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# Glucose Metabolism: Glycolysis, Link Reaction, Krebs Cycle & ETC

**Study Guide — Metabolism**

Pre-med/IB-level practice on cellular respiration from glycolysis (cytosol) to pyruvate oxidation (link reaction), citric acid cycle (Krebs), anaerobic vs aerobic ATP yield, mitochondrial structure, electron transport chain, chemiosmosis, and ATP synthase—focused on concept traps and multi-step reasoning.

**50 items — Study Guide with Answers**

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**1** Where does glycolysis occur in a typical human cell?

- A Mitochondrial matrix
- B Inner mitochondrial membrane
- C Cytosol ✓
- D Nucleus
- E Endoplasmic reticulum lumen

► **Explanation:** Glycolysis takes place in the cytosol and does not require mitochondria. The mitochondrial matrix houses the link reaction and Krebs cycle, while the inner membrane contains the ETC and ATP synthase.



**2** What is the net ATP yield from glycolysis per molecule of glucose (assuming it proceeds to pyruvate)?

- A 0 ATP
- B 1 ATP
- C 2 ATP ✓
- D 4 ATP
- E 36 ATP

► **Explanation:** Glycolysis uses 2 ATP (investment phase) and produces 4 ATP (payoff phase), giving a net gain of 2 ATP per glucose. 36 ATP refers to older estimates for total aerobic respiration, not glycolysis alone.



**3** Which set of products is generated by glycolysis per glucose molecule (before fermentation or mitochondrial oxidation)?





- A 2 pyruvate, 2 NADH, net 2 ATP ✓**
- B 2 acetyl-CoA, 2 NADH, net 2 ATP
- C 2 pyruvate, 2 FADH<sub>2</sub>, net 2 ATP
- D 6 CO<sub>2</sub>, 2 NADH, net 2 ATP
- E 2 lactate, 0 NADH, net 4 ATP

► **Explanation:** Glycolysis converts glucose (6C) into 2 pyruvate (3C each), producing 2 NADH and net 2 ATP. Acetyl-CoA is produced in the link reaction, FADH<sub>2</sub> is mainly from Krebs cycle, and CO<sub>2</sub> release is not a feature of glycolysis.

**4 Glycolysis can continue without oxygen only if the cell can regenerate which molecule?**



- A FAD
- B Coenzyme A
- C NAD<sup>+</sup> ✓**
- D O<sub>2</sub>
- E ATP synthase

► **Explanation:** Glycolysis requires NAD<sup>+</sup> at the glyceraldehyde-3-phosphate dehydrogenase step; without regenerating NAD<sup>+</sup>, glycolysis stops. Fermentation regenerates NAD<sup>+</sup> in anaerobic conditions; oxygen is not required for glycolysis itself.

**5 Which step of glycolysis directly requires NAD<sup>+</sup> as a reactant?**



- A Glucose → glucose-6-phosphate
- B Fructose-6-phosphate → fructose-1,6-bisphosphate
- C Glyceraldehyde-3-phosphate → 1,3-bisphosphoglycerate ✓**





- D 2-phosphoglycerate → phosphoenolpyruvate
- E Phosphoenolpyruvate → pyruvate

► **Explanation:** NAD<sup>+</sup> is reduced to NADH when glyceraldehyde-3-phosphate is oxidized to 1,3-bisphosphoglycerate. The other listed steps involve ATP use, rearrangements, dehydration, or substrate-level ATP formation but not NAD<sup>+</sup> reduction.

6 Which statement best defines substrate-level phosphorylation?



- A ATP formation using energy from a proton gradient across a membrane
- B ATP formation by direct transfer of a phosphate group from a high-energy substrate to ADP ✓**
- C ATP formation only in the presence of oxygen
- D ATP formation by splitting glucose in half
- E ATP formation by attaching phosphate to glucose

► **Explanation:** Substrate-level phosphorylation is direct phosphate transfer to ADP (e.g., in glycolysis and one step of Krebs). ATP synthase uses oxidative phosphorylation via a proton gradient, which is different.

