Chapter 16 The Citric Acid Cycle

Multiple Choice Questions

1. Which of the following is not true of the reaction catalyzed by the pyruvate dehydrogenase complex?
   A) Biotin participates in the decarboxylation.
   B) Both NAD+ and a flavin nucleotide act as electron carriers.
   C) The reaction occurs in the mitochondrial matrix.
   D) The substrate is held by the lipoyl-lysine “swinging arm.”
   E) Two different cofactors containing —SH groups participate.

2. Which of the below is not required for the oxidative decarboxylation of pyruvate to form acetyl-CoA?
   A) ATP
   B) CoA-SH
   C) FAD
   D) Lipoic acid
   E) NAD+

3. Which of the following is not true of the citric acid cycle?
   A) All enzymes of the cycle are located in the cytoplasm, except succinate dehydrogenase, which is bound to the inner mitochondrial membrane.
   B) In the presence of malonate, one would expect succinate to accumulate.
   C) Oxaloacetate is used as a substrate but is not consumed in the cycle.
   D) Succinate dehydrogenase channels electrons directly into the electron transfer chain.
   E) The condensing enzyme is subject to allosteric regulation by ATP and NADH.

4. Malonate is a competitive inhibitor of succinate dehydrogenase. If malonate is added to a mitochondrial preparation that is oxidizing pyruvate as a substrate, which of the following compounds would you expect to decrease in concentration?
   A) Citrate
   B) Fumarate
   C) Isocitrate
   D) Pyruvate
   E) Succinate

5. Which of the following is not an intermediate of the citric acid cycle?
   A) Acetyl-coA
   B) Citrate
   C) Oxaloacetate
   D) Succinyl-coA
   E) α-Ketoglutarate

6. In mammals, each of the following occurs during the citric acid cycle except:
   A) formation of α-ketoglutarate.
   B) generation of NADH and FADH₂.
   C) metabolism of acetate to carbon dioxide and water.
   D) net synthesis of oxaloacetate from acetyl-CoA.
   E) oxidation of acetyl-CoA.
7. Conversion of 1 mol of acetyl-CoA to 2 mol of CO₂ via the citric acid cycle results in the net production of:
   A) 1 mol of citrate.
   B) 1 mol of FADH₂.
   C) 1 mol of NADH.
   D) 1 mol of oxaloacetate.
   E) 7 mol of ATP.

8. The oxidative decarboxylation of α-ketoglutarate proceeds by means of multistep reactions in which all but one of the following cofactors are required. Which one is not required?
   A) ATP
   B) Coenzyme A
   C) Lipoic acid
   D) NAD⁺
   E) Thiamine pyrophosphate

9. The reaction of the citric acid cycle that is most similar to the pyruvate dehydrogenase complex catalyzed conversion of pyruvate to acetyl-CoA is the conversion of:
   A) citrate to isocitrate.
   B) fumarate to malate.
   C) malate to oxaloacetate.
   D) succinyl-CoA to succinate.
   E) α-ketoglutarate to succinyl-CoA.

10. Which one of the following enzymatic activities would be decreased by thiamine deficiency?
    A) Fumarase
    B) Isocitrate dehydrogenase
    C) Malate dehydrogenase
    D) Succinate dehydrogenase
    E) α-Ketoglutarate dehydrogenase complex

11. The reaction of the citric acid cycle that produces an ATP equivalent (in the form of GTP) by substrate level phosphorylation is the conversion of:
    A) citrate to isocitrate.
    B) fumarate to malate.
    C) malate to oxaloacetate.
    D) succinate to fumarate.
    E) succinyl-CoA to succinate.

12. For the following reaction, ΔG°' = 29.7 kJ/mol.
    \[ \text{L-Malate} + \text{NAD}^+ \rightarrow \text{oxaloacetate} + \text{NADH} + \text{H}^+ \]
    The reaction as written:
    A) can never occur in a cell.
    B) can only occur in a cell if it is coupled to another reaction for which ΔG°' is positive.
    C) can only occur in a cell in which NADH is converted to NAD⁺ by electron transport.
    D) may occur in cells at certain concentrations of substrate and product.
    E) would always proceed at a very slow rate

13. The oxidative steps of the citric acid cycle are linked to the reduction of NAD⁺ except the reaction catalyzed by:
    A) isocitrate dehydrogenase.
    B) malate dehydrogenase.
    C) pyruvate dehydrogenase
    D) succinate dehydrogenase.
    E) the α-ketoglutarate dehydrogenase complex.
14. Which of the following cofactors is required for the conversion of succinate to fumarate in the citric acid cycle?
   A) ATP
   B) Biotin
   C) FAD
   D) NAD^+
   E) NADP^+

15. The conversion of 1 mol of pyruvate to 3 mol of CO\(_2\) via pyruvate dehydrogenase and the citric acid cycle also yields _____ mol of NADH, _____ mol of FADH\(_2\), and _____ mol of ATP (or GTP).
   A) 2; 2; 2
   B) 3; 1; 1
   C) 3; 2; 0
   D) 4; 1; 1
   E) 4; 2; 1

16. Entry of acetyl-CoA into the citric acid cycle is decreased when:
   A) [AMP] is high.
   B) NADH is rapidly oxidized through the respiratory chain.
   C) the ratio of [ATP]/[ADP] is low.
   D) the ratio of [ATP]/[ADP] is high.
   E) the ratio of [NAD^+]/[NADH] is high.

17. Citrate synthase and the NAD^+-specific isocitrate dehydrogenase are two key regulatory enzymes of the citric acid cycle. These enzymes are inhibited by:
   A) acetyl-CoA and fructose 6-phosphate.
   B) AMP and/or NAD^+.
   C) AMP and/or NADH.
   D) ATP and/or NAD^+.
   E) ATP and/or NADH.

