

UNIVERSITY OF TORONTO

FACULTY OF ARTS AND SCIENCE

BIOCHEMISTRY 210H

DECEMBER FINAL EXAMINATION 2006

DURATION: 3 hours

EXAMINERS: Dr. R.R. Baker, Dr. S. Andreopoulos

Candidates may use simple, non-programmable calculators (supplied by candidates).

This examination is worth 50% of the final grade for the course. There are 30 multiple choice questions worth one mark each for a total of 30 marks and 10 short answer questions, worth two marks each for a total of 20 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.

*****CAREFULLY fill in the appropriate circles on the computer card for your name and student number WITH PENCIL. Please also print your name and number on the card.**

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(s) provided.

Please print your name and student number on your examination booklet(s).

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PART I: MULTIPLE CHOICE QUESTIONS (30 MARKS)

1. Which ONE of the following concerning hemoglobin and myoglobin is INCORRECT?

a) Fe^{2+} is found in heme, and a human oxyhemoglobin tetramer can carry 4 molecules of bound O_2 .

b) Heme is buried in a crevice within α and β subunits to prevent the oxidation of heme Fe^{2+} .

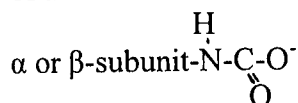
c) At oxygen pressures of $p\text{O}_2 = 20\text{-}40$ torr, one subunit in hemoglobin binds oxygen more efficiently than myoglobin.

d) A mutation in myoglobin that changes His 64 (His E-7) to Asp will likely lower the oxygen binding efficiency of this mutated myoglobin.

2. Which ONE of the following concerning hemoglobin is INCORRECT?

a) A decrease in pH at the tissues will promote the unloading of oxygen from oxyhemoglobin at higher oxygen pressures ($p\text{O}_2$).

b) Cellular respiration results in the formation of CO_2 and this will promote the formation of a carbamate at the N-terminus of each deoxyhemoglobin subunit, with the structure:



c) Smokers and those living at high altitude will have elevated levels of 2,3-bisphosphoglycerate in their red cells.

d) At the lungs, rising pH and the release of CO_2 from red cells will promote the transition $\text{R}_4 \rightarrow \text{T}_4$.

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3. Considering the Case Study Nat, which ONE of the following is INCORRECT?

a) It is quite likely that the unusual noise (flow irregularities) the neurologist hears over Nat's left carotid artery is associated with Nat's stenosis.

b) The elevation of LDL in Nat's blood is mainly caused by foods rich in cholesterol (dairy, red meat) that he has eaten in his diet.

c) Carotid plaque is often found near a branch point in this artery.

d) LPL (lipoprotein lipase) attacks chylomicrons and VLDL in the blood and reduces both the triglyceride content and size of these lipoproteins.

4. Which ONE of the following statements concerning Nat is INCORRECT?

a) Nat's doctor prescribed the statin drug Lipitor to reduce his LDL levels, which can be elevated due to the intake of dietary monounsaturated fatty acids.

b) Elevated HDL levels would benefit Nat, since HDL functions to carry cholesterol back to the liver for disposal.

c) Nat's loss of speech was likely a result of an ischemic blockage caused by emboli depriving his speech center of reasonable blood supply.

d) Foods that are made with modified hydrogenated oils will elevate Nat's LDL levels and reduce his HDL levels.

5. Your 47 year-old father (who is a smoker) receives the following values after he has seen his GP and given blood for analysis. He is currently taking no medications.

BP: 138/90

TC: 6.8 mM

LDL-C: 5.1 mM

HDL-C: 1.2 mM

TG (Triglycerides): 1.5 mM

Using these figures and the risk sheet given as the last page in this exam, which value below is closest to the 10 year risk your father has for coronary artery disease?

a) 12%

c) 20%

b) 16%

d) 25%

Continued...

6. Which ONE of the following concerning lipoproteins is INCORRECT?

- a) Triglycerides are composed of glycerol esterified to three fatty acids.
- b) A defect in the LDL receptor leads to lower levels of oxidized LDL in the blood.
- c) Chylomicrons are lipoproteins assembled by cells lining the intestine, following fat digestion.
- d) HDL levels can be elevated by moderate daily alcohol consumption and also by eating diets enriched in olive oil.