7 Which pair of glycolysis steps produces ATP directly by substrate-level phosphorylation?



- A Hexokinase and phosphofructokinase-1
- B Glyceraldehyde-3-phosphate dehydrogenase and enolase
- C Phosphoglycerate kinase and pyruvate kinase ✓**
- D Aldolase and triose phosphate isomerase
- E Pyruvate dehydrogenase and citrate synthase





► **Explanation:** ATP is formed at 1,3-BPG → 3-PG (phosphoglycerate kinase) and PEP → pyruvate (pyruvate kinase). Hexokinase and PFK-1 consume ATP; PDH and citrate synthase are not glycolysis enzymes.

8 Which glycolysis enzyme catalyzes the committed, rate-limiting step in many cells?



- A Hexokinase
- B Phosphofruktokinase-1 (PFK-1) ✓**
- C Pyruvate kinase
- D Lactate dehydrogenase
- E ATP synthase

► **Explanation:** PFK-1 converts fructose-6-phosphate to fructose-1,6-bisphosphate, a major committed step and key control point. Hexokinase is also regulated but is not the classic committed step; lactate dehydrogenase is fermentation, and ATP synthase is mitochondrial.

9 High ATP levels in a cell would most directly tend to:



- A Activate PFK-1 to speed up glycolysis
- B Inhibit PFK-1 to slow down glycolysis ✓**
- C Force pyruvate to become lactate
- D Increase oxygen binding to hemoglobin
- E Block glucose entry into the cell in all tissues

► **Explanation:** ATP is a signal of high energy status and typically inhibits PFK-1, slowing glycolysis. Lactate formation is mainly driven by the need to regenerate  $\text{NAD}^+$  when aerobic oxidation is limited, not directly by ATP levels.





**10** A high AMP (or ADP) level in a cell generally indicates low energy. Which effect is most expected?



- A** Inhibition of PFK-1, slowing glycolysis
- B** Activation of PFK-1, speeding glycolysis ✓
- C** Immediate stop of electron transport chain
- D** Conversion of acetyl-CoA into glucose in humans
- E** Direct synthesis of ATP without substrates

► **Explanation:** AMP/ADP signal low energy and typically activate glycolysis by stimulating PFK-1 (and other pathways that generate ATP). They do not magically create ATP; they shift regulation to increase ATP production.

**11** What is the main purpose of fermentation in human muscle during intense exercise?



- A** To produce large amounts of ATP directly from lactate
- B** To regenerate  $\text{NAD}^+$  so glycolysis can continue producing ATP ✓
- C** To produce acetyl-CoA for the Krebs cycle
- D** To transport oxygen into mitochondria
- E** To convert glucose into  $\text{CO}_2$  in the cytosol

► **Explanation:** Fermentation (lactate production) oxidizes NADH back to  $\text{NAD}^+$ , allowing glycolysis to keep running when mitochondrial oxidation is limited. It does not add extra ATP beyond glycolysis and does not produce acetyl-CoA.





**12** In lactic acid fermentation, pyruvate is converted to lactate. What happens to NADH in this reaction?

- A NADH is produced from  $\text{NAD}^+$
- B NADH is oxidized to  $\text{NAD}^+$  ✓**
- C NADH is converted into  $\text{FADH}_2$
- D NADH is pumped across the mitochondrial membrane
- E NADH becomes acetyl-CoA

► **Explanation:** Lactate dehydrogenase uses NADH to reduce pyruvate to lactate, regenerating  $\text{NAD}^+$ . The other options describe processes that do not occur in fermentation.



