UNIVERSITY OF TORONTO
FACULTY OF ARTS AND SCIENCE
BIOCHEMISTRY 210HF

Final Examination: December 13th, 2010
Total Duration: 3 hours

Examiners: Drs. R. Andreopoulos and R.R. Baker

Candidates may use simple calculators (supplied by candidates).

This examination is worth 50% of the final grade for the course. There are 35 multiple choice questions worth 1 mark each for a total of 35 marks and 8 short answer questions worth a total of 15 marks.

For the multiple choice questions you are to choose ONE answer for each question and fill in the appropriate circle on the computer card with a soft lead pencil (**not pen!**). Marks are not deducted for wrong choices but no marks are given if more than one circle is filled in per question.

We cannot help you if you make transcriptional errors. It is thus not a good idea to leave entering your answers on the card to the last few minutes of the exam.

When not entering answers on your card you should cover the answer card with your question paper.

Please note that the examiners make every effort to ensure there is only one suitable answer for each multiple choice question. However, if you are convinced that a particular question has two answers, you should select the answer that seems **MOST** appropriate.

Answer all the multiple choice questions and all the short answer questions. Place your short answers in the examination booklet provided and number the booklets accordingly if more than one is used.

MULTIPLE CHOICE SECTION: Answer all questions

Dr. Andreopoulos' Section

1. Which ONE of the following statement(s) regarding Michaelis-Menten kinetics is INCORRECT?

   a) Doubling the enzyme concentration (from 5μM to 10μM) in an enzymatic reaction will result in a Lineweaver Burke plot showing a 1/Vmax value that is half the value of the enzymatic reaction using 5μM of enzyme.

   b) Ki is the dissociation constant for an inhibitor binding to the enzyme (either as EI or ESI).

   c) At [S] <<< Km, an enzyme is almost saturable and displays first order kinetics.

   d) The rate limiting reaction rate for an enzymatic reaction is the formation of the ES complex and not the EI complex.

   e) On the Lineweaver Burke plot, the lowest value of 1/[S] will allow for determination of Vmax since this is the highest [S] value.

2. If a person (whose total body water is 40 L) inadvertently drinks 10 mL of a 35% methanol (by composition) windshield washer fluid, at what approximate rate (expressed as a percentage of Vmax) will liver alcohol dehydrogenase convert the methanol to formaldehyde. Assume the density of methanol is 0.791 g/mL, the Km of liver alcohol dehydrogenase is 15 mM and that methanol freely enters all fluid compartments.

   a) 1%
   b) 11%
   c) 21%
   d) 31%
   e) None of the above

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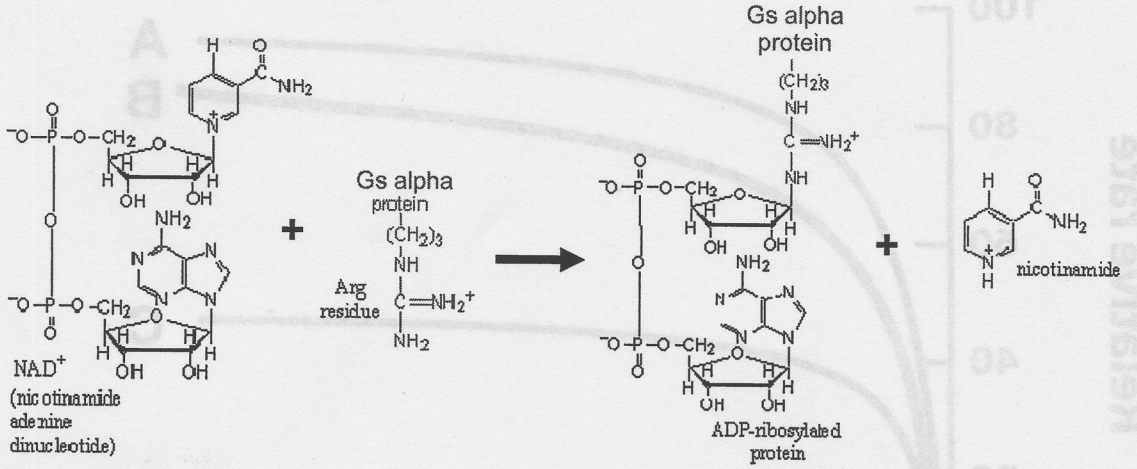
3. Cholera toxin catalyzes covalent modification of a specific arginine in the Gs alpha subunit of the G-protein heterotrimer preventing its GTPase activity (see reaction below). Which ONE enzyme classification best describes the action of cholera toxin?