7. Which ONE of the following statements is INCORRECT?

- a) Arachidonate has 4 cis double bonds, is a member of the omega 6 family of fatty acids and is polyunsaturated.
- b) Arachidonate can be released from membranes by the Ca^{2+} activated enzyme cPLA2.
- c) ASA is an effective non-steroidal anti-inflammatory pain killer whose action can reversibly block the COX tunnel leading to the arachidonate binding site.
- d) EPA, which is an omega 3 fatty acid, can compete with arachidonate for COX leading to the formation of the eicosanoid TXA3.

8. Which ONE of the following statements concerning carbohydrates is INCORRECT?

- a) Carbohydrates such as glyceraldehyde, dihydroxyacetone and sucrose have the general formula $(\text{CH}_2\text{O})_n$.
- b) Monosaccharides can be considered to be hydrates of carbon having a H:O ratio of 2:1 and can be classified as either polyhydroxy aldehydes or ketones in their straight chain form.
- c) Hexoses are the most abundant monosaccharides compared with pentoses and trioses.
- d) Except for ketotriose, all monosaccharides have one or more chiral carbons.

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9. Which ONE of the following concerning D-glucose in its straight chain form is INCORRECT?

- a) The straight chain form of D-glucose does not participate in the reducing sugar test
- b) The straight chain form of D-glucose allows mutarotation of the two anomers of D-glucopyranose.
- c) The straight chain form of D-glucose has 4 chiral carbons.
- d) D-Glucose in its straight chain form is one of 16 different aldohexose stereoisomers.

10. Which ONE of the following concerning the cyclization reaction of the straight chain form of D-glucose is INCORRECT?

- a) A hemiacetal is formed by the chemical reaction of the -OH group at C5 with the aldehyde.
- b) Two anomers can be formed by this cyclization: α -D-glucopyranose and β -D-glucopyranose.
- c) A water molecule is released during the cyclization.
- d) A chemical equilibrium exists between the two anomers.

11. Which ONE of the following statements is INCORRECT?

- a) For β -maltose, the α -anomer of D-glucose is joined to the β -anomer of D-glucose through an $\alpha(1\rightarrow4)$ glycosidic linkage between C-1 of the α anomer and C-4 of the β anomer.
- b) The common disaccharide that contains α -D-glucopyranose and β -D-fructofuranose can be broken down in the intestine by sucrase.
- c) α -D-glucose-6-phosphate, α -D-glucosamine and α -D-glucose-1-phosphate cannot be described by the general formula $(\text{CH}_2\text{O})_n$, however are all classified as reducing sugars.
- d) Starch can be found in two forms, α -amylose and amylopectin, the latter of which is comprised of branched chains of α -D-glucose linked by $\alpha(1\rightarrow4)$ and $\alpha(1\rightarrow6)$ glycosidic linkages.

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12. Which ONE of the following statements concerning metabolism is INCORRECT?

- a) An important role of metabolism is the generation of molecules such as RNA, lipids, triglycerides and glucose.
- b) Two examples of anabolic reactions include the β -oxidation of fatty acids and the synthesis of glycogen from glucose.
- c) The pathways involved in the synthesis or breakdown of molecules can be either linear or circular in nature, the latter of which usually involves the regeneration of the first substrate in the last enzymatic step.
- d) Catabolic reactions usually involve the liberation of energy while anabolic reactions require energy to synthesize more complex molecules.

13. The reaction catalyzed by creatine kinase (CK) is shown below:



If phosphocreatine has a ΔG° of hydrolysis of -43 KJ/mol, which value below is closest to the equilibrium constant (K'_{eq}) for the CK reaction?

($R = 8.315 \text{ J/K}^\circ \cdot \text{mol}$)

- a) 52
- b) 190
- c) 375
- d) 642

14. Which ONE of the following statements concerning Soon Yi during her warm-ups is INCORRECT?

- a) Soon Yi's muscles cells first access her resting cellular ATP, and as ATP levels fall, utilize creatine phosphate to sustain ATP levels for a short time.
- b) Her initial source of fuel is glucose from her blood and this enters her muscle cells using the glucose transporter GLUT4.
- c) Aerobic glycolysis, taking place in Soon Yi's muscle cells, converts α -D-glucose to 2 molecules of pyruvate, with a net gain of 7 ATP per α -D-glucose.
- d) The ATP investment steps in the first stage in glycolysis include the hexokinase reaction that generates α -D-glucose-6-phosphate and the PFK-1 reaction that generates β -D-fructose -1,6-bisphosphate.