**13** Which statement about ATP yield is correct?

- A Fermentation produces additional ATP beyond glycolysis
- B Anaerobic metabolism yields the same ATP per glucose as aerobic metabolism
- C Without oxygen, the net ATP per glucose from glycolysis is still 2 ✓**
- D Without oxygen, glycolysis yields 0 ATP because NADH cannot form
- E Without oxygen, the Krebs cycle speeds up to compensate

► **Explanation:** Even anaerobically, glycolysis yields net 2 ATP per glucose (if  $\text{NAD}^+$  is regenerated via fermentation). Fermentation's key role is  $\text{NAD}^+$  regeneration, not extra ATP production; Krebs/ETC slow without oxygen.



**14** Which process directly produces  $\text{CO}_2$  from pyruvate before the Krebs cycle begins?

- A Glycolysis





- B Link reaction (pyruvate oxidation by pyruvate dehydrogenase) ✓**
- C ATP synthase activity
- D Lactic acid fermentation
- E Phosphorylation of glucose by hexokinase

► **Explanation:** The link reaction converts pyruvate (3C) to acetyl-CoA (2C) and releases CO<sub>2</sub> (1C), producing NADH. Glycolysis does not release CO<sub>2</sub>, and lactate fermentation does not produce CO<sub>2</sub> in humans.

**15** During the link reaction, one pyruvate molecule (3 carbons) becomes:



- A One acetyl-CoA (2C) + one CO<sub>2</sub> (1C) + NADH ✓**
- B One acetyl-CoA (3C) + one CO<sub>2</sub> (0C) + FADH<sub>2</sub>
- C Two acetyl-CoA (2C each) + one CO<sub>2</sub>
- D One lactate (3C) + NADH
- E One citrate (6C) directly

► **Explanation:** Pyruvate dehydrogenase removes one carbon as CO<sub>2</sub> and transfers the remaining 2-carbon acetyl group to CoA, generating NADH. Citrate forms later when acetyl-CoA combines with oxaloacetate.

**16** Where do the link reaction and Krebs cycle occur in eukaryotic cells?



- A Cytosol
- B Mitochondrial matrix ✓**
- C Outer mitochondrial membrane
- D Inner mitochondrial membrane





**E** Nucleus

► **Explanation:** The link reaction (pyruvate → acetyl-CoA) and the Krebs cycle enzymes are located in the mitochondrial matrix. The ETC and ATP synthase are embedded in the inner mitochondrial membrane.

**17** Per acetyl-CoA entering the Krebs cycle, which set of reduced electron carriers is produced?



- A** 2 NADH and 2 FADH<sub>2</sub>
- B** 3 NADH and 1 FADH<sub>2</sub> ✓
- C** 1 NADH and 3 FADH<sub>2</sub>
- D** 4 NADH and 0 FADH<sub>2</sub>
- E** 0 NADH and 0 FADH<sub>2</sub>

► **Explanation:** Each acetyl-CoA yields 3 NADH and 1 FADH<sub>2</sub> in the Krebs cycle (plus 1 GTP/ATP and 2 CO<sub>2</sub>). The other combinations are incorrect and are common counting traps.

**18** How many CO<sub>2</sub> molecules are released per acetyl-CoA during the Krebs cycle itself (not counting the link reaction)?



- A** 0
- B** 1
- C** 2 ✓
- D** 3
- E** 6

► **Explanation:** In the Krebs cycle, two decarboxylation steps release 2 CO<sub>2</sub> per acetyl-CoA. A third CO<sub>2</sub> per pyruvate is released earlier in the link reaction, not in the cycle itself.





19 Which step produces GTP (or ATP equivalent) directly in the Krebs cycle?



- A Citrate synthase step
- B Isocitrate →  $\alpha$ -ketoglutarate
- C **Succinyl-CoA → succinate** ✓
- D Succinate → fumarate
- E Malate → oxaloacetate

► **Explanation:** Succinyl-CoA synthetase performs substrate-level phosphorylation to generate GTP (or ATP). The other steps produce NADH/FADH<sub>2</sub> or are condensation/rearrangement reactions, not direct ATP/GTP formation.

20 Which statement best explains why the Krebs cycle is considered 'aerobic' even though O<sub>2</sub> is not used directly in the cycle?



