BIOL/CHEM 3361 and BIOL 6352 **FORM A**

EXAM No. 4 Spring 2012, Marsh and Spiro

PLEASE MAKE SURE TO BUBBLE YOUR NAME AND STUDENT ID ON THE SCANTRON

There are 50 multiple choice questions, and two short answer questions (on the last page). Write your answer to the short answer questions and your name on the back of the Scantron.

GLUCONEOGENESIS

1. Which of the following are major sites of gluconeogenesis?

   (i) brain
   (ii) liver
   (iii) muscle
   (iv) kidney

   a. (i) and (iii).
   b. (i).
   c. (iii).
   d. (ii) and (iv).
   e. all four.

2. Which of the following mediates the reciprocal regulation of the interconversion of fructose-6-phosphate and fructose-1,6-bisphosphate?

   a. Fructose.
   b. Fructose-1-phosphate.
   c. Fructose-6-phosphate.
   d. Fructose-1,6-bisphosphate.
   e. Fructose-2,6-bisphosphate.

3. Which enzyme in the gluconeogenesis pathway requires biotin as a prosthetic group?

   a. Pyruvate carboxylase.
   b. Phosphoenolpyruvate carboxykinase.
   c. Fructose-1,6-bisphosphatase.
   d. Glucose-6-phosphatase.
   e. None of the above.

4. In gluconeogenesis, how many molecules of NADH are oxidized to NAD^+ for each glucose molecule synthesized?

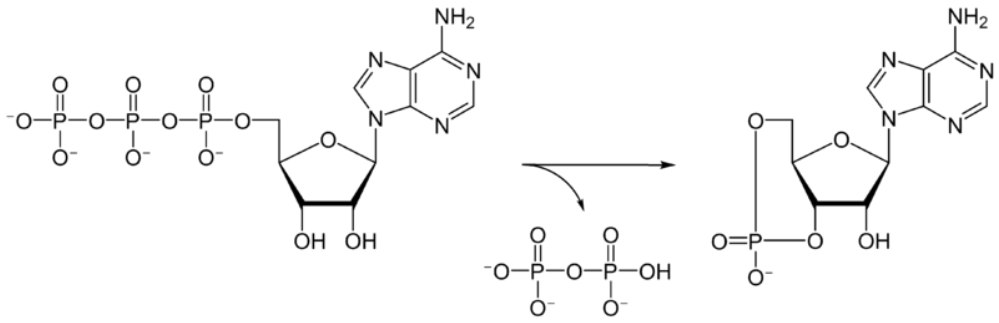
a. 0
b. 0.5
c. 1
d. 2
e. 4

5. If one molecule of glucose is converted to 2pyruvate by glycolysis then back to glucose by gluconeogenesis, what is the NET number of nucleoside triphosphates (ATP + GTP) consumed?

a. 2
b. 3
c. 4
d. 5
e. 6

GLYCOGEN METABOLISM AND THE PENTOSE PHOSPHATE PATHWAY
PLEASE NOTE THAT WE ARE NOT COVERING THE PENTOSE PHOSPHATE PATHWAY THIS SEMESTER

6. What enzyme catalyzes the reaction shown below?



a. Cyclic AMP dependent protein kinase.
b. Adenylate kinase.
c. G protein.
d. The glucagon receptor.
e. Adenylyl cyclase.

7. The reaction catalyzed by glycogen phosphorylase is a:

a. Hydrolysis.
b. Phosphorylation.
c. Cyclization.
d. Dephosphorylation.
e. Phosphorolysis.

8. What is the effect of phosphorylation on glycogen phosphorylase?

a. The enzyme is inactivated.
b. The enzyme becomes persistently active.
c. None - glycogen phosphorylase is not normally phosphorylated.
d. The enzyme becomes more sensitive to allosteric regulation.
e. The enzyme is converted from the a form to the b form.

9. What is the role of cAMP-dependent protein kinase in the cascade regulation of glycogen phosphorylase?

a. It phosphorylates glycogen phosphorylase.
b. It cyclizes ATP to make cAMP.
c. It phosphorylates adenylyl cyclase.
d. It phosphorylates the G protein.
e. It phosphorylates phosphorylase kinase.

