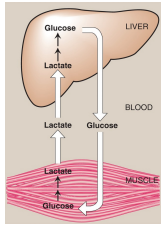
oxidized By **glycerol 3-phosphate dehydrogenase**

dihydroxyacetone phosphate

lactate

released from - muscles
- RBCs

Blood stream → liver → glucose



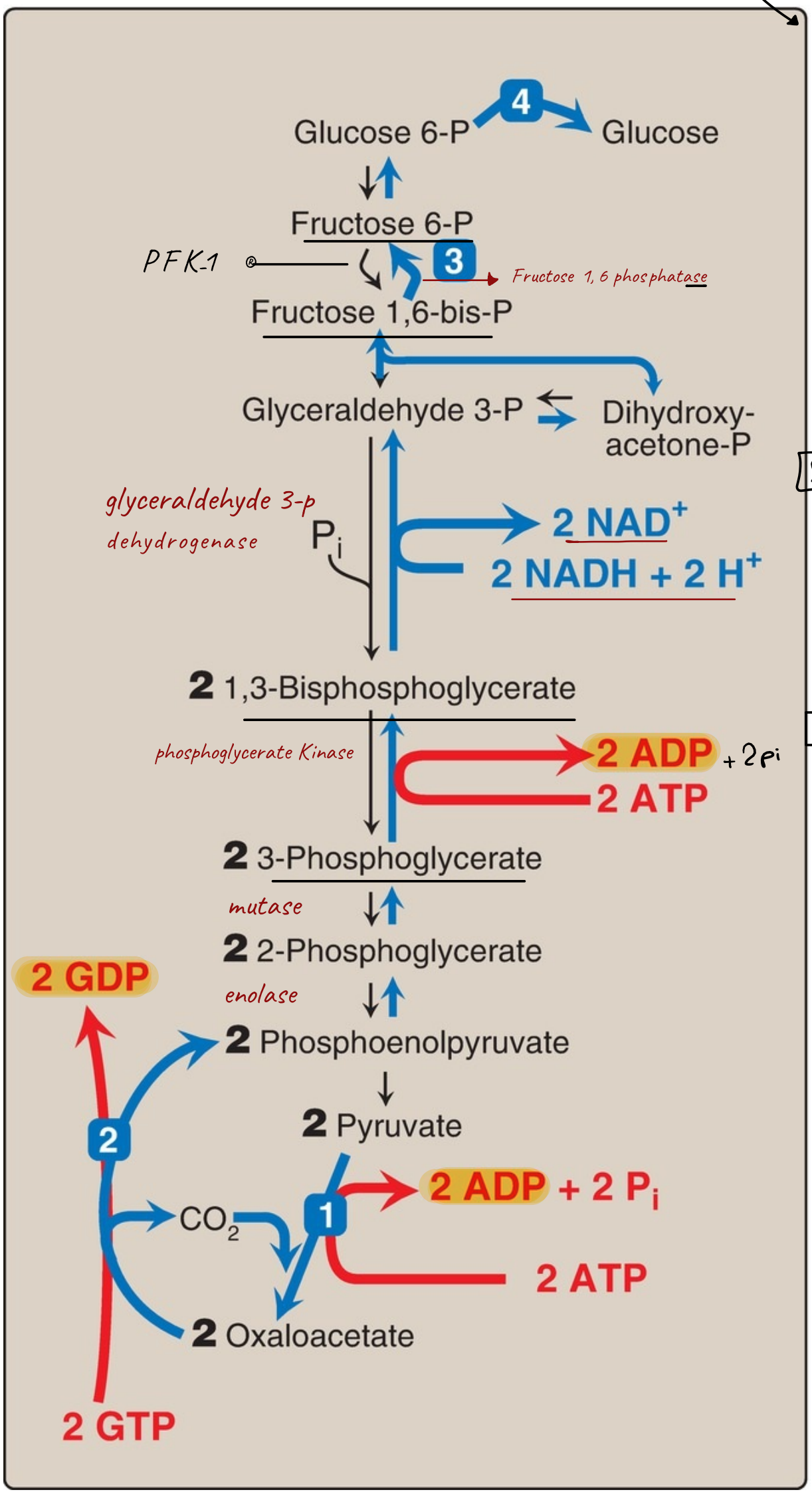
amino acids

- hydrolysis of tissue proteins

Source	End Product	Can it become Glucose?	Why?
Glucogenic AAs	Pyruvate / OAA	Yes	They enter the pathway before/at the OAA stage.
Ketogenic AAs	Acetyl CoA	No	PDHC reaction is irreversible; no path back to pyruvate.

turn into α-Ketoacids - oxaloacetate
- α-Ketoglutarate

Protein → Amino Acids → α-keto acids → TCA Cycle → Oxaloacetate → Glucose



1 2 pyruvate → 2 oxaloacetate

By pyrovate carboxylase PC

helper? Biotin (vitamin B7) carries CO_2

2ATP -> 2 ADP + 2Pi

regulated by Acetyl CoA

activates PC

صح حسا معنا OAA بساما يقدر يطلع منا
الـ mitochondria شو نعمل إذا

oxaloacetate → malate

By malate dehydrogenase

cytosol لـ يطلع

malate → oxaloacetate

By cystolic malate dehydrogenase

2 2 oxaloacetate -> 2 phosphoenolpyruvate (PEP)

By pep carboxykinase (PEPCK)