- A O<sub>2</sub> is a substrate in the citrate synthase reaction
- B **The cycle requires NAD<sup>+</sup> and FAD, which are regenerated mainly by the electron transport chain that depends on O<sub>2</sub>** ✓
- C The cycle occurs in the lungs, where O<sub>2</sub> is abundant
- D O<sub>2</sub> is produced by the cycle, so it must be aerobic
- E The cycle only occurs during exercise

► **Explanation:** The Krebs cycle needs oxidized NAD<sup>+</sup> and FAD; these are regenerated when NADH/FADH<sub>2</sub> donate electrons to the ETC, which requires oxygen as the final electron acceptor. Without O<sub>2</sub>, NADH accumulates and the cycle slows/stops.





21 Where is the electron transport chain (ETC) located in eukaryotic cells?



- A Cytosol
- B Mitochondrial matrix
- C Outer mitochondrial membrane
- D Inner mitochondrial membrane ✓
- E Nuclear envelope

► **Explanation:** ETC complexes (I–IV) are embedded in the inner mitochondrial membrane, pumping protons into the intermembrane space. The matrix contains Krebs enzymes; the outer membrane is relatively permeable and does not host the ETC complexes.

22 The final electron acceptor in aerobic respiration is:



- A  $\text{NAD}^+$
- B FAD
- C Oxygen ( $\text{O}_2$ ) ✓
- D Carbon dioxide ( $\text{CO}_2$ )
- E Glucose

► **Explanation:** In aerobic respiration, oxygen accepts electrons at the end of the ETC (complex IV) and is reduced to water.  $\text{CO}_2$  is a waste product from decarboxylation reactions, not an electron acceptor.

23 Which complexes pump protons across the inner mitochondrial membrane in the ETC?



- A I, II, and III
- B II, III, and IV





- C I, III, and IV ✓**
- D I and II only
- E All complexes I–IV pump protons equally

► **Explanation:** Complexes I, III, and IV pump protons from the matrix to the intermembrane space. Complex II (succinate dehydrogenase) transfers electrons to ubiquinone but does not pump protons—a classic trap.

**24** In mitochondria, protons are pumped by the ETC from the:



- A Intermembrane space into the matrix
- B Matrix into the intermembrane space ✓**
- C Cytosol into the nucleus
- D Outer membrane into the cytosol
- E ER lumen into the cytosol

► **Explanation:** ETC complexes pump  $H^+$  out of the matrix into the intermembrane space, creating a proton gradient. ATP synthase allows protons to flow back into the matrix, driving ATP formation.

**25** ATP synthase makes ATP primarily by:



- A Using oxygen to directly phosphorylate ADP
- B Using light energy absorbed by chlorophyll
- C Allowing protons to flow down their electrochemical gradient through the enzyme, driving conformational changes that synthesize ATP ✓**
- D Breaking ATP to release energy and build more ATP
- E Transferring phosphate directly from glucose to ADP





► **Explanation:** ATP synthase couples proton flow (chemiosmosis) to ATP synthesis (oxidative phosphorylation). Oxygen is used at the end of the ETC to keep electrons flowing, but ATP synthase itself uses the proton gradient—not oxygen directly.

26 In mitochondria, the catalytic 'head' (F<sub>1</sub>) of ATP synthase faces the:



- A Intermembrane space
- B Mitochondrial matrix ✓**
- C Cytosol
- D Outer mitochondrial membrane
- E Nucleus

► **Explanation:** In mitochondria, protons flow from the intermembrane space back into the matrix through ATP synthase, and ATP is produced on the matrix side (F<sub>1</sub> faces the matrix). Confusing matrix vs intermembrane space is a common trap.