a) Synthase
b) Ligase
c) Lyase
d) Synthetase
e) None of the above

4. Which ONE of the following is NOT a characteristic of enzyme active sites?

a) The interaction of the enzyme and substrate at the active site promotes the formation of the transition state.

b) Active sites may include amino acid residues that have been brought together from different parts of the polypeptide chain.

c) The active site consists of a small percentage of the total volume of an enzyme.

d) The specificity of substrate binding to all known enzymes depends solely on the precise arrangement of particular atoms in the active site.

e) Binding of the substrate to the active site results in the release of maximal free energy since only the correct substrate can participate in the reaction.

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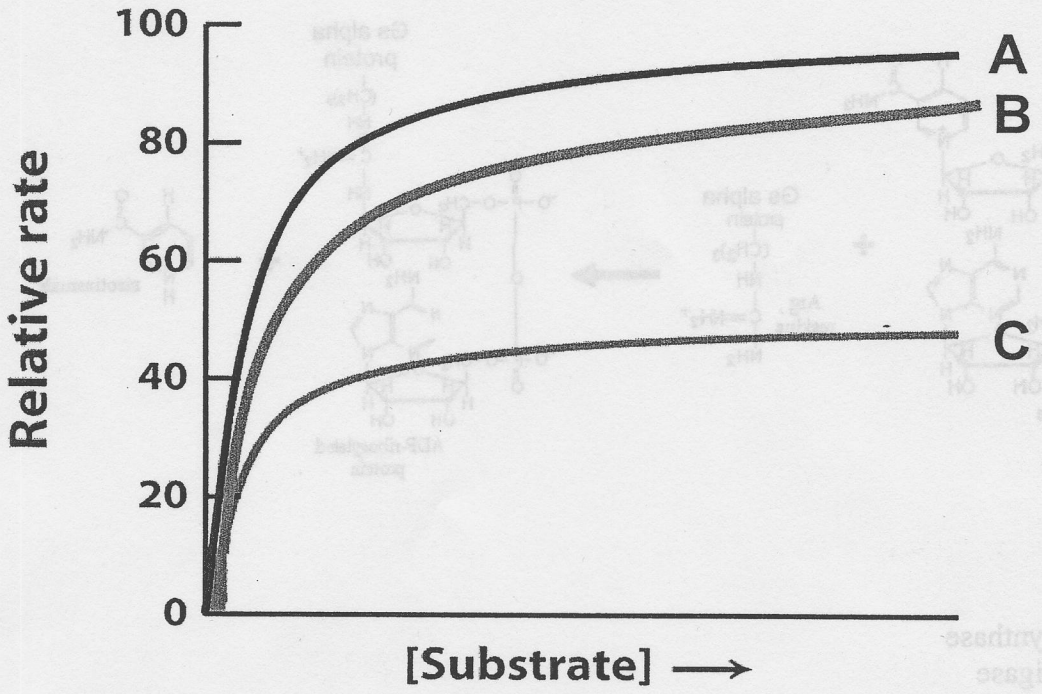
5. Using the Vo vs [S] graph below, select the one statement that is MOST APPROPRIATE.



a) When comparing line A with line C, line A represents a control reaction whereas line C represents a noncompetitive inhibitor of the control reaction.

b) When comparing line A with line C, line A represents a reaction with 25 μM enzyme whereas line C represents a reaction with 12.5 μM enzyme.

c) When comparing line B with line C, line B represents an enzyme using substrate X whereas line C represents an enzyme using substrate Y.

d) When comparing line A with line B, line A represents a control reaction whereas line B represents an inhibitor of the control reaction whose inhibition can be overcome by increasing [S].

e) All the statements are appropriate.

cont'd...

6. Which ONE of the following statement(s) is INCORRECT?

a) Allosteric enzymes can transduce information via their subunits leading to modification of their catalytic activity.

b) The binding of CTP to the catalytic subunit of ATCase stabilizes the T state while ATP binding stabilizes the R state.

c) The generation of 3'nucleoside monophosphate by RNAse occurs subsequent to the entry of H_2O.

d) Iodoacetate is an alkylating agent often used to permanently modify sulfhydryl groups.

e) RNAse catalysis involves the formation of two transition states and the generation of two products.