2 GTP → 2 GDP

$-CO_2$

reverse glycolysis نكمل

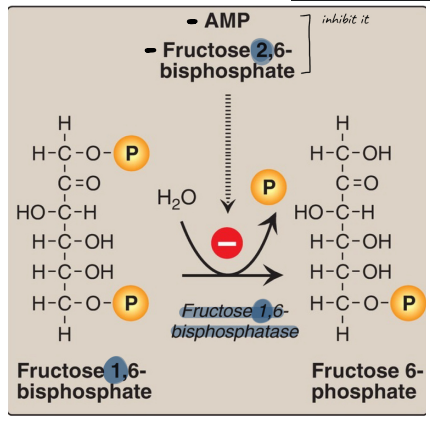
3 Fructose 1.6 Bisphosphate

Fructose 1, 6 Bisphoatase

Fructose - 6 - P

- **Inhibited by:** AMP and Fructose 2,6-bisphosphate (signals that the cell needs energy/has sugar, so stop making glucose).
- **Stimulated by:** High ATP (signals the cell has plenty of energy, so start making glucose).

low AMP



4 glucose-6-p → glucose

By glucose-6-phosphatase

Reactions unique to gluconeog

- Seven of the glycolysis reactions are reversible and are used for gluconeogensis while three of them are irreversible (Pyruvate kinase, phosphofructokinase and hexokinase)

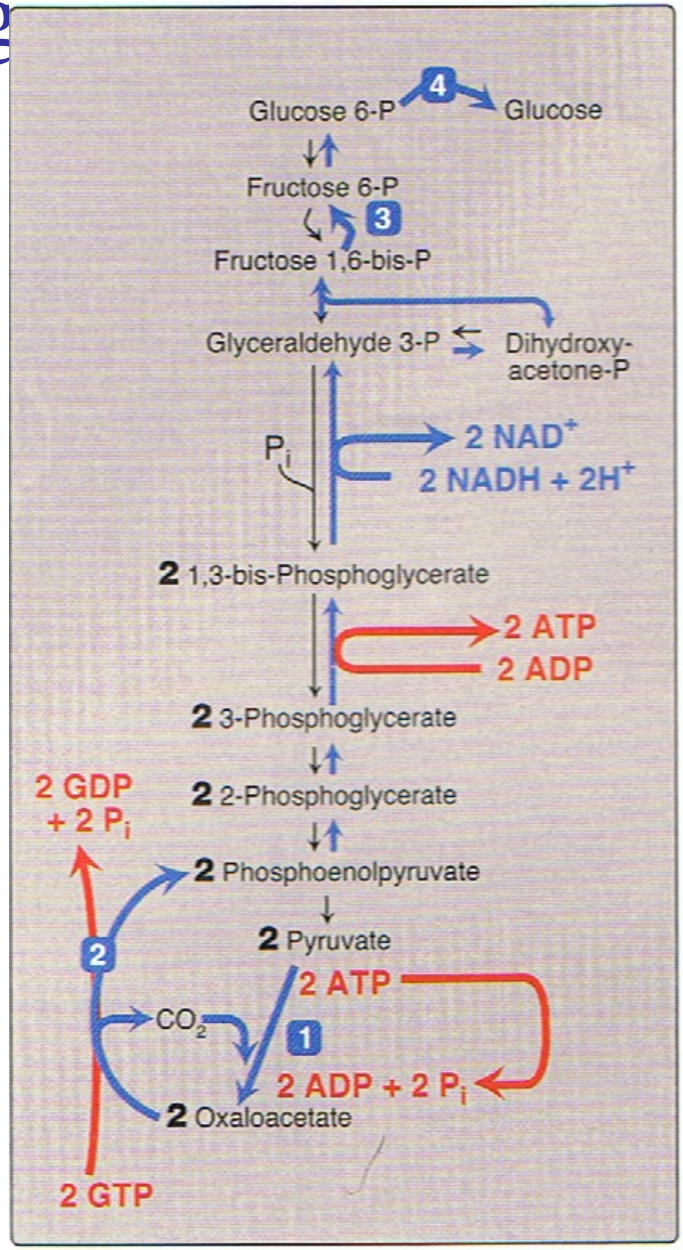
1. Pyruvate carboxylase: Pyruvate is converted to phosphoenolpyruvate (PEP) by pyruvate carboxylase and PEP caboxykinase

amino group

- Biotin: covalently bound to the N of lysine in the pyruvate carboxylase, requires CO2 and ATP for the convertion of pyruvate to oxaloacetate. It occurs in mitochondria of liver and kidney. Muscles contain also pyruvate carboxylase for the use of OAA in TCA.
- Allosteric regulation: it is allosterically activated by Acetyl coA.

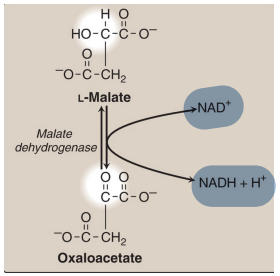
activates PC

pyruvate كاربكيز
there is too much of me!
Don't turn into me! go another way (to OAA)



Reactions unique to gluconeogenesis

2. Transport of oxaloacetate to the cytosol: oxaloacetate can't cross the mitochondrial membrane so it is reduced to malate by malate dehydrogenase that can cross. In cytosol malate is reoxidized to oxaloacetate by cytosolic malate dehydrogenase.



$-CO_2$ $2GTP \rightarrow 2GDP + 2P_i$

3. Oxaloacetate is decarboxylated and phosphorylated in the cytosol by PEP carboxykinase which utilize 1 GTP. PEP will continue in the reverse of glycolysis until reach fructose 1,6- biphosphate.