27 Which statement best distinguishes oxidative phosphorylation from substrate-level phosphorylation?



- A Oxidative phosphorylation happens in the cytosol; substrate-level phosphorylation happens in mitochondria only
- B Oxidative phosphorylation requires a proton gradient and ATP synthase; substrate-level phosphorylation uses direct phosphate transfer from a metabolic intermediate ✓**
- C Substrate-level phosphorylation requires oxygen; oxidative phosphorylation does not
- D Oxidative phosphorylation produces lactate; substrate-level phosphorylation produces CO<sub>2</sub>
- E They are different names for the same process





► **Explanation:** Oxidative phosphorylation couples electron transport and a proton gradient to ATP synthase activity. Substrate-level phosphorylation forms ATP (or GTP) directly from phosphorylated intermediates (e.g., in glycolysis and one Krebs step).

28 Which molecule donates electrons to Complex I of the ETC?



- A NADH ✓
- B FADH<sub>2</sub>
- C ATP
- D CO<sub>2</sub>
- E O<sub>2</sub>

► **Explanation:** NADH donates electrons to Complex I. FADH<sub>2</sub> donates electrons through Complex II (succinate dehydrogenase) or related entry points, which is why NADH generally yields more proton pumping than FADH<sub>2</sub>.

29 Complex II is unique among ETC complexes because it:



- A Is located in the mitochondrial matrix and never touches the membrane
- B Pumps the most protons
- C Transfers electrons from NADH to oxygen
- D Is the same enzyme as succinate dehydrogenase from the Krebs cycle and does not pump protons ✓
- E Directly makes ATP from ADP

► **Explanation:** Complex II is succinate dehydrogenase (a Krebs cycle enzyme) embedded in the inner membrane and passes electrons to ubiquinone without pumping protons. ATP synthase makes ATP; Complex II does not.





**30** Why does NADH typically produce more ATP than FADH<sub>2</sub> in oxidative phosphorylation?



- A FADH<sub>2</sub> cannot donate electrons to the ETC
- B NADH enters at Complex I, which pumps protons; FADH<sub>2</sub> enters at Complex II, which does not pump protons ✓**
- C FADH<sub>2</sub> is used only in glycolysis
- D NADH is produced only in the nucleus
- E FADH<sub>2</sub> directly turns into lactate

► **Explanation:** NADH donates electrons to Complex I, enabling proton pumping at I, III, and IV. FADH<sub>2</sub> donates electrons via Complex II (no proton pumping there), so fewer protons are pumped overall and less ATP is generated.

**31** A student claims: "Oxygen is needed for glycolysis." Which is the best correction?



- A True—glycolysis uses oxygen directly to split glucose
- B True—without oxygen, glycolysis cannot make any ATP
- C False—glycolysis does not use oxygen directly, but it requires NAD<sup>+</sup> regeneration, which can be supported by fermentation when oxygen is absent ✓**
- D False—glycolysis occurs in mitochondria where oxygen binds ATP synthase
- E False—glycolysis occurs only in plants

► **Explanation:** Glycolysis itself is anaerobic (no O<sub>2</sub> required). The real requirement is NAD<sup>+</sup>; oxygen matters indirectly because aerobic metabolism regenerates NAD<sup>+</sup> via the ETC, but fermentation can regenerate NAD<sup>+</sup> without oxygen.





32 Red blood cells (RBCs) rely heavily on anaerobic glycolysis mainly because they:



- A Have no mitochondria for Krebs cycle and oxidative phosphorylation ✓
- B Have no cytosol for glycolysis
- C Use photosynthesis for ATP
- D Cannot take up glucose
- E Contain chloroplasts instead of mitochondria

► **Explanation:** Mature RBCs lack mitochondria, so they cannot perform the link reaction, Krebs cycle, or ETC. They must generate ATP via cytosolic glycolysis and regenerate  $\text{NAD}^+$  by converting pyruvate to lactate.