7. Which ONE of the following statement(s) regarding chymotrypsin's catalytic mechanism is INCORRECT?

a) The negatively charged oxygen (the oxyanion) of the tetrahedral intermediate is stabilized by the NH groups of Gly-193 and Ser-195.

b) His 57 donates a proton to the nitrogen of the amine product leading to the collapse of E-TI_2.

c) Hydrolysis of the acyl-enzyme intermediate occurs when the ^-OH group from water attacks the carbonyl group of the ester.

d) Chymotrypsin employs both acid-base and covalent catalysis.

e) Regeneration of the catalytic triad occurs as the carboxylate product is released from the active site.

8. Which ONE of the following pairs is INCORRECTLY matched?

a) ATP : cosubstrate
b) NAD^+ : loosely bound coenzyme
c) Heme: prosthetic group tightly bound
d) ATCase Zn^{2+} : metal ion tightly bound
e) None of the above, all are correctly paired.

cont'd...

Dr. Baker's Section

9. Which ONE of the following comparisons of hemoglobin (Hb) and myoglobin (Mb) is INCORRECT?

a) Mb binds oxygen more efficiently than Hb at low pO_2 values (around 20 torr).

b) Heme is found in both Mb and Hb and serves as an oxygen binding site.

c) If Mb (instead of Hb) were found in red blood cells it would be difficult to unload oxygen from the red cells at the tissues where the pO_2 is about 20 torr.

d) Near 100 torr, the pO_2 found at the lungs, Mb and Hb bind oxygen with similar affinity.

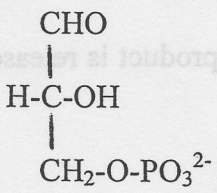
e) Exposure of Hb and Mb to CO_2 will likely lead to a shift in the oxygen binding curves for Hb and Mb to the left.

10. Considering the binding of oxygen to a heme group in hemoglobin (Hb) which ONE of the following is INCORRECT?

a) The imidazole side chain of a His residue H bonds with oxygen, and oxygen also binds with the Fe^{2+} ion at the centre of the heme group.

b) In forming oxyHb, the Fe^{2+} of the heme group is pulled more closely into the plane of the protoporphyrin ring.

c) The presence of this molecule increases the affinity of hemoglobin for oxygen:



d) The transition from deoxyHb to oxyHb is accompanied by a T_4 to R_4 conformational change within the Hb tetramer.

e) As the pH falls below 7.4 the pO_2 needed to saturate half of the heme sites in Hb increases in value.

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11. Considering the Case Study Nat, who suffered a TIA, which ONE of the following is INCORRECT?

a) Nat's LDL is formed from VLDL made by his liver.

b) LDL can be chemically oxidized and this modification promotes the accumulation of LDL within the artery wall.

c) Nat's LDL levels can be raised by the presence of trans and saturated fats in Nat's diet.

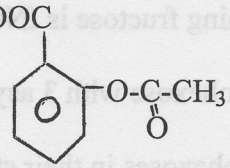
d) LDL is formed in the blood by the action of lipoprotein lipase, an enzyme that increases the percentage content of cholesterol in its product lipoprotein particles.

e) If Nat could now eliminate cholesterol from his diet, he would likely substantially reduce the size of his atherosclerotic plaque.

12. Which ONE of the following features of platelets is INCORRECT?

a) Platelets are small cells, found in the blood, that have no nucleus but they can make TXA_2.

b) The compound below directly inhibits the release of arachidonic acid (20:4 ω-6) from activated platelets:



c) Platelets activated by the turbulent blood flow over an atherosclerotic plaque can promote thrombus formation at the plaque surface.

d) Emboli are formed from thrombi and are aggregates of platelets and other blood cells.

e) If Nat takes Lipitor he can reduce the inflammatory process that is the basis of atherosclerotic plaque formation.