18. During seed germination, the glyoxylate pathway is important to plants because it enables them to:
   A) carry out the net synthesis of glucose from acetyl-CoA.
   B) form acetyl-CoA from malate.
   C) get rid of isocitrate formed from the aconitase reaction.
   D) obtain glyoxylate for cholesterol biosynthesis.
   E) obtain glyoxylate for pyrimidine synthesis.

19. A function of the glyoxylate cycle, in conjunction with the citric acid cycle, is to accomplish the:
   A) complete oxidation of acetyl-CoA to CO\(_2\) plus reduced coenzymes.
   B) net conversion of lipid to carbohydrate.
   C) net synthesis of four-carbon dicarboxylic acids from acetyl-CoA.
   D) net synthesis of long-chain fatty acids from citric acid cycle intermediates.
   E) both B and C are correct

20. The glyoxylate cycle is:
   A) a means of using acetate for both energy and biosynthetic precursors.
   B) an alternative path of glucose metabolism in cells that do not have enough O\(_2\).
   C) defective in people with phenylketonuria.
   D) not active in a mammalian liver.
   E) the most direct way of providing the precursors for synthesis of nucleic acids (e.g., ribose).
Short Answer Questions

1. Balance Sheet for the Citric Acid Cycle The citric acid cycle has eight enzymes: citrate synthase, aconitase, isocitrate dehydrogenase, a-ketoglutarate dehydrogenase, succinyl-CoA synthetase, succinate dehydrogenase, fumarase, and malate dehydrogenase.
   (a) Write a balanced equation for the reaction catalyzed by each enzyme.
   (b) Name the cofactor(s) required by each enzyme reaction.
   (c) For each enzyme determine which of the following describes the type of reaction(s) catalyzed: condensation (carbon–carbon bond formation); dehydration (loss of water); hydration (addition of water); decarboxylation (loss of CO2); oxidation-reduction; substrate-level phosphorylation; isomerization.
   (d) Write a balanced net equation for the catabolism of acetyl-CoA to CO2.

2. Net Equation for Glycolysis and the Citric Acid Cycle Write the net biochemical equation for the metabolism of a molecule of glucose to CO2, including all cofactors.

3. Pyruvate Dehydrogenase Cofactors and Mechanism Describe the role of each cofactor involved in the reaction catalyzed by the pyruvate dehydrogenase complex.

4. Thiamine Deficiency Individuals with a thiamine-deficient diet have relatively high levels of pyruvate in their blood. Explain this in biochemical terms.

5. Cofactors for the Citric Acid Cycle Suppose you have prepared a mitochondrial extract that contains all of the soluble enzymes of the matrix but has lost (by dialysis) all the low molecular weight cofactors. What must you add to the extract so that the preparation will oxidize acetyl-CoA to CO2?

6. Riboflavin Deficiency How would a riboflavin deficiency affect the functioning of the citric acid cycle?

7. Oxaloacetate Pool What factors might decrease the pool of oxaloacetate available for the activity of the citric acid cycle? How can the pool of oxaloacetate be replenished?

8. Energy Yield from the Citric Acid Cycle The reaction catalyzed by succinyl-CoA synthetase produces the high-energy compound GTP. How is the free energy contained in GTP incorporated into the cellular ATP pool?

9. Respiration Studies in Isolated Mitochondria Cellular respiration can be studied in isolated mitochondria by measuring oxygen consumption under different conditions. If 0.01 M sodium malonate is added to actively respiring mitochondria that are using pyruvate as fuel source, respiration soon stops and a metabolic intermediate accumulates.
   (a) What is the structure of this intermediate?
   (b) Explain why it accumulates.
   (c) Explain why oxygen consumption stops.
   (d) Aside from removal of the malonate, how can this inhibition of respiration be overcome?

10. Role of the Vitamin Thiamine People with beriberi, a disease caused by thiamine deficiency, have elevated levels of blood pyruvate and a-ketoglutarate, especially after consuming a meal rich in glucose. How are these effects related to a deficiency of thiamine?
11. Synthesis of Oxaloacetate by the Citric Acid Cycle Oxaloacetate is formed in the last step of the citric acid cycle by the NAD-dependent oxidation of L-malate. Can a net synthesis of oxaloacetate from acetyl-CoA occur using only the enzymes and cofactors of the citric acid cycle, without depleting the intermediates of the cycle? Explain. How is oxaloacetate that is lost from the cycle (to biosynthetic reactions) replenished?

12. Oxaloacetate Depletion Mammalian liver can carry out gluconeogenesis using oxaloacetate as the starting material (Chapter 14). Would the operation of the citric acid cycle be affected by extensive use of oxaloacetate for gluconeogenesis? Explain your answer.

13. Regulation of the Pyruvate Dehydrogenase Complex In animal tissues, the rate of conversion of pyruvate to acetyl-CoA is regulated by the ratio of active, phosphorylated to inactive, unphosphorylated PDH complex. Determine what happens to the rate of this reaction when a preparation of rabbit muscle mitochondria containing the PDH complex is treated with (a) pyruvate dehydrogenase kinase, ATP, and NADH; (b) pyruvate dehydrogenase phosphatase and Ca²⁺; (c) malonate.

14. Effect of [NADH]/[NAD⁺] on the Citric Acid Cycle How would you expect the operation of the citric acid cycle to respond to a rapid increase in the [NADH]/[NAD⁺] ratio in the mitochondrial matrix? Why?