Medical Biochemistry Examination II
October 29, 1997
Kresge Auditorium

Please follow these directions:

1. Do not begin the exam until all students have received a copy of the exam. You will be instructed as to when to break the seal.

2. The exam consists of 78 questions on 19 pages, with this title page considered page 1. There are 125 points on this exam. The point value for each question is indicated by the question. For multiple answer questions without a defined number of answers 0.25 points will be deducted for each incorrect answer, although the lowest point value assigned for a question is 0. No multiple answer question will have more than 4 correct answers. If a question has a defined number of answers, there is no penalty for guessing.

3. Place your ID number on every page of the exam booklet and on the answer sheet you will hand in. Also, print your name on the line provided on the answer sheet.

4. The answer sheet for questions 1-73 is a computer graded form. Use a No. 2 pencil only. Fill in the circle for the correct answer(s) completely. If you believe that a question has more than one correct answer fill in all answers for that question completely. If you wish to change an answer, be sure to erase cleanly. Make sure that you use your biochemistry ID number to fill in the ID box. You should convert your number to a three digit number (001, 010, etc) and use the three leftmost boxes to insert your number. Five questions (74-78) should be answered within the exam booklet itself.

5. When you are finished with the exam, return both the test booklet and the answer sheet. The test booklet will be returned to you when the grading is complete. Be sure to pick up the next section of the course syllabus as you leave.

6. Questions will not be allowed during the exam. If you believe there is a typographical error do the best you can with the information available. Do not spend extra time on the question. If it is determined that the information presented is ambiguous, or in error, then the question will not be counted in the final scoring.

7. There is a piece of graph paper attached to the exam booklet after page 19. Following that there are two blank pages, and then a page which contains a sheet for you to list your answers. You can take this sheet with you from the exam, and use it to check your answers against the posted answers (outside of room 3109 MSB). Answers will be posted on October 30th, at 2:00 pm, assuming that all students attend the exam at its scheduled time.

8. You will have 4 hours (until 4:30 pm) to complete this exam. Good luck.
Questions 1-3 (1 point each) are based on the following pairs of metabolites. Answer the following questions using the answers presented as A-F. A question may have more than one correct answer, and an answer may be used more than once. Indicate all correct answers on the answer sheet.

1. Which of the 6 reactions (A to F) involves an oxidation-reduction reaction?

A. \( \text{CH}_3\text{C}-\text{COOH} \) and \( \text{CH}_3\text{C}-\text{SCoA} \)

B. \( \text{CH}_3\text{C} = \text{CH}_2\text{-COOH} \) and \( \text{CH}_3\text{C} = \text{CH}_3 \)

C. \( \text{CH}_2\text{C} = \text{CH} \) and \( \text{CH}_2\text{C} = \text{CH} \)

2. Which of the 6 reactions represents an enol-keto conversion?

D. \( \text{CH}_2\text{OH} \) and \( \text{CH}_2\text{PO}_3^-2 \)

3. Which of the 6 reactions requires, in biological systems, the participation of thiamine pyrophosphate?

E. \( \text{CH}_2\text{OH} \) and \( \text{CH}_2\text{C} = \text{CH}_2 \)

F. \( \text{CH}_2\text{COO}^- \) and \( \text{O}^-\text{SCoA} \)
4. (1 point) A culture of hepatocytes, under anaerobic conditions, is presented with glucose as a sole carbon source. Lactate can be demonstrated to be produced under these conditions, as well as a net synthesis of ATP. Arsenate is a phosphate analog which can replace phosphate in biochemical reactions. The problem with arsenate is that the arseno-bonds formed are very susceptible to hydrolysis, whereas the phospho-bonds are stable to hydrolysis. Which TWO of the following statements are correct concerning glycolysis in the hepatocyte, under anaerobic conditions, in the presence of arsenate? Assume that the experiment is started at time = 0 when glucose is added to the cells.

A. Lactate will be formed for a short period of time, and then lactate formation will stop.
B. Lactate production will never occur.
C. There will be no effect on lactate formation.
D. ATP levels will drop dramatically after a short period of time.
E. ATP levels will remain constant.
F. There will be net synthesis of ATP as glycolysis proceeds.

5. (2 points) Which of the following reactions are used to bypass the irreversible reactions of glycolysis?