33 If oxygen suddenly becomes unavailable, which immediate change is most likely inside mitochondria?



- A Electron transport accelerates because there is less competition
- B **NADH levels rise and  $\text{NAD}^+$  levels fall because electrons cannot be passed to oxygen** ✓
- C  $\text{CO}_2$  production increases sharply because Krebs cycle speeds up
- D ATP synthase produces more ATP because the proton gradient increases forever
- E Glycolysis stops because it requires oxygen directly

► **Explanation:** Without oxygen, electrons back up in the ETC, so NADH cannot be efficiently oxidized to  $\text{NAD}^+$ . This raises NADH/ $\text{NAD}^+$  ratio, slowing the link reaction and Krebs cycle and forcing reliance on fermentation for  $\text{NAD}^+$  regeneration.

34 Cyanide poisoning inhibits Complex IV. Which outcome is most expected?





- A Oxygen consumption increases and ATP production increases
- B Electron flow stops, oxygen cannot be reduced to water, and ATP production by oxidative phosphorylation falls dramatically ✓**
- C Glycolysis stops instantly in all tissues because Complex IV is in the cytosol
- D CO<sub>2</sub> production from glycolysis increases
- E Fermentation becomes impossible because NAD<sup>+</sup> becomes too abundant

► **Explanation:** Complex IV transfers electrons to oxygen; cyanide blocks this step, stopping the ETC, collapsing ATP production from oxidative phosphorylation, and reducing oxygen consumption. Glycolysis can still occur, often increasing fermentation to regenerate NAD<sup>+</sup>.

**35** Oligomycin blocks the proton channel of ATP synthase. What is the best prediction for oxygen consumption?



- A Oxygen consumption increases because electrons flow faster
- B Oxygen consumption decreases because the proton gradient cannot be used and electron transport slows due to backpressure ✓**
- C Oxygen consumption is unchanged because ATP synthase is unrelated to the ETC
- D Oxygen consumption becomes negative (oxygen is produced)
- E Oxygen consumption increases only if glycolysis is blocked

► **Explanation:** If protons cannot flow back through ATP synthase, the proton gradient builds and makes further proton pumping energetically difficult, slowing the ETC and lowering oxygen consumption. ATP production also falls.

**36** A chemical uncoupler makes the inner mitochondrial membrane more permeable to protons. Which combination is most expected?



- A Decreased oxygen consumption, increased ATP production, decreased heat





- B Increased oxygen consumption, decreased ATP production, increased heat ✓**
- C No change in oxygen consumption or ATP, because uncouplers act only on glycolysis
- D Increased ATP production because the gradient is larger
- E Stopped electron transport but increased ATP production

► **Explanation:** Uncouplers dissipate the proton gradient, so ATP synthase makes less ATP. The ETC may speed up trying to restore the gradient, increasing oxygen consumption, and the energy is released as heat.

**37 Which stage(s) of glucose metabolism produce(s) ATP directly by substrate-level phosphorylation?**



- A Electron transport chain only
- B Glycolysis and one step of the Krebs cycle ✓**
- C Link reaction only
- D ATP synthase only
- E Krebs cycle only at every step

► **Explanation:** Substrate-level ATP (or GTP) formation occurs at specific reactions: two in glycolysis and one in the Krebs cycle (succinyl-CoA → succinate). The ETC/ATP synthase produce ATP via oxidative phosphorylation, not direct phosphate transfer.

**38 Which statement correctly tracks carbon atoms during complete oxidation of one glucose molecule in aerobic respiration?**



- A Glucose (6C) becomes 6 CO<sub>2</sub> (1C each) overall ✓**
- B Glucose (6C) becomes 2 CO<sub>2</sub> overall
- C Glucose (6C) becomes 4 CO<sub>2</sub> overall





- D** Glucose (6C) becomes 6 lactate (3C each) overall
- E** Glucose carbons are conserved as water in aerobic respiration

► **Explanation:** Complete oxidation of one glucose releases all 6 carbons as CO<sub>2</sub> (2 from the link reactions and 4 from two turns of the Krebs cycle). Lactate formation occurs in anaerobic conditions and does not fully oxidize carbon to CO<sub>2</sub>.

**39** How many molecules of CO<sub>2</sub> are produced from one glucose molecule by the link reaction (pyruvate oxidation) alone?