15. Which ONE of the following statements is INCORRECT?

- a) In the absence of ADP or AMP, high ATP levels inhibit PFK-1, while high levels of β -D-fructose-6-phosphate accelerate glycolysis by promoting activation of PFK-2.
- b) In the ATP production phase of glycolysis, 1,3-bisphosphoglycerate is made in an oxidation-reduction reaction that also produces NADH.
- c) The first ATP generating step in glycolysis is catalyzed by the enzyme phosphoglycerate kinase.
- d) Pyruvate kinase catalyzes the second ATP generating step in glycolysis and this reaction is slowed by increasing levels of cytoplasmic β -D-fructose-1,6-bisphosphate.

16. Which ONE of the following statements concerning anaerobic glycolysis is INCORRECT?

- a) Starting with one molecule of α -D-glucose, anaerobic glycolysis produces less ATP than aerobic glycolysis.
- b) The production of lactate involves the reduction of pyruvate.
- c) There is a loss of NADH and a decrease in muscle cell pH when pyruvate is converted to lactate by lactate dehydrogenase.
- d) Athletes can readily convert lactate back to pyruvate by the action of lactate dehydrogenase which also produces NADH in this reaction.

17. Which ONE of the following statements is INCORRECT?

- a) Following activation of the muscle adrenergic receptor by epinephrine, cAMP-activated PKA inactivates glycogen synthase a by phosphorylation.
- b) Following activation of the muscle adrenergic receptor by epinephrine, cAMP-activated PKA inactivates phosphorylase kinase by phosphorylation.
- c) Glycogen phosphorylase a catalyzes the release of α -D-glucose-1-phosphate from glycogen.
- d) The glycosidic bonds found in glycogen are $\alpha(1 \rightarrow 4)$ and $\alpha(1 \rightarrow 6)$.

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18. Which ONE of the following statements is INCORRECT?

- a) The pyruvate dehydrogenase complex generates $\text{CH}_3\text{-C}(=\text{O})\text{-S-CoA}$, CO_2 and NADH from one molecule of pyruvate.
- b) Regulation of the Krebs cycle can take place at the citrate synthase site and at two other enzyme sites of NADH production.
- c) Succinyl CoA synthetase catalyzes a substrate level phosphorylation.
- d) The pyruvate dehydrogenase complex along with the Krebs cycle will generate 8 NADH and 2 FADH_2 for each pyruvate entering the mitochondrion.

19. Which ONE of the following statements is INCORRECT?

- a) Citrate is formed by the transfer of acetyl CoA to oxaloacetate by citrate synthase.
- b) Acetyl CoA is an energy rich molecule whose thioester linkage conserves some of the energy produced by the decarboxylation of pyruvate by the PDH complex.
- c) There are three dehydrogenase reactions in the Krebs cycle.
- d) α -ketoglutarate dehydrogenase and isocitrate dehydrogenase catalyze both oxidation and decarboxylation.

20. Which ONE of the following statements is INCORRECT?

- a) During electron transport from NADH to O_2 , the energy released is used to transfer protons into the mitochondrial intermembrane space and the proton gradient drives ATP synthesis by $\text{F}_0\text{F}_1\text{ATPase}$.
- b) 2, 4-DNP uncouples mitochondrial oxidation from phosphorylation by promoting proton passage into the matrix by $\text{F}_0\text{F}_1\text{ATPase}$.
- c) If the transfer of one proton into the matrix is associated with a ΔG° of -19 kJ/mol then $>$ one proton must be translocated for every ATP molecule made.
- d) Unlike Complex I, III and IV, Complex II does not directly contribute to the formation of the proton concentration gradient.

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21. Which ONE of the following statements is INCORRECT?

- a) Disruption of the IMM by detergents can result in dissipation of the H^+ gradient and subsequent loss of ATP production.
- b) 5 ATP equivalents are generated by the PDH complex for every two pyruvate molecules used by the PDH complex.
- c) In some parts of the world, releasing rotenone into waterways can aid in paralyzing fish since electron flow from NADH to Q will be blocked.
- d) Cytochrome oxidase inhibitors such as CO will not block the electron transport chain as effectively as CN^- .