10. Which of the following is the monomeric substrate for glycogen synthase?

a. Glucose.
b. Glucose-1-phosphate.
c. Glucose-6-phosphate.
d. UDP-glucose.
e. Glycogenin.

11. How many nucleoside triphosphates (ATP + UTP) are consumed for each molecule of glucose that is incorporated into glycogen?

a. 0.
b. 1.
c. 2.
d. 3.
e. 4.

12. The main function of the oxidative reactions of the pentose phosphate pathway is to:

a. Generate NADH.
b. Provide NADPH for biosynthetic metabolism.
c. Provide ribose-5-phosphate for biosynthetic metabolism.
d. Generate ATP by substrate level phosphorylation.
e. All are true.

13. When a cell with the pentose phosphate pathway requires both ribose-5-phosphate and NADPH the following happens:

    a. The oxidative reactions are active, NADPH and ribose-5-phosphate are consumed in biosynthetic metabolism, so the non-oxidative reactions are inactive.
    b. The oxidative and non-oxidative branches of the pentose phosphate pathway are both active.
    c. The non-oxidative enzymes produce pentose phosphates from fructose-6-phosphate and glyceraldehyde-3-phosphate.
    d. Glucose-6-phosphate is oxidized to CO_2, fructose-6-phosphate and glyceraldehyde-3-phosphate are converted back to glucose by gluconeogenesis.
    e. None is true.

THE TCA CYCLE

14. What is the sequence of the first five reactions of the TCA cycle?

    A. α-ketoglutarate dehydrogenase.
    B. Succinyl CoA synthetase.
    C. Citrate synthase.
    D. Isocitrate dehydrogenase
    E. Aconitase.

    a. C, E, D, A, B.
    b. A, B, C, D, E.
    c. E, C, D, A, B.
    d. C, D, E, A, B.
    e. B, A, D, E, C.

15. The pyruvate dehydrogenase complex reaction is a(n):

    a. Respiration.
    b. Oxidative decarboxylation.
    c. Substrate level phosphorylation.
    d. Oxidative phosphorylation.
    e. Reductive decarboxylation.

16. What is the function of the E3 component of the pyruvate dehydrogenase complex?

    a. To reoxidize reduced lipoamide.
    b. To transfer an acetyl group from acetyl dihydrolipoamide to coenzyme A forming acetyl CoA
    c. To transfer a 2 carbon unit to lipoamide forming acetyl dihydrolipoamide.
    d. To decarboxylate pyruvate forming hydroxyethyl TPP.
    e. To allow the 'swinging arm' of lipoamide to visit the active sites of E1 and E2

17. Which of the following is NOT an intermediate of the TCA cycle?

    a. Oxaloacetate.
    b. Succinyl CoA.
    c. Malate.
    d. Glyoxylate.
    e. Isocitrate.

18. Which of the following cofactors and prosthetic groups does NOT have a role in the pyruvate dehydrogenase complex reaction?

    a. Thiamine pyrophosphate
    b. $FAD/FADH_2$
    c. $NAD^+/NADH$
    d. Fe-S clusters
    e. Lipoamide

19. The _____ cluster of _____ functions to _____ during the reaction

    a. 2Fe-2S; aconitase; transfer electrons
    b. 4Fe-4S; aconitase; transfer electrons
    c. 3Fe-4S; aconitase; coordinate the substrate
    d. 4Fe-4S; citrate synthase; coordinate the substrate
    e. 4Fe-4S; aconitase; coordinate the substrate

20. Fluoroacetate is a suicide substrate inhibitor of the TCA cycle. The product of fluoroacetate metabolism is _____ which inhibits _____:

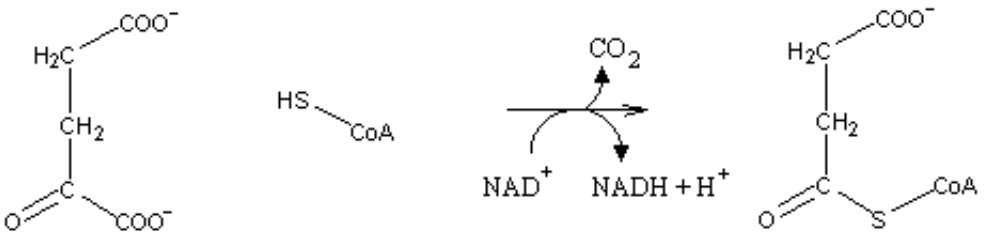
    a. Fluorocitrate; citrate synthase
    b. Fluorocitrate; aconitase
    c. Fluoroacetyl CoA; acetyl CoA synthetase
    d. Fluoroacetyl CoA; citrate synthase
    e. Fluoroaconitate; aconitase