- A** 0
- B** 1
- C** 2 ✓
- D** 4
- E** 6

► **Explanation:** One glucose produces 2 pyruvate, and each pyruvate releases 1 CO<sub>2</sub> when converted to acetyl-CoA. Therefore, the link reaction produces 2 CO<sub>2</sub> per glucose.

**40** Which of the following is the most direct reason mitochondria have highly folded cristae?



- A** To increase the surface area of the inner membrane for ETC complexes and ATP synthase ✓
- B** To increase DNA replication speed in the nucleus
- C** To allow glycolysis enzymes to attach to the membrane
- D** To increase the thickness of the outer membrane to prevent diffusion of CO<sub>2</sub>
- E** To store glucose as glycogen inside mitochondria





► **Explanation:** Cristae are folds of the inner mitochondrial membrane, increasing the area available for the ETC and ATP synthase, boosting capacity for oxidative phosphorylation. Glycolysis occurs in the cytosol, and glycogen is stored in the cytoplasm.

41 Which process directly produces the proton gradient that ATP synthase uses?



- A Glycolysis enzymes in the cytosol
- B Pyruvate dehydrogenase reaction in the matrix
- C **Electron transport chain proton pumping across the inner mitochondrial membrane**
- D Lactate dehydrogenase converting pyruvate to lactate
- E Citrate synthase condensing acetyl-CoA with oxaloacetate

► **Explanation:** The ETC uses energy from electron transfers to pump protons into the intermembrane space, creating the proton motive force. ATP synthase uses that gradient but does not create it; glycolysis and fermentation occur in the cytosol.

42 If the inner mitochondrial membrane suddenly became freely permeable to  $H^+$ , what would happen to ATP production by oxidative phosphorylation?



- A It would increase because protons can reach ATP synthase faster
- B **It would decrease sharply because the proton gradient would collapse** ✓
- C It would be unaffected because ATP synthase does not use protons
- D It would stop glycolysis in the cytosol
- E It would increase  $CO_2$  production in glycolysis

► **Explanation:** Oxidative phosphorylation depends on an intact proton gradient. If protons leak freely, the gradient collapses and ATP synthase cannot efficiently produce ATP, even if electron transport continues.



**43 Which description best matches the link reaction?**

- A** Glucose is split into two 3-carbon molecules and 2 ATP are produced
- B** A 3-carbon pyruvate is oxidized to a 2-carbon acetyl group attached to CoA, producing NADH and releasing CO<sub>2</sub> ✓
- C** Acetyl-CoA combines with oxygen to make water
- D** Protons flow down a gradient to phosphorylate ADP
- E** Pyruvate is reduced to lactate to produce ATP

► **Explanation:** The link reaction (pyruvate oxidation) connects glycolysis to the Krebs cycle by generating acetyl-CoA, NADH, and CO<sub>2</sub>. It does not directly produce ATP, and proton flow/ATP synthase are part of oxidative phosphorylation, not the link reaction.

**44 Which statement about NADH is correct in cellular respiration?**

- A** NADH is the final electron acceptor in the ETC
- B** NADH carries high-energy electrons to the ETC where their energy helps pump protons to build a gradient ✓
- C** NADH is produced only during oxidative phosphorylation
- D** NADH is used to directly phosphorylate ADP by transferring phosphate groups
- E** NADH is a structural protein of the mitochondrial membrane

► **Explanation:** NADH is a reduced electron carrier produced in glycolysis, the link reaction, and the Krebs cycle. It donates electrons to the ETC, powering proton pumping; oxygen, not NADH, is the final electron acceptor.