22. Which ONE of the following is closest to the ATP production that comes from the entry of one molecule of pyruvate into the mitochondrial matrix, considering the complete catabolic metabolism of pyruvate by the PDH complex, Krebs cycle and the associated actions of electron transport and oxidative phosphorylation?

- a) 10
- b) 12.5
- c) 15.5
- d) 30

23. Which ONE of the following statements is INCORRECT?

- a) After Soon-yi's training session, she consumes an omelette rich in 18:3, a fatty acid that can be converted to the omega-6 fatty acid, 20:4.
- b) After her run, Soon-yi consumes her classic smoothie made of blueberries and strawberries, which contain high levels of antioxidants.
- c) After Soon-yi's meal, the pancreas will release insulin which terminates the metabolic effects of glucagon and adrenaline.
- d) Depolarization of the β cell in the pancreas will result in the vesicular secretion of insulin.

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24. Which ONE of the following statements is INCORRECT?

- a) Upon the removal of the C-peptide fragment from proinsulin, the mature double chain form of insulin is formed.
- b) Preproinsulin contains an N-terminal signal sequence along with 3 sets of disulfide bridges.
- c) In skeletal muscle, insulin activates protein phosphatase-1 and inhibits glycogenolysis.
- d) Excess glucose from the diet can be used to extend glycogen chains at their non-reducing ends.

25. Which ONE of the following statements is INCORRECT?

- a) Fat mobilization involves phosphorylation and inactivation of hormone sensitive lipase (HSL).
- b) The purpose of drinking a small cup of coffee prior to the start of the marathon for Soon-yi was to inhibit cAMP hydrolysis via cAMP phosphodiesterase.
- c) Fat mobilization involves binding of adrenaline to adrenergic receptors at the surface of fat cells.
- d) Fatty acids released from fat cells are bound to albumin in the blood to ensure their efficient transfer to muscle and other cells.

26. Which ONE of the following statements is INCORRECT?

- a) Activation of fatty acids by acyl-CoA synthetase results in the formation of a high energy thioester linkage and the release of AMP and PPi.
- b) The carnitine shuttle is an important mode of regulation for fatty acid β -oxidation.
- c) CAT II will reverse the actions of CAT I, regenerating acylcarnitine in the mitochondrial matrix.
- d) 8 acetyl CoA molecules along with 7 NADH and 7 FADH₂ can be generated by the complete β -oxidation of palmitoyl-CoA.

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27. Which ONE of the following statements is INCORRECT?

- a) More than 100 molecules of ATP can be generated by Soon-yi's complete degradation of 1 molecule of 16:0 CoA by β -oxidation, the Krebs cycle and the associated actions of electron transport and oxidative phosphorylation.
- b) Fatty acid β -oxidation will supply a large number of H_2O molecules, effectively reversing the dehydration effects felt by Soon-yi in the marathon.
- c) Glycerol released from triglyceride hydrolysis can be used to make glucose via a process termed gluconeogenesis.
- d) In gluconeogenesis, activated PKA accelerates the activation of PFK-2 activity and the inactivation of fructose-2,6-bisphosphatase activity.

28. Which ONE of the following statements is INCORRECT?

- a) A diet rich in saturated and trans fats such as 16:0 and 18:0 will increase the risk of cardiovascular disease and type II diabetes.
- b) The excess carbohydrates consumed with a Big Mac supersize meal will be converted by the liver into fatty acids and triglycerides.
- c) After a meal rich in carbohydrate, liver can convert malonyl CoA into acetyl CoA by the action of acetyl CoA carboxylase.
- d) Fatty acid synthase has a number of active sites and one will catalyze the condensation reaction that joins an acetyl and a malonyl group with a release of carbon dioxide.

29. Which ONE of the following statements is INCORRECT?

- a) Type I diabetes is a result of the lack of insulin due to an autoimmune reaction which kills off β -cells in the pancreas.
- b) The lack of insulin allows the predominance of catabolism by the effects of glucagon and adrenaline on muscle and fat tissue.
- c) A lack of insulin will greatly increase the rate of mitochondrial β -oxidation and the loss of both glycogen and fat reserves in the body.
- d) High concentrations of acetyl CoA in liver mitochondria support the formation of β -hydroxybutyrate by the enzymatic oxidation of acetoacetate using NAD^+ .

Continued...