13. If calcium levels could be lowered inside the cytoplasm of cells, how many of the following cellular enzyme activities would be reduced?

lipoprotein lipase, phosphorylase kinase , phospholipase A_2 ($cPLA_2$), COX, carnitine acyltransferase I, pyruvate dehydrogenase phosphatase (PDH phosphatase)

a) 1 b) 2 c) 3 d) 4 e) 5

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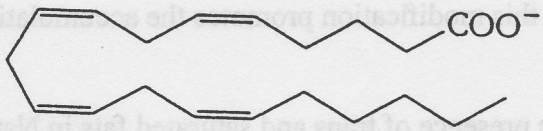
14. Which ONE of the following is INCORRECT concerning the enzyme COX?

a) COX uses the following compound as substrate fatty acid:



b) COX catalyzes oxygenation reactions that add 2 molecules of oxygen (O_2) to arachidonate.

c) Some fish, like salmon, have the fatty acid EPA, and adding salmon to Nat's diet can reduce the formation of TXA_2 by platelets.

d) Elevating Nat's HDL level will likely reduce the conversion of arachidonate to TXA_2.

e) Irreversible inhibition of COX can have undesirable side effects like gastric bleeding.

15. Which ONE of the following concerning fructose is INCORRECT?

a) In its straight chain structure it is a ketohexose with 3 asymmetric or chiral carbons.

b) There are 8 possible structures for ketohexoses in their straight chain form and 4 of these will be D-stereoisomers.

c) The cyclization reaction that produces α-D-fructofuranose results in a new asymmetric centre at carbon 2, which is the anomeric carbon for this molecule.

d) Hemiketals are formed by the cyclization of ketohexoses.

e) The enzymatic action of sucrase and lactase in your intestine each liberates the monosaccharide β-D-fructofuranose from a common dietary disaccharide.

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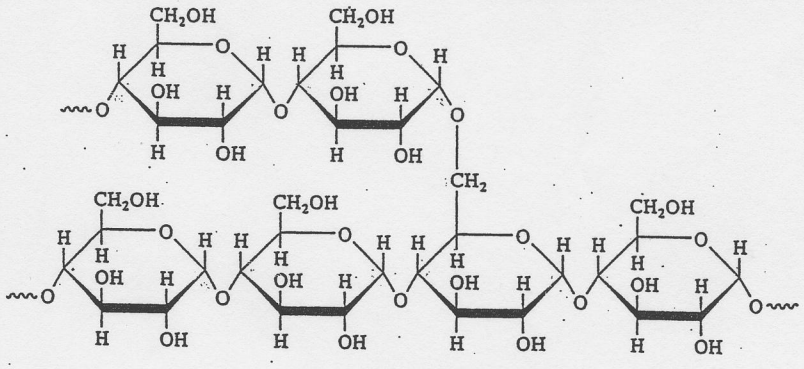
16. Which ONE of the following concerning the structure X below is INCORRECT?



a) X is a polysaccharide composed of α-D-glucose units linked by glycosidic bonds.

b) There are two types of glycosidic bond in X: α (1→4) and α (1→6).

c) It is possible to form the β-anomer of maltose following the digestion of X by amylase.

d) Water molecules are liberated when glycosidic bonds are broken chemically.

e) If X is broken down by amylase in the intestine, the α anomer of maltose is a product of the enzyme.

17. Which ONE of the following would you NOT expect for an enzyme that catalyzes the catabolic reaction A → C + D?

a) There should be a positive change in enthalpy (ΔH).

b) ΔS should be a positive value for the reaction

c) The overall change in free energy should be a negative value.

d) At equilibrium, under standard conditions, $\log_{10}$ [C][D]/[A] is a positive value.

e) If this catabolic reaction starts with A as substrate, at equilibrium losses in A will be balanced by the formation of equal numbers of product molecules C and D.

cont'd...

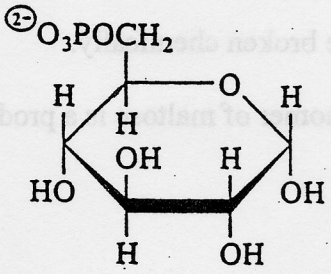
18. If the standard free energy change of hydrolysis for the molecule PEP is -62 kJ/mol, which value below is closest to the equilibrium constant (K'eq) for the reaction catalyzed by pyruvate kinase, under standard conditions?