21. Which reactions of the TCA cycle generate NADH?

(i) Citrate synthase.
(ii) Isocitrate dehydrogenase.
(iii) α-ketoglutarate dehydrogenase.
(iv) Succinate dehydrogenase.
(v) Malate dehydrogenase

a. (i)
b. (ii), (iii), (iv) and (v)
c. (iv)
d. (ii), (iii) and (v)
e. (ii) and (iv)

22. The reaction shown is a(n) _____ catalyzed by _____.



a. Substrate level phosphorylation; α-ketoglutarate dehydrogenase.
b. Oxidative decarboxylation; pyruvate dehydrogenase.
c. Oxidative decarboxylation; succinyl CoA synthetase.
d. Substrate level phosphorylation; succinyl CoA synthetase.
e. Oxidative decarboxylation; α-ketoglutarate dehydrogenase.

23. The α-ketoglutarate dehydrogenase is similar to:

a. Pyruvate dehydrogenase.
b. Citrate synthase
c. Isocitrate dehydrogenase.
d. Succinate dehydrogenase.
e. Malate dehydrogenase.

24. The succinyl CoA synthetase reaction is unique to the TCA cycle because:

a. It generates NADH.
b. It generates CO_2.
c. It is a substrate level phosphorylation.
d. It generates a reduced flavin adenine dinucleotide.
e. It is an oxidative decarboxylation.

25. Succinate dehydrogenase is unique to the TCA cycle because:

(i) It is membrane bound.
(ii) It contains an iron-sulfur cluster.
(iii) It contains heme.
(iv) It delivers electrons to the electron transfer chain.

a. (i)
b. (ii)
c. (iv)
d. (i), (iii) and (iv)
e. (i), (ii), (iii) and (iv)

26. The oxidation of malate to oxaloacetate is not thermodynamically favored under standard state conditions. It occurs because:

a. It involves substrate-level phosphorylation.
b. It is coupled with a strong reduction.
c. It is coupled with ATP hydrolysis.
d. Oxaloacetate is used in the next reaction which has a negative ΔG.
e. The previous reaction has a large negative ΔG.

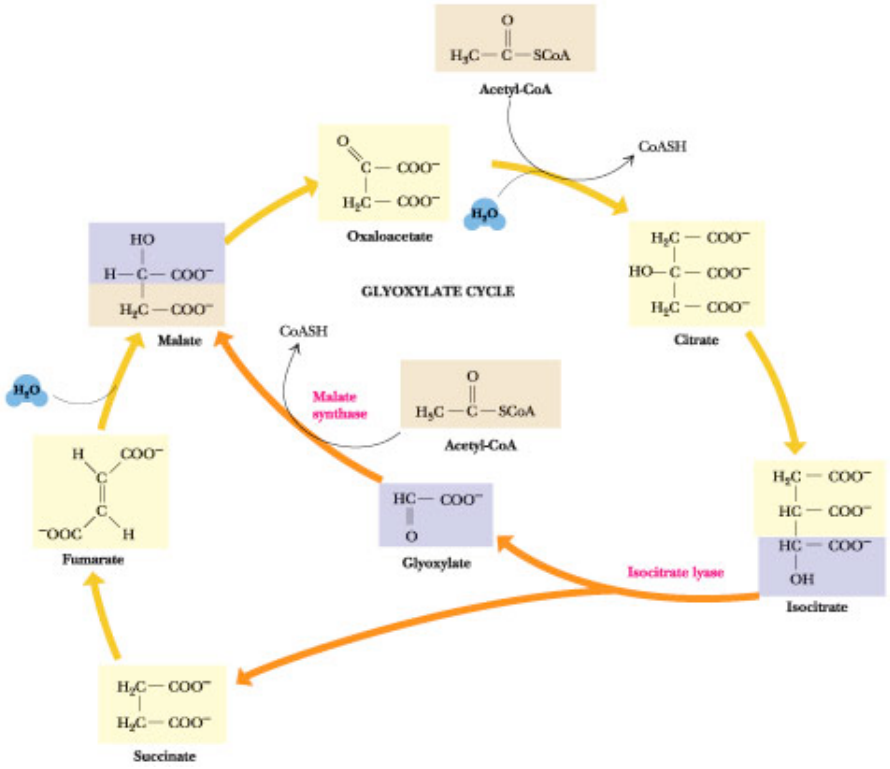
27. When glucose is metabolized by glycolysis and the TCA cycle how many NADH are generated per molecule of glucose?