30. Which ONE of the following statements is INCORRECT?

- a) Insulin will shut down β -oxidation of fatty acids by accelerating the action of the carnitine shuttle.
- b) Insulin given to a diabetic patient by injection will decrease fatty acid mobilization, decrease fatty acid β -oxidation and decrease ketogenesis.
- c) Hyperglycemia will cause glycosylation of proteins, including hemoglobin, and can cause retinal degeneration and circulatory problems.
- d) Polyuria is a consequence of type I diabetes and involves the loss of copious amounts of water as a result of increased ketone body formation.

**PART II: SHORT ANSWER QUESTIONS (20 MARKS TOTAL):
2 MARKS EACH. PLEASE USE EXAMINATION BOOKLET.**

1. What are the first two structural changes you see when one subunit in the hemoglobin tetramer binds oxygen?
2. Nat has FH. What is FH and what defective protein causes it?
3. Draw the structure of β -D-glucopyranose in Haworth projection.
4. What is likely the K'_{eq} value for the auxiliary kinase in mitochondria that forms ATP from GTP? Briefly give your reasoning.
5. Is activated glycogen phosphorylase a hydrolase? Briefly explain your reasoning.
6. Define P/O ratio and explain why NADH has a P/O = 2.5.
7. Explain the difference between glycogenolysis activated by glucagon in liver and glycogenolysis activated by adrenaline in muscle.
8. Explain Standard Reduction Potential (E°) and give an example of a modest step down in energy in mitochondria.
9. A tofu burger has 100 g of carbohydrate, 38 g of fat and 50 g of protein. Which supplies the most and which supplies the least number of calories? Show your calculations.
10. In the MSI case Selene, why does Selene need i.v. glucose when she has glycogen stores in her liver?

Model for estimating the 10-year risk of coronary artery disease in a patient without diabetes mellitus or clinically evident cardiovascular disease, using data from the Framingham Heart Study*

MEN						WOMEN					
Risk factor	Risk points					Risk factor	Risk points				
Age group, yr						Age group, yr					
20-34	-9					20-34	-7				
35-39	-4					35-39	-3				
40-44	0					40-44	0				
45-49	3					45-49	3				
50-54	6					50-54	6				
55-59	8					55-59	8				
60-64	10					60-64	10				
65-69	11					65-69	12				
70-74	12					70-74	14				
75-79	13					75-79	16				
Total cholesterol level, mmol/L						Total cholesterol level, mmol/L					
	Age group, yr						Age group, yr				
	20-39	40-49	50-59	60-69	70-79		20-39	40-49	50-59	60-69	70-79
< 4.14	0	0	0	0	0	< 4.14	0	0	0	0	0
4.15-5.19	4	3	2	1	0	4.15-5.19	4	3	2	1	1
5.20-6.19	7	5	3	1	0	5.20-6.19	8	6	4	2	1
6.20-7.20	9	6	4	2	1	6.20-7.20	11	8	5	3	2
≥ 7.21	11	8	5	3	1	≥ 7.21	13	10	7	4	2
Smoker						Smoker					
No	0	0	0	0	0	No	0	0	0	0	0
Yes	8	5	3	1	1	Yes	9	7	4	2	1
HDL-C level, mmol/L						HDL-C level, mmol/L					
≥ 1.55	-1					≥ 1.55	-1				
1.30-1.54	0					1.30-1.54	0				
1.04-1.29	1					1.04-1.29	1				
< 1.04	2					< 1.04	2				
Systolic blood pressure, mm Hg						Systolic blood pressure, mm Hg					
	Untreated		Treated				Untreated		Treated		
< 120	0		0			< 120	0		0		
120-129	0		1			120-129	1		3		
130-139	1		2			130-139	2		4		
140-159	1		2			140-159	3		5		
≥ 160	2		3			≥ 160	4		6		
Total risk points						Total risk points					
	10-year risk, %						10-year risk, %				
< 0	< 1					< 9	< 1				
0-4	1					9-12	1				
5-6	2					13-14	2				
7	3					15	3				
8	4					16	4				
9	5					17	5				
10	6					18	6				
11	8					19	8				
12	10					20	11				
13	12					21	14				
14	16					22	17				
15	20					23	22				
16	25					24	27				
≥ 17	≥ 30					≥ 25	≥ 30				

10-year risk:
_____ %

10-year risk:
_____ %