(R = 8.315 J/K°.mol)

a) 100
b) 1,100
c) 55,600
d) 275,000
e) 412,000

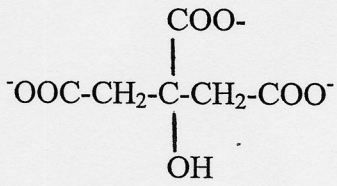
19. In Soon-yi's muscle cells which ONE of the following regulatory molecules or mechanisms would NOT lead to a slowing of glycolysis?

a) Rising levels of the compound:



b) Rising levels of ATP

c) Rising cytoplasmic levels of the compound:



d) Rising levels of cytoplasmic cAMP

e) A mutation that decreases the activity of the enzyme PFK-2.

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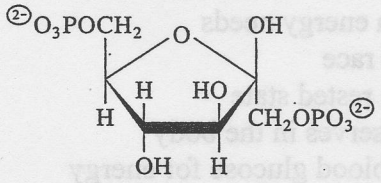
20. Considering the molecule Y, shown below, which ONE of the following is INCORRECT?



a) Y can be formed by a kinase reaction in glycolysis.

b) The kinase catalyzed reaction that forms Y is a very favourable reaction.

c) Y can serve as a substrate for the enzyme aldolase and be converted to phosphate esters of an aldotriose and a ketotriose.

d) Y is also an intermediate found within the gluconeogenesis pathway and is a substrate for the reaction catalyzed by FBP-1.

e) Increased levels of phosphocreatine in muscle will lead to increased rates of formation of Y.

21. A patient has a mutation in glycogen phosphorylase that eliminates a key serine phosphorylation site in the conversion of glycogen phosphorylase b to glycogen phosphorylase a. Which ONE of the following is LIKELY to occur when the patient begins to exercise?

a) cAMP levels will be depressed in her muscle cells.

b) The patient will have severe acidosis because of lactate buildup.

c) The patient may become dizzy and unable to continue her exercises.

d) Activation of phosphorylase kinase will be inhibited.

e) Glycogen synthase will be activated.

cont'd...

22. During Soon-yi's marathon run, which ONE of the options listed below gives the best description of liver? Consider the following properties:

i) provider ii) consumer iii) produces α-D-glucose for release into blood
iv) keeps its intracellular glycogen to supply its own energy needs
v) can minimize glycolytic rates during a prolonged race
vi) has considerable creatine phosphate stores in the rested state
vii) a storage depot for most of the fatty acid fuel reserves in the body
vii) no significant fuel reserves, very dependent on blood glucose for energy
viii) can rely on fatty acid oxidation to provide most of its ATP needs

a) i, iii, v, viii
b) ii, vii
c) i, iii, vi, vii
d) ii, iii, vi
e) i, iii, iv, v

23. If a patient has a mutation that inactivates the PDH kinase activity found in the PDH complex, which ONE of the following is CORRECT?

a) There will likely be an accumulation of the compound $CH_3CHOHCOO^-$ in the patient's cytoplasm

b) Likely rising levels of mitochondrial NADH will lead to a decline in the formation of CH_3-C(=O)-S-CoA by the PDH complex.

c) There will be reduced Krebs cycle activity and reductions in electron transport.

d) Likely PDH complex activity won't keep pace with rates of glycolysis in the cytoplasm

e) Likely the $\Delta G^{o'}$ value for the PDH complex reaction will decline.

cont'd...

24. Considering the compound Z shown below formed during the Krebs cycle:

$^{-}OOC\text{-}CH_2\text{-}CH_2\text{-}COO^{-}$

Which ONE of the following is INCORRECT?

a) Z has no asymmetric carbons

b) The production of Z is accompanied by the activation of G proteins.

c) Z is formed from a thioester compound that contains coenzyme A.

d) A nucleotide is generated by the mitochondrial enzyme activity that produces Z.

e) The production of Z involves sufficient liberation of free energy to support the synthesis of GTP from GDP and inorganic phosphate.