a. 4
b. 5
c. 6
d. 8
e. 10

28. What is the role of the anaplerotic reactions associated with the TCA cycle?

a. To reoxidize NADH.
b. To generate ATP.
c. To replenish cycle intermediates that are used for biosynthesis.
d. To allow growth on acetate as a carbon and energy source.
e. To reduce the velocity of the TCA cycle when cells are energy sufficient.

29. The diagram below shows the glyoxylate cycle. Note that two acetyl CoA are consumed in each turn of the cycle, and that some details are omitted from this diagram. Use your knowledge of the TCA cycle to calculate the number of NADH molecules generated per acetyl CoA metabolized by the glyoxylate cycle (*ie* the ratio NADH produced/acetyl CoA consumed).



a. 0
b. 0.5
c. 1
d. 2
e. 2.5

ELECTRON TRANSPORT AND OXIDATIVE PHOSPHORYLATION

30. In the reaction between oxygen and hydrogen, which of the following is the donor couple?

a. O_2 and H_2O
b. H_2 and O_2
c. H^+ and e^-
d. H^+ and O_2
e. H^+ and H_2

31. What is the terminal electron acceptor in the mitochondrial electron transport chain?

a. Oxygen.
b. Ubiquinone.
c. NADH.
d. NAD^+.
e. Ubiquinol.

32. In *Escherichia coli*, the transfer of electrons from NADH to oxygen requires two enzymes. What are they?

a. NADH dehydrogenase and cytochrome oxidase.
b. Succinate dehydrogenase and quinol oxidase.
c. NADH dehydrogenase and quinol oxidase.
d. NADH dehydrogenase and cytochrome *c*.
e. NAD dehydrogenase and coenzyme Q.

33. Which of the following proteins reduce ubiquinone?

a. Complex 1 and cytochrome *c*
b. Complex 1 and complex 2
c. Complex 1 and complex 4
d. Complex 2 and complex 4
e. Complex 2 and cytochrome *c*

34. Which of the following act as electron donors to the mitochondrial electron transport chain?

a. NADH and ubiquinone
b. H_2O and NADH
c. NADH and succinate
d. NADH and oxygen
e. oxygen and succinate

35. In mitochondria, which component accepts electrons from cytochrome *c*?

a. Complex 1.
b. Complex II.
c. Complex III.
d. Complex IV.
e. Uniquinone.

36. The O_2/H_2O redox couple has a large _____ reduction potential, and so has a strong tendency to undergo _____ and oxygen is a good _____ of electrons.

a. positive; reduction; donor
b. negative; oxidation; donor
c. negative; reduction; acceptor
d. positive; reduction; acceptor
e. positive; oxidation; acceptor

37. Which complex reduces molecular oxygen?

a. Complex I.
b. Complex II.
c. Complex III.
d. UQH/UQH_2 pool.
e. Complex IV.

38. Which statement is an accurate description of the mechanism of proton translocation by NADH dehydrogenase (Complex 1)?

a. Protons are translocated by a redox loop mechanism involving oxidation and reduction of an enzyme-bound coenzyme Q.
b. Protons are translocated by proton pumps in the enzyme.
c. Protons are translocated by a redox loop and by proton pumps.
d. NADH dehydrogenase is not a proton pump.
e. Protons are translocated by a redox loop mechanism involving oxidation and reduction of NADH.

39. Succinate dehydrogenase couples the oxidation of succinate to the reduction of:

a. Ubiquinone.
b. Ubiquinol.
c. NAD^+.
d. Fumarate.
e. Cytochrome *c*.

40. Complex IV is unique in the electron transport chain because it contains:

a. Heme.
b. Coenzyme Q.
c. Fe-S clusters.
d. Copper.
e. FAD.