$-PO_4^{3-}$

4. Dephosphorylation of frucose 1,6- biphosphate by frucose 1,6-biphosphatase to produce fructose 6-phosphate will bypass the irreversible PFK reaction.

The enzyme is inhibited by high levels of AMP and fructose 2,6- biphosphate, while high level of ATP and low AMP stimulate gluconeogenesis

needs a lot of ATP

Reactions unique to gluconeogenesis

5. Dephosphorylation of glucose 6-phosphate: occurs by glucose 6-phosphatase. This occurs only in liver and kidney. Two enzymes are required (glucose 6-phosphate translocase to transfer glucose 6-phosphate to ER and glucose 6-phosphatase)

Type 1a glycogen storage disease results from inherited diffeciency of one of them which has the following symptoms: (glucose-6-phosphatase)

- Hypoglycemia (low blood sugar)
- Hepatomegaly and liver problems (enlarged liver)
- Lactic acidosis
- Growth failure

Glycolysis Step (Irreversible)	Gluconeogenesis "Bypass" Enzyme	Location
Pyruvate Kinase	Pyruvate Carboxylase & PEPCK	Mitochondria & Cytosol
Phosphofructokinase (PFK-1)	Fructose 1,6-bisphosphatase	Cytosol
Hexokinase / Glucokinase	Glucose 6-phosphatase	ER (Liver/Kidney only)

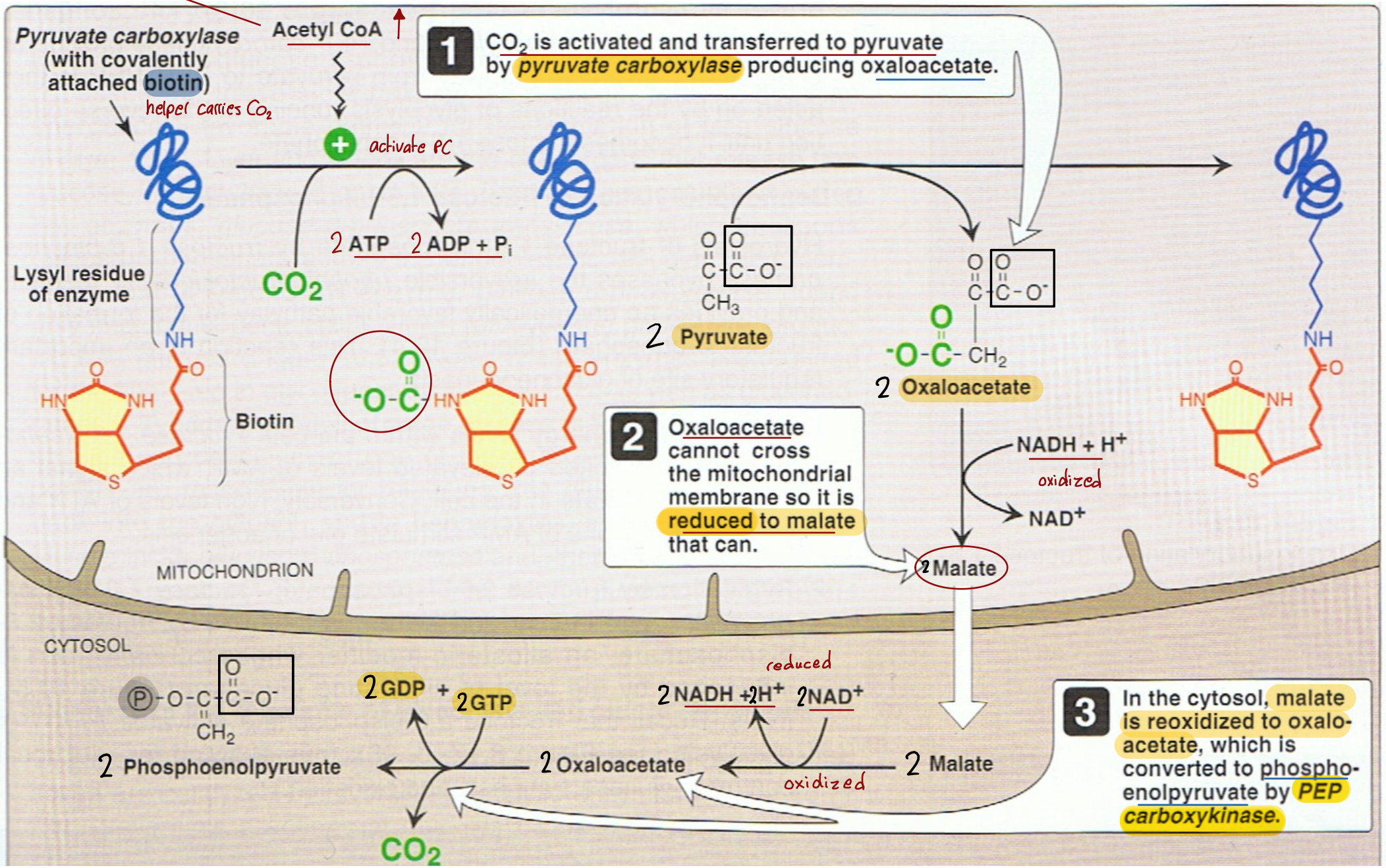
Key Takeaway: Gluconeogenesis is "expensive"—it costs ATP and GTP to push the reactions uphill against the flow of glycolysis.

pyruvate كاربكيلاز

there is too much of me!