25. Which ONE of the following concerning electron transport and oxidative phosphorylation is INCORRECT?

a) The use of electron transport inhibitors such as CO, CN^{-} or N_3^{-} will lead to a build up of oxidized carriers along the electron transport chain.

b) $FADH_2$ and $CoQH_2$ have lower P/O ratios than that shown by NADH.

c) Likely the P/O ratio for NADH will be reduced below 2.5 if the mitochondrial inner membrane is made leaky.

d) Electron transport and oxidative phosphorylation for the complete breakdown of α-D-glucose will yield 30 molecules of ATP (net) and 36 molecules of water (net) in muscle.

e) If one molecule of D-glyceraldehyde-3-phosphate is added to the cytoplasm of an actively respiring muscle cell, the resulting generation of ATP by the action of glycolysis, PDH complex, Krebs cycle and electron transport/oxidative phosphorylation will be 16.

cont'd...

26. If mitochondria are suspended in a medium that is mildly acidic, and are supplied with ADP and inorganic phosphate, which ONE of the following is MOST LIKELY to occur?

a) FoF1 ATPase will utilize the artificial proton gradient created across the inner mitochondrial membrane to produce ATP and water.

b) The production of ATP will depend upon electron transport and the pumping of protons across the mitochondrial membrane.

c) If the mitochondria are not also supplied with pyruvate, there will be no ATP production by oxidative phosphorylation.

d) The addition of amytal or rotenone will decrease ATP production by hindering electron transport.

e) Likely the mitochondria will produce ATP but there won't be significant water production associated with it.

27. Considering the large breakfast Soon-yi had after her run, which of the following BEST describes the reasons for her eating an omellete prior to drinking her classic smoothie.

a) The smoothie has ingredients that are harder to digest than the omellete.

b) Carbohydrate will assist the digestion of proteins and fats in the omellete and stabilize the quantity of circulating lipoproteins.

c) The omelette will likely slow the digestion of carbohydrate and allow a more gradual rise in blood sugar.

d) The omellete is the best way for Soon-yi to get her daily vegetable requirement and provides 18:3, which is the most effective anti-inflammatory omega 3 dietary fatty acid.

e) Insulin spikes occur following the increased presentation of GLUT4 transporters on the surface of fat and muscle cells.

cont'd...

28. Which ONE of the following is NOT a response to rising blood sugar that Soon-yi experiences after her meal?

a) Insulin, made up of an A and a B chain, is released from beta cells of the endocrine pancreas and insulin binds with its receptor at the plasma membrane of insulin responsive cells.

b) There is an increased formation of glucose-1-phosphate from glycogen and this serves as a substrate in the formation of UDP-glucose.

c) Glycolytic rates increase in liver as a result of increased glucose supply and reversal of the effects of PKA catalyzed enzyme phosphorylation.

d) Glycogenolysis declines and glycogen synthesis is activated in muscle via the action of protein phosphatase 1.

e) β-oxidation of fatty acids declines because of specific inhibition of the carnitine shuttle at carnitine acyltransferase 1.

29. At the 38 km mark of her marathon, Soon-yi has lost 200g of glycogen, 44g of fat and also has had a net loss of 350 ml of body water through sweat, breathing and renal filtration. On average how many kcal has Soon-yi expended per km of her race?

a) 23.3

b) 31.5

c) 36.8

d) 44.2

e) 51.5

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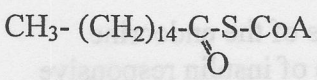
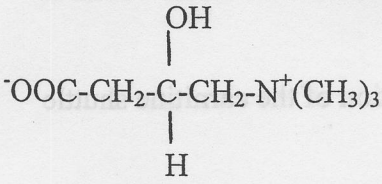
30. Which ONE of the following is INCORRECT concerning the molecule A shown below?



a) Molecule A is formed by the action of acyl CoA synthetase, a ligase that uses 1 molecule of ATP for each molecule of A formed.

b) During exercise, A can be made in muscle cells following the arrival of fatty acids liberated during fat mobilization in fat cells.

c) Molecule A can be used as a substrate by the enzyme carnitine acyltransferase I to form the compound shown below that is transported into the mitochondrial matrix:



d) The first enzyme in β-oxidation converts A to an acyl CoA molecule containing a trans double bond.

e) The standard free energy change for the hydrolysis of the thioester link in A is similar to the standard free energy change seen for the hydrolysis of ATP to ADP + Pi.

31. The complete breakdown of one molecule of 22:0 CoA by the actions of β-oxidation and the Krebs cycle and the use of electron transport and oxidative phosphorylation will generate the following quantity of ATP and water:

	ATP	H_2O
a)	108	123
b)	122	136
c)	150	181
d)	163	210
e)	198	242

cont'd...