**45** Which statement is most accurate about anaerobic vs aerobic conditions in human cells?

- A Anaerobic conditions allow Krebs cycle and ETC to run normally
- B Anaerobic conditions prevent glycolysis from producing ATP
- C Aerobic conditions allow NADH to be oxidized by the ETC, supporting continued Krebs cycle activity ✓
- D Oxygen is used directly in glycolysis to split glucose
- E Fermentation occurs in mitochondria to make CO<sub>2</sub> and water

► **Explanation:** Aerobic respiration uses oxygen at the end of the ETC, enabling NADH oxidation to NAD<sup>+</sup> and supporting continued operation of the link reaction and Krebs cycle. In anaerobic conditions, the ETC slows/stops, and cells rely on fermentation to regenerate NAD<sup>+</sup> for glycolysis.



**46** Which step is the main reason glycolysis is considered to have an 'investment phase'?

- A NAD<sup>+</sup> is reduced to NADH
- B ATP is used to phosphorylate intermediates before ATP is produced later ✓
- C CO<sub>2</sub> is produced early
- D FADH<sub>2</sub> is consumed to start the pathway
- E Oxygen is used to activate glucose

► **Explanation:** In the investment phase, ATP is spent to phosphorylate glucose and fructose-6-phosphate, priming the molecule for later energy payoff. CO<sub>2</sub> is not produced in glycolysis, and oxygen is not used.



**47** A student says: "The mitochondrion is where glucose is broken into two pyruvates." Which correction is best?





- A Correct—glycolysis occurs in the mitochondrial matrix
- B Correct—glycolysis occurs on the inner mitochondrial membrane
- C Incorrect—glycolysis occurs in the cytosol; mitochondria oxidize pyruvate and run the Krebs cycle and ETC ✓**
- D Incorrect—glucose is broken into CO<sub>2</sub> directly in the nucleus
- E Incorrect—glucose is broken into lactate only inside mitochondria

► **Explanation:** Glycolysis is cytosolic. Mitochondria primarily carry out pyruvate oxidation, the Krebs cycle, and oxidative phosphorylation. Confusing location is a common exam trap.

48 Which of the following happens directly at Complex IV of the ETC?



- A NADH donates electrons to ubiquinone
- B Succinate is oxidized to fumarate
- C Electrons are transferred to oxygen to form water ✓**
- D ATP is made by direct phosphate transfer from PEP
- E Glucose is phosphorylated to glucose-6-phosphate

► **Explanation:** Complex IV (cytochrome c oxidase) passes electrons to oxygen, producing water and allowing the chain to continue. Succinate oxidation occurs at Complex II; NADH oxidation starts at Complex I; ATP from PEP is glycolysis.

49 Which statement best captures why ATP synthase is not considered a 'pump' in the same way as ETC complexes I, III, and IV?



- A ATP synthase actively pumps protons from matrix to intermembrane space using ATP
- B ATP synthase mainly allows protons to flow down their gradient and uses that energy to synthesize ATP ✓**





- C** ATP synthase is located in the cytosol and uses glucose directly
- D** ATP synthase transfers electrons to oxygen
- E** ATP synthase converts CO<sub>2</sub> into glucose

► **Explanation:** ETC complexes pump protons uphill (against gradient) using electron-transfer energy. ATP synthase harnesses downhill proton flow (with the gradient) to drive ATP synthesis—opposite direction of energy use.

**50** Cytosolic NADH produced by glycolysis cannot cross the inner mitochondrial membrane directly. In many cells, it is shuttled into mitochondria. Why does this matter for ATP yield?



- A** Because cytosolic NADH is always wasted and produces 0 ATP
- B** Because different shuttles can transfer the electrons in ways that enter the ETC at different points, affecting how many protons are pumped and thus ATP yield ✓
- C** Because cytosolic NADH is converted into glucose in the shuttle
- D** Because shuttles are only used during fermentation
- E** Because shuttles move oxygen into mitochondria

► **Explanation:** Electron shuttles move the reducing power of cytosolic NADH into mitochondria. If electrons enter as NADH at Complex I (e.g., malate-aspartate shuttle), more proton pumping occurs than if they enter downstream as FADH<sub>2</sub>-equivalents (e.g., glycerol phosphate shuttle), changing ATP yield per glucose.