Don't turn into me! go another way (to OAA)

Pyruvate carboxylase



Regulation of gluconeogenesis

Activates glycolysis by activating PFK.1

Inhibit glyconeogensis by inhibiting fructose 1,6phosphatase

- Glucagon: stimulates gluconeogenesis in three mechanisms:
  - **Change in allosteric effectors:** it lowers level of fructose 2,6-biphosphate leading to activation of fructose 1,6-biphosphatase and inhibition of phosphofructokinase.
  - **Covalent modification of enzyme activity:** it elevate cAMP leading to activation of cAMP-dependent protein kinase activity which will phosphorylate pyruvate kinase to its inactive form.
  - **Induction of enzyme synthesis:** it increases the transcription of PEP carboxykinase gene.
- Substrate availability: like glucogenic amino acids
- Allosteric activation of pyruvate carboxylase by acetyl coA.
- Allosteric inhibition of fructose 1,6-bisphosphatase by AMP

low energy state

Note: ATP and NADH are produced in large quantities during fasts from fatty acid oxidation is required for gluconeogenesis.

glyconeogensis is expensive حكينا ATP بيها كتير

0.1. Which one of the following statements concerning gluconeogenesis is correct?

A. It is an energy-producing (exergonic) process.

B. It is important in maintaining blood glucose during a 2-day fast.

C. It is inhibited by a fall in the insulin/glucagon ratio.

D. It occurs in the cytosol of muscle cells.

E. It uses carbon skeletons provided by fatty acid degradation.

Correct answer = B. During a 2-day fast, glycogen stores are depleted, and gluconeogenesis maintains blood glucose. This is an energy-requiring (endergonic) pathway (both ATP and GTP get hydrolyzed) that occurs primarily in the liver, with the kidneys becoming major glucose producers in prolonged fasting. Gluconeogenesis uses both mitochondrial and cytosolic enzymes and is stimulated by a fall in the insulin/glucagon ratio. Fatty acid degradation yields acetyl coenzyme A (CoA), which cannot be converted to glucose. This is because there is no net gain of carbons from acetyl CoA in the tricarboxylic acid cycle, and the pyruvate dehydrogenase complex is physiologically irreversible. It is the carbon skeletons of most amino acids that are glucogenic.

0.3. Which one of the following reactions is unique to gluconeogenesis?

A. 1,3-Bisphosphoglycerate → 3-phosphoglycerate

B. Lactate → pyruvate

C. Oxaloacetate → phosphoenolpyruvate

D. Phosphoenolpyruvate → pyruvate

Correct answer = C. The other reactions are common to both gluconeogenesis and glycolysis.

0.4. Use the chart below to show the effect of adenosine monophosphate (AMP) and fructose 2,6-bisphosphate on the listed enzymes of gluconeogenesis and glycolysis.

Enzyme	Fructose 2,6-bisphosphate	AMP
Fructose 1,6-bisphosphatase		
Phosphofructokinase-1		

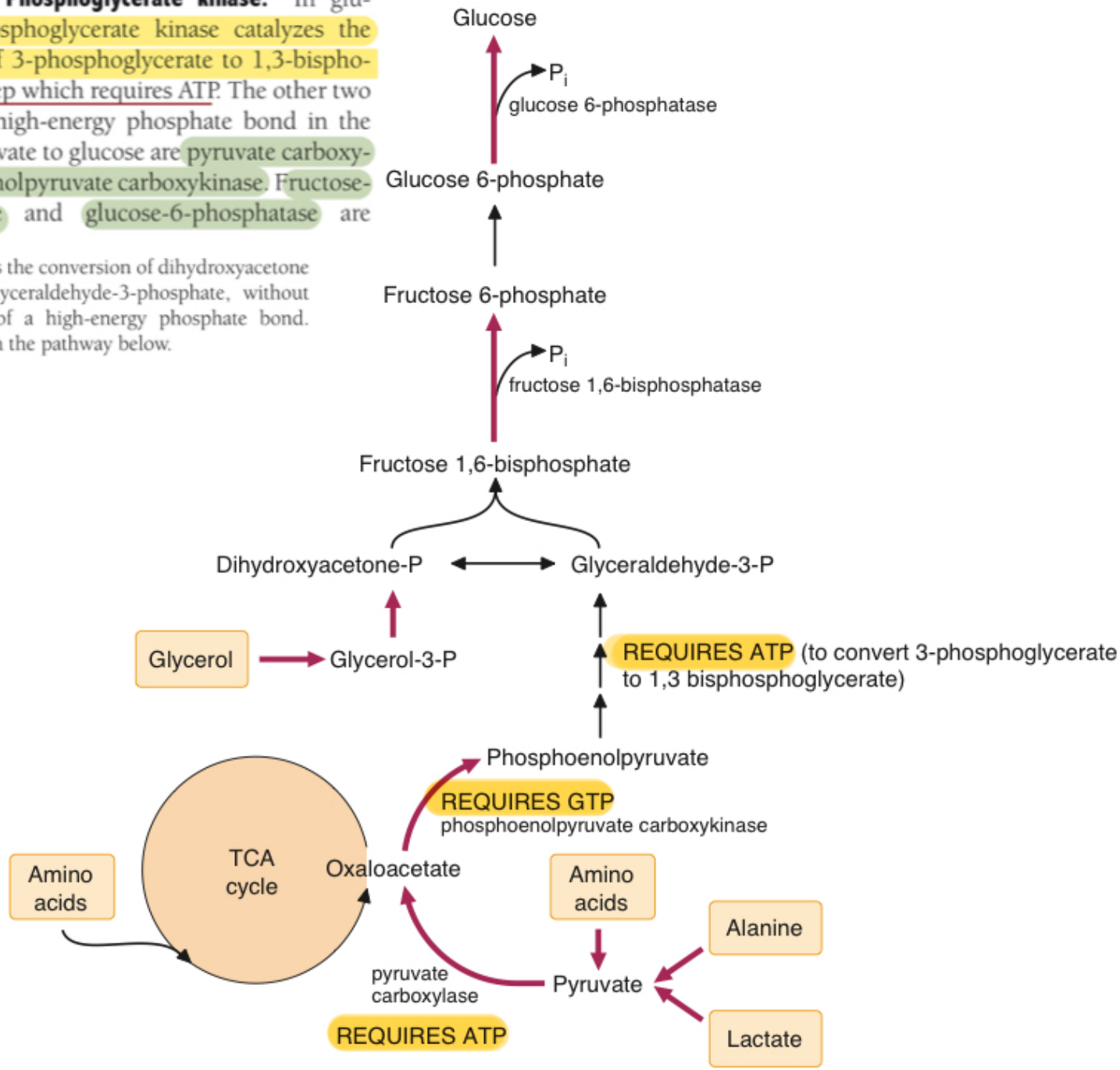
Both fructose 2,6-bisphosphate and adenosine monophosphate inhibit fructose 1,6-bisphosphatase of gluconeogenesis and activate phosphofructokinase-1 of glycolysis. This results in reciprocal regulation of the two pathways.