32. Which ONE of the following concerning gluconeogenesis and glycolysis in Soon-yi at the 38 km mark of the race is INCORRECT?

a) Most of the glucose Soon-yi produces is made in her liver by the action of the liver specific enzyme glucose-6-phosphatase.

b) PKA is found in its active form in liver and phosphorylates and inactivates pyruvate kinase and fructose-1,6-bisphosphatase.

c) Fructose-2,6-bisphosphate is actively degraded by FBP-2.

d) Adenylate cyclase is activated in Soon-yi's liver.

e) The coffee Soon-yi drank just before her race increases her fat mobilization and also boosts the activity of her gluconeogenesis pathway.

33. Considering Julian, after he has consumed a calorie dense, carbohydrate rich fast food meal, which ONE of the following is INCORRECT?

a) Fat in his diet is digested and fatty acids are absorbed and assembled into triacylglycerols that are loaded into chylomicrons made by the intestine.

b) Rising blood glucose in Julian triggers insulin release and likely promotes more insulin synthesis in β-cells of the pancreas.

c) Julian's liver actively forms malonyl CoA.

d) If Julian's fast food meal is rich in 18:2 (linoleate), this will support the synthesis of the omega 3 fatty acid 20:5 in Julian's body.

e) Liver acetyl CoA carboxylase actively catalyzes a lyase reaction in the carboxylation of $CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-S-CoA}$.

cont'd...

34. Which ONE of the following concerning the fatty acid synthase (FAS) complex in Julian's liver is INCORRECT?

a) In the FAS complex, two reduction reactions are involved that each require NADPH.

b) In the synthesis of 16:0 CoA by the FAS complex, a number of cycles are involved, each involving the decarboxylation of malonyl-S-ACP in a condensation step.

c) Like β-oxidation, the action of the FAS complex involves a hydration step.

d) 16:0, released by the FAS complex (as its last step), can be used in the synthesis of liver triglycerides and VLDL.

e) Fatty acids made by the liver FAS complex can end up in depot fat in fat cells.

35. Considering Adil, the hyperglycemic case study, which one of the following concerning Adil's very active liver ketogenesis (before his insulin shot) is INCORRECT?

a) Acetyl CoA, produced by high rates of fatty acid β-oxidation, is used to make the molecule: $CH_3\text{-}\overset{\overset{O}{\|}}{C}\text{-}CH_2\text{-}COO^-$

b) NADH is used in the synthesis of acetoacetate from β-hydroxybutyrate.

c) Ketone bodies can have either 3 or 4 carbons.

d) Rising levels of ketone bodies in the blood promote cellular dehydration.

e) It might be possible to control Adil's hyperglycemia and acidosis by greatly restricting his carbohydrate, fat and protein intake.

SHORT ANSWER QUESTIONS: 15 Marks Total
Answer all questions in the booklets provided

36. By drawing the chemical structures for the catalytic triad of chymotrypsin, describe what effect the substitution of Asp 102 with Tyr 102 would have on the catalytic mechanism of the enzyme (2 marks).

37. Briefly compare three distinctive features of competitive and non competitive inhibitors (2 marks)

38. Draw the structure of 2,3-bisphosphoglycerate and explain how it controls the affinity of hemoglobin for oxygen (2 marks).

cont'd...

39. Explain how aspirin inhibits COX activity (2 marks)

40. Explain why it is so critical for Soon-yi to have enough muscle glycogen to last until the end of her marathon. (2 marks)

41. The molecule 2,4-dinitrophenol (2,4-DNP) has been used since the 1930's as a dieting aid. Individuals who take this compound experience an accelerated loss of weight when they exercise. Explain what 2,4-DNP does and suggest why DNP has this effect in weight loss. (2 marks)

42. When it was first discovered, L-carnitine was suggested as a possible supplement to promote weight loss. Explain why simply taking L-carnitine (with no other lifestyle changes) would not lead to significant loss of body fat. (2 marks)

43. The case study Selene, who has type 1 diabetes, collapsed in class because of low blood sugar. It was determined that Selene had very good glycogen stores in her body.

Explain why Selene was hypoglycemic, even though she had lots of glycogen. (1 mark)