41. Which of the following mediate electron transfer between protein complexes?

A. UQ/UQH_2
B. Cyt *c*
C. Complex III

a. A only
b. B only
c. C only
d. B & C
e. A & B

42. In the Q cycle, Complex III oxidizes _____ molecule(s) of ubiquinol, reduces _____ molecule(s) of ubiquinone, and reduces _____ molecule(s) of cytochrome *c*.

a. One; two; two.
b. Two; zero; two.
c. One; zero; two.
d. Two; one; one.
e. Two; one; two.

43. In mitochondria, how many protons are thought to be translocated across the inner membrane for each molecule of NADH that is oxidized?

a. 0.
b. 4.
c. 6.
d. 8.
e. 10.

44. The reduction of half a molecule of oxygen (O_2) to one molecule of water requires how many electrons?

a. two
b. three
c. four
d. eight
e. six

45. What molecule is the electron donor to complex I?

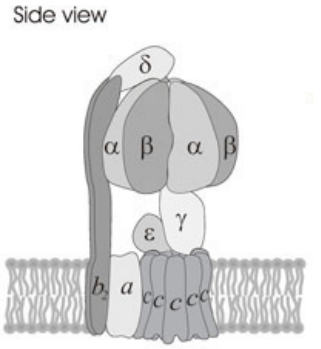
a. Cytochrome *c*
b. UQH_2
c. NADH
d. Succinate
e. $FADH_2$

46. Which of the following complex(es) translocate protons in the inner mitochondrial membrane?

1. Complex I
2. Complex II
3. Complex III
4. Complex IV

a. 1, 3 & 4
b. 1 & 2
c. 1, 2 & 4
d. 4 only
e. all of the above

47. The diagram is a schematic of the structure of ATP synthase. During catalysis, which components of the enzyme rotate?



a. c and γ.
b. α and β.
c. a, c and γ.
d. b, a, c and γ.
e. c, γ, α and ß.

48. Look again at the diagram of ATP synthase. Which of the following statements is <u>INCORRECT</u>?

a. The F_1 component is attached to the integral membrane component F_O.
b. Protons pass through the enzyme by moving through channels in the a subunit.
c. The active site for ADP phosphorylation is located in the ß subunit.
d. The F_1 component is located in the inter-membrane space.
e. The γ subunit is a stalk connecting the ring of c subunits to the α and ß subunits.

49. Which of the following statements about uncouplers is INCORRECT?

a. Oxygen consumption continues in the presence of an uncoupler.
b. NADH oxidation continues in the presence of an uncoupler.
c. The proton gradient is collapsed in the presence of an uncoupler.
d. ATP synthesis continues in the presence of an uncoupler.
e. Energy is dissipated as heat in the presence of an uncoupler.

50. What provides the driving force for the export of ATP from mitochondria?

a. Rotary catalysis by the ATP synthase.
b. Proton pumps.
c. ATP hydrolysis.
d. The ATP/ADP translocase.
e. The proton motive force.

PLEASE WRITE YOUR NAME ON THE FRONT OF THE QUESTION PAPER AND TURN EVERYTHING IN AT THE END (WITHOUT SEPARATING), OR YOU WILL GET NO CREDIT. WRITE YOUR ANSWERS ON THIS PAGE NOT THE SCANTRON.

1. You are studying oxidative phosphorylation in a sample of bacteria, and find that 10 protons are translocated across the cytoplasmic membrane for each NADH that is oxidized. You estimate experimentally that the bacteria make 2 ATP for each 2 electrons that enter electron transport from NADH. Assuming your estimate is correct, how many c subunits does the organism's ATP synthase have? Remember that bacteria do not need to export ATP (so there is no need to account for export). You do not need a calculator – leave the answer as a fraction if necessary. **[5 points]**

2. An oxygen electrode is a device that allows for the measurement of oxygen consumption by isolated mitochondria. Suppose you have a preparation of mitochondria that actively oxidize NADH and phosphorylate ADP to make ATP. (a) What would you expect to happen to the rate of oxygen consumption in the presence of an inhibitor of the ATP synthase? (b) In the presence of an uncoupler you discover that the rate of oxygen consumption increases. Can you suggest an explanation? In both cases, explain your reasoning briefly for full credit. **[5 points]**