12 The synthesis of one mole of glucose from two moles of lactate requires six moles of ATP. Which one of the following steps requires ATP in the gluconeogenic pathway?

(A) Pyruvate kinase
(B) Triosephosphate isomerase
(C) Glucose-6-phosphatase
(D) Fructose-1,6-bisphosphatase
(E) Phosphoglycerate kinase

The answer is E: Phosphoglycerate kinase. In gluconeogenesis, phosphoglycerate kinase catalyzes the phosphorylation of 3-phosphoglycerate to 1,3-bisphosphoglycerate, a step which requires ATP. The other two steps requiring a high-energy phosphate bond in the conversion of pyruvate to glucose are pyruvate carboxylase and phosphoenolpyruvate carboxykinase. Fructose-1,6-bisphosphatase and glucose-6-phosphatase are

isomerase catalyzes the conversion of dihydroxyacetone phosphate and glyceraldehyde-3-phosphate, without the involvement of a high-energy phosphate bond. These are shown in the pathway below.



Medical Biochemistry Question Bank

Metabolism, Glycolysis, TCA Cycle & Gluconeogenesis

Section 1: Cell Signaling & Global Regulation

1. Adenylyl cyclase is activated by:

A) Binding of GTP to the α-subunit of Gs protein.

B) Binding of GDP to the βγ complex.

C) Hydrolysis of GTP on the α-subunit.

D) Phosphorylation of the G-protein coupled receptor.

Answer: A

2. The primary role of cAMP-dependent protein kinase (PKA) is to:

A) Directly catalyze the breakdown of glycogen.

B) Phosphorylate specific enzymes to change their activity.

C) Increase the transcription of the GLUT-4 gene.

D) Dephosphorylate pyruvate kinase.

Answer: B

3. Termination of the G-protein signal occurs when:

A) cAMP is converted to AMP by phosphodiesterase.

B) The α-subunit hydrolyzes its bound GTP to GDP.

C) The receptor is internalized by the cell.

D) PKA phosphorylates the G-protein.

Answer: B

4. Metabolism is "convergent" during catabolism because:

A) Many complex molecules are broken down into a few simple end products.

B) Simple precursors are used to build various complex structures.

C) All metabolic pathways occur within the mitochondria.

D) It requires the simultaneous use of ATP and NADH.

Answer: A

5. Which hormone is primarily responsible for promoting storage and glycolysis?

A) Glucagon

B) Epinephrine

C) Insulin

D) Cortisol

Answer: C

Section 2: Glucose Transport

6. Which GLUT transporter is insulin-dependent?

A) GLUT-1

B) GLUT-2

C) GLUT-3

D) GLUT-4

Answer: D

7. GLUT-2 is characterized by having:

A) High affinity and low Km for glucose.

B) Low affinity and high Km for glucose.

C) A requirement for Sodium co-transport.

D) Expression only in the blood-brain barrier.

Answer: B

8. Sodium-monosaccharide cotransporter (SGLT1) is an example of:

A) Simple diffusion.

B) Facilitated diffusion.

C) Primary active transport.

D) Secondary active transport.

Answer: D

9. The GLUT-3 transporter is primarily found in:

A) Liver and Pancreas.

B) Muscle and Adipose.

C) Neurons and Brain.

D) Erythrocytes.

Answer: C

10. In which tissue does GLUT-2 allow for bidirectional glucose flux?

A) Skeletal muscle.

B) Heart.

C) Liver.

D) Brain.

Answer: C

Section 3: Glycolysis

11. Which enzyme catalyzes the "first committed step" of glycolysis?

A) Hexokinase

B) Phosphofructokinase-1 (PFK-1)

C) Pyruvate Kinase

D) Phosphoglucose Isomerase

Answer: B

12. Glucokinase differs from Hexokinase because Glucokinase:

A) Is inhibited by glucose 6-phosphate.

B) Has a very low Km for glucose.

C) Is induced by insulin in the liver.

D) Is found in all peripheral tissues.

Answer: C

13. The conversion of Phosphoenolpyruvate (PEP) to Pyruvate produces:

A) 1 NADH.

B) 1 ATP via substrate-level phosphorylation.

C) 1 CO_2.

D) 1 $FADH_2$.

Answer: B

14. Arsenate poisoning inhibits glycolysis by competing with:

A) Glucose for Hexokinase.

B) Inorganic phosphate in the G-3-P dehydrogenase reaction.

C) ATP in the PFK-1 reaction.

D) Magnesium ions.

Answer: B

15. Which glycolytic enzyme is inhibited by Fluoride in blood samples?

A) Enolase

B) Pyruvate Kinase

C) Aldolase

D) Phosphoglycerate kinase

Answer: A

16. The reduction of Pyruvate to Lactate is essential in anaerobic conditions to:

A) Produce extra ATP.

B) Regenerate NAD+ for continued glycolysis.

C) Reduce the pH of the cell.

D) Generate CO_2 for the Krebs cycle.

Answer: B

17. Which molecule is a potent allosteric activator of PFK-1?

A) ATP

B) Citrate

C) Fructose 2,6-bisphosphate

D) Glucose 6-phosphate

Answer: C

18. A deficiency in Pyruvate Kinase most commonly leads to:

A) Hemolytic anemia.

B) Muscle cramping.

C) Diabetes mellitus.

D) Congenital lactic acidosis.

Answer: A

19. What is the net ATP yield of anaerobic glycolysis per molecule of glucose?

A) 2 ATP

B) 7 ATP

C) 32 ATP

D) 38 ATP

Answer: A

20. Which reaction in glycolysis is reversible?

A) Hexokinase

B) PFK-1

C) Phosphoglycerate kinase

D) Pyruvate kinase

Answer: C

Section 4: Pyruvate Oxidation (PDH)

21. The Pyruvate Dehydrogenase (PDH) complex converts pyruvate into:

A) Lactate

B) Acetyl CoA

C) Oxaloacetate

D) Malate

Answer: B

22. Which of the following coenzymes is NOT required by the PDH complex?

A) Thiamine pyrophosphate (TPP)

B) Lipoic acid

C) Biotin

D) FAD

Answer: C

23. PDH kinase regulates the PDH complex by:

A) Phosphorylating it to an inactive state.

B) Dephosphorylating it to an active state.

C) Allosterically activating it with Calcium.

D) Cleaving the enzyme into subunits.

Answer: A

24. Congenital Lactic Acidosis is often caused by a deficiency in:

A) Glucokinase

B) Pyruvate Dehydrogenase E1 subunit

C) Lactate dehydrogenase

D) Citrate synthase

Answer: B

25. PDH complex activity is increased by high levels of:

A) ATP

B) NADH

C) Acetyl CoA

D) Pyruvate and Ca2+

Answer: D

Section 5: The Krebs Cycle (TCA)

26. Where do the reactions of the Krebs cycle occur?

A) Cytosol

B) Mitochondrial matrix

C) Inner mitochondrial membrane

D) Endoplasmic reticulum

Answer: B

27. The first step of the Krebs cycle combines Acetyl CoA with:

A) Citrate

B) Isocitrate

C) Oxaloacetate

D) Succinate

Answer: C

28. Which enzyme is the rate-limiting step of the TCA cycle?

A) Citrate synthase

B) Isocitrate dehydrogenase

C) α-Ketoglutarate dehydrogenase

D) Malate dehydrogenase

Answer: B

29. α-Ketoglutarate dehydrogenase requires the same cofactors as:

A) Hexokinase

B) Pyruvate Dehydrogenase

C) Pyruvate Carboxylase

D) Lactate Dehydrogenase

Answer: B

30. One turn of the TCA cycle produces how many NADH molecules?

A) 1

B) 2

C) 3

D) 4

Answer: C

31. Substrate-level phosphorylation in the TCA cycle occurs at the step catalyzed by:

A) Succinate thiokinase (Succinyl CoA synthetase)
B) Succinate dehydrogenase
C) Fumarase
D) Aconitase

Answer: A

32. Which TCA cycle enzyme is also part of the Electron Transport Chain (Complex II)?

A) Isocitrate dehydrogenase
B) Succinate dehydrogenase
C) Malate dehydrogenase
D) Citrate synthase

Answer: B

33. The oxidation of one Acetyl CoA in the TCA cycle yields approximately how many ATP?

A) 2 ATP
B) 10 ATP
C) 12 ATP
D) 20 ATP

Answer: B

34. Fluoroacetate is a toxin that inhibits the TCA cycle at which enzyme?

A) Citrate synthase

B) Aconitase

C) Isocitrate dehydrogenase

D) Fumarase

Answer: B

35. High levels of NADH will:

A) Stimulate the TCA cycle.

B) Inhibit the TCA cycle.

C) Have no effect on the TCA cycle.

D) Stimulate the conversion of Malate to Oxaloacetate.

Answer: B

Section 6: Gluconeogenesis

36. Gluconeogenesis occurs primarily in the:

A) Muscle and Brain.

B) Liver and Kidney.

C) Adipose tissue.

D) Erythrocytes.

Answer: B

37. Which of the following is NOT a substrate for gluconeogenesis?

A) Lactate

B) Glycerol

C) Glucogenic amino acids

D) Acetyl CoA

Answer: D

38. Pyruvate carboxylase requires which vitamin cofactor?

A) Thiamine (B1)

B) Riboflavin (B2)

C) Biotin (B7)

D) Niacin (B3)

Answer: C

39. The conversion of Oxaloacetate to PEP is catalyzed by:

A) PEP carboxykinase

B) Pyruvate kinase

C) Pyruvate carboxylase

D) Malate dehydrogenase

Answer: A

40. Fructose 1,6-bisphosphatase is inhibited by:

A) ATP

B) Citrate

C) Fructose 2,6-bisphosphate

D) Glucagon

Answer: C

41. Glucose 6-phosphatase is located in the:

A) Cytosol

B) Mitochondria

C) Endoplasmic reticulum (ER)

D) Golgi apparatus

Answer: C

42. Type 1a Glycogen Storage Disease (Von Gierke) is caused by a deficiency in:

A) Pyruvate kinase

B) Glucose 6-phosphatase

C) Glucokinase

D) Phosphofructokinase

Answer: B

43. Which hormone stimulates gluconeogenesis by inducing PEP carboxykinase gene expression?

A) Insulin

B) Glucagon

C) Growth Hormone

D) Melatonin

Answer: B

44. The energy required for gluconeogenesis is primarily derived from:

A) Glycolysis

B) Fatty acid oxidation

C) The Pentose Phosphate Pathway

D) Protein synthesis

Answer: B

45. Acetyl CoA acts as an allosteric activator for:

A) Pyruvate kinase

B) Pyruvate carboxylase

C) PDH complex

D) Phosphofructokinase

Answer: B

Section 7: Integrated Metabolism

46. What is the total ATP yield for the complete aerobic oxidation of 1 glucose molecule?

A) 2 ATP

B) 7 ATP

C) 30-32 ATP

D) 100 ATP

Answer: C

47. During fasting, which enzyme is inactivated by phosphorylation?

A) Pyruvate carboxylase

B) Pyruvate kinase

C) PEP carboxykinase

D) Citrate synthase

Answer: B

48. Which molecule serves as a signal of "high energy" in the cell?

A) AMP

B) ADP

C) ATP

D) NAD+

Answer: C

49. Lactate produced in the muscle is sent to the liver to be converted to glucose via:

A) The Krebs Cycle.

B) The Cori Cycle.

C) The Urea Cycle.

D) The Pentose Phosphate Pathway.

Answer: B

50. Which reaction produces FADH2?

A) Isocitrate to α-Ketoglutarate

B) Succinate to Fumarate

C) Malate to Oxaloacetate

D) Pyruvate to Acetyl CoA

Answer: B

Section 8: Additional Advanced Concepts

51. In the adenylyl cyclase pathway, which molecule acts as the "second messenger"?

A) Insulin

B) ATP

C) cAMP

D) GTP

Answer: C

52. Which enzyme is responsible for the degradation of cAMP to 5'-AMP?

A) Adenylyl cyclase
B) Protein kinase A
C) Phosphodiesterase
D) Phosphatase

Answer: C

53. The G-protein α-subunit has intrinsic enzymatic activity that allows it to:

A) Phosphorylate glucose.
B) Hydrolyze GTP to GDP.
C) Synthesize ATP.
D) Bind to insulin receptors.

Answer: B

54. Which hormone is released when blood glucose is low?

A) Insulin
B) Glucagon
C) Melatonin
D) Acetylcholine

Answer: B

55. Insulin promotes movement of glucose into muscle/adipose via:

A) GLUT-1
B) GLUT-2
C) GLUT-3
D) GLUT-4

Answer: D

56. Which enzyme bypasses PFK-1 in gluconeogenesis?

A) Pyruvate carboxylase
B) Fructose 1,6-bisphosphatase
C) Glucose 6-phosphatase
D) Aldolase

Answer: B

57. Aldolase cleaves Fructose 1,6-bisphosphate into:

A) Two G-3-P molecules.
B) DHAP and G-3-P.
C) Glucose and Fructose.
D) Pyruvate and Acetyl CoA.

Answer: B

58. Which enzyme isomerizes DHAP to G-3-P?

A) Enolase

B) Triose phosphate isomerase

C) Mutase

D) Isocitrate dehydrogenase

Answer: B

59. Aerobic glycolysis net ATP (including NADH in ETC) is:

A) 2 ATP

B) 5 ATP

C) 7 ATP

D) 32 ATP

Answer: C

60. High ATP effect on PFK-1:

A) Allosteric activation

B) Allosteric inhibition

C) No effect

D) Competitive activation

Answer: B

61. Enzyme shifting phosphate from C3 to C2 in 3-PG:

A) Phosphoglycerate kinase
B) Phosphoglycerate mutase
C) Enolase
D) Pyruvate kinase

Answer: B

62. Energy Investment Phase consumes how many ATP?

A) 1
B) 2
C) 4
D) 0

Answer: B

63. Lactic acidosis occurs due to:

A) Failure in oxygen transport to tissues.
B) Glycogen synthesis failure.
C) Gut glucose absorption failure.
D) Liver conversion of lactate to pyruvate.

Answer: A

64. Energy Payoff Phase gross ATP production is:

A) 2

B) 4

C) 7

D) 32

Answer: B

65. Precursor for 2,3-BPG synthesis in RBCs:

A) 1,3-Bisphosphoglycerate

B) Phosphoenolpyruvate

C) Glucose 6-phosphate

D) Citrate

Answer: A

66. Aconitase converts Citrate into:

A) Isocitrate

B) Malate

C) α-Ketoglutarate

D) Fumarate

Answer: A

67. Reaction releasing the first CO2 in TCA:

A) Citrate to Isocitrate

B) Isocitrate to α-Ketoglutarate

C) α-Ketoglutarate to Succinyl CoA

D) Succinate to Fumarate

Answer: B

68. α-Ketoglutarate dehydrogenase is inhibited by:

A) ATP

B) Succinyl CoA

C) Citrate

D) Oxaloacetate

Answer: B

69. Fumarase adds what molecule to form Malate?

A) CO2

B) Phosphate

C) Water (H2O)

D) Hydrogen

Answer: C

70. TCA intermediate used for fatty acid synthesis:

A) Succinyl CoA
B) Citrate
C) Malate
D) Isocitrate

Answer: B

71. TCA intermediate used for Heme synthesis:

A) α-Ketoglutarate
B) Succinyl CoA
C) Fumarate
D) Oxaloacetate

Answer: B

72. Malate to Oxaloacetate proceeds because:

A) Oxaloacetate is rapidly consumed by Citrate Synthase.
B) NADH drives the reaction forward.
C) ATP is hydrolyzed.
D) It occurs in the cytosol.

Answer: A

73. Arsenite specifically inhibits:

A) Citrate Synthase

B) α-Ketoglutarate dehydrogenase complex

C) Malate dehydrogenase

D) Aconitase

Answer: B

74. CO_2 molecules produced per Glucose in TCA:

A) 1

B) 2

C) 4

D) 6

Answer: C

75. Succinate dehydrogenase is unique because it is:

A) In the cytosol.

B) In the inner mitochondrial membrane.

C) Independent of cofactors.

D) Inhibited by Insulin.

Answer: B

76. Main source of Glycerol for gluconeogenesis:

A) Protein breakdown.

B) Adipose TAG hydrolysis.

C) Muscle glycogen breakdown.

D) Dietary fiber.

Answer: B

77. Cori cycle location:

A) Muscle to Liver.

B) Liver to Brain.

C) Kidney to Muscle.

D) Brain to Liver.

Answer: A

78. Why can't muscle contribute to blood glucose?

A) Lacks Glucokinase.

B) Lacks Glucose 6-phosphatase.

C) Cannot perform glycolysis.

D) Lacks GLUT-4.

Answer: B

79. Von Gierke lactic acidosis cause:

A) Excess glucose to lactate.

B) G-6-P accumulation shunted to lactate.

C) Krebs cycle insulin inhibition.

D) Mitochondrial pyruvate entry failure.

Answer: B

80. Most important glucogenic precursor amino acid:

A) Leucine

B) Lysine

C) Alanine

D) Tryptophan

Answer: C

81. Pyruvate carboxylase allosteric activator:

A) Acetyl CoA

B) AMP

C) Citrate

D) Insulin

Answer: A

82. Fructose 1,6-bisphosphatase inhibitor:

A) ATP
B) AMP
C) Citrate
D) Glucagon

Answer: B

83. Gluconeogenesis energy source:

A) Glucose oxidation.
B) Fatty acid oxidation.
C) Amino acid oxidation.
D) Ethanol metabolism.

Answer: B

84. Secondary gluconeogenesis site (starvation):

A) Spleen
B) Kidney
C) Pancreas
D) Heart

Answer: B

85. Acetyl CoA inhibits which enzyme?

A) Pyruvate Carboxylase
B) PDH
C) Isocitrate dehydrogenase
D) Citrate synthase

Answer: B

86. PDH muscle contraction activator:

A) Sodium
B) Potassium
C) Calcium (Ca2+)
D) Iron

Answer: C

87. Link between glycolysis and TCA:

A) Pyruvate
B) Acetyl CoA
C) Lactate
D) Citrate

Answer: B

88. Anaerobic net ATP:

A) 2

B) 7

C) 10

D) 32

Answer: A

89. Fluoride enzyme inhibition target:

A) Hexokinase

B) PFK-1

C) Enolase

D) Pyruvate kinase

Answer: C

90. Thiamine (B1) deficiency target:

A) Glucokinase

B) PDH

C) Lactate dehydrogenase

D) Glucose 6-phosphatase

91. Divergent pathway example:

A) Glycolysis

B) TCA

C) Anabolism

D) Catabolism

Answer: C

92. PKA-phosphorylated Pyruvate Kinase:

A) Active.

B) Inactive.

C) Moves to mitochondria.

D) Changes substrate to Fructose.

Answer: B

93. Brain-ensuring high affinity transporters:

A) GLUT-1 and GLUT-3

B) GLUT-2

C) GLUT-4

D) SGLT-1

Answer: A

94. Von Gierke hepatomegaly cause:

A) Glucose accumulation.
B) Glycogen accumulation.
C) Pyruvate accumulation.
D) Acetyl CoA accumulation.

Answer: B

95. Insulin-induced glucose promoter:

A) Glucokinase
B) Pyruvate carboxylase
C) PEP carboxykinase
D) Fructose 1,6-bisphosphatase

Answer: A

96. Glucose to G-6-P reaction type:

A) Reversible.
B) Irreversible.
C) Non-enzymatic.
D) Liver-only.

Answer: B

97. ATP molecules to synthesize one Glucose from two Pyruvate:

A) 2
B) 4
C) 6
D) 12

Answer: C

98. PDH electron acceptor from FADH2:

A) TPP
B) NAD+
C) Lipoic acid
D) CoA

Answer: B

99. Overall Krebs cycle purpose:

A) Glucose production.
B) Acetyl CoA oxidation & electron capture.
C) Cytosolic fatty acid synthesis.
D) ADP regeneration.

Answer: B

100. PFK-1 is the rate-limiting enzyme for:

A) Glycolysis.

B) Gluconeogenesis.

C) TCA Cycle.

D) Glycogenolysis.

Answer: A