A. Glucose-6-phosphate yields glucose + Pi
B. Fructose 1,6 bisphosphate yields fructose-6-phosphate + Pi
C. 1,3 bisphosphoglycerate + NADH yields glyceraldehyde-3-phosphate + Pi + NAD^+
D. Malate + NAD^+ yields oxaloacetate + NADH
E. Pyruvate + NAD^+ + CoA yields acetyl-CoA + NADH + CO_2
F. Fructose-6-phosphate yields glucose-6-phosphate

6. (2 points) Which TWO of the following are major roles of the glycolytic pathway in metabolism?

A. A pathway of energy generation from carbohydrates.
B. A pathway for the conversion of six and five carbon sugars.
C. Generation of biosynthetic precursors from carbohydrates.
D. Production of acetyl-CoA for fat biosynthesis.
E. Generation of NADPH for biosynthetic purposes.
F. Oxidation of NADH for energy generation.
Answer questions 7-10 (1 point each) from the lettered list (A-L) below. There may be more than one correct answer per question, indicate all correct answers on the answer sheet. An answer may be used for more than one question.

7. Requires an active sulphydryl group
   A. Aldolase
   B. Enolase
   C. Fatty Acid Synthase

   D. Fumarase
   E. Glucokinase

9. Catalyzes a substrate-level phosphorylation reaction.
   F. Glyceraldehyde-3-phosphate dehydrogenase
   G. Hexokinase

10. Catalyzes an oxidative decarboxylation reaction.
    H. Isocitrate Dehydrogenase
    I. Phosphofructokinase-I
    J. Phosphoglycerate kinase
    K. Phosphoglycerate mutase
    L. Pyruvate dehydrogenase

Answer questions 11-17 (1.5 points each) from the lettered list A-K below, in which the disease needs to be matched to an appropriate protein defect. **PICK THE ONE BEST ANSWER FOR EACH QUESTION.** An answer may be used more than once.

11. Von Gierke’s Disease
    A. Aldolase
    B. Citrate synthase
    C. Glucagon receptor
    D. Glucokinase

12. MODY
    E. Glucose-6-phosphatase
    F. Glucose-6-phosphate dehydrogenase
    G. Hexokinase

13. Red cell oxidation in the presence of oxidizing agents
    H. Insulin
    I. Insulin receptor
    J. MCAD
    K. Muscle phosphorylase

14. Inefficient fatty acid oxidation

15. Acanthosis nigricans

16. Type I diabetes

17. Hereditary fructose intolerance
18. (1 point) Which of the following statements are CORRECT concerning glycogen synthesis and degradation?

A. Both glycogen synthesis and degradation occur in the cytoplasm.
B. Both pathways require the participation of pyridoxal phosphate.
C. Both pathways require the use of nucleotide sugars.
D. Both pathways result in the hydrolysis of ATP, with the loss of one high energy bond.
E. Both pathways are regulated, in part, by covalent modification of key enzymes.
F. Both pathways in muscle, can, in part, be regulated by the levels of ATP.

19. (1 point) Which of the following statements are CORRECT concerning the allosteric regulators of glycogen metabolism?

A. Glucose, in the liver, can modulate phosphorylase a activity.
B. ATP, in the muscle, can modulate phosphorylase a activity.
C. F6P, in the liver, can modulate glycogen synthase D activity.
D. Calcium ions, in the muscle, can modulate phosphorylase kinase b activity.
E. AMP, in the liver, can modulate phosphorylase b activity.
F. Creatine-phosphate, in the liver, can modulate phosphorylase a activity.

Questions 20 and 21 (2 points each) should be answered from the lettered list of choices, A through K below. There may be more than one correct answer per question, and an answer may be used more than once.

20. Under conditions of epinephrine release in a normal adult human, indicate which of the enzymes in the list would be ACTIVE and phosphorylated.

A. Acetyl-CoA carboxylase
B. Glycogen synthase
C. Glucagon receptor
D. Guanine nucleotide binding protein
E. Hormone-sensitive lipase
F. Insulin Receptor

21. Under conditions of epinephrine release in a normal adult human, indicate which of the enzymes in the list would be INACTIVE and phosphorylated.

G. Phosphorylase
H. Phosphorylase kinase
I. Protein phosphatase I
J. Pyruvate carboxylase
K. Pyruvate dehydrogenase (liver)
22. (2 points) Which **TWO** of the following statements are correct concerning Gibbs free energy and biochemical reactions?

A. $\Delta G = \Delta H - T\Delta S$ is the equation relating Gibbs free energy to enthalpy and entropy.

B. $\Delta G^\circ$ refers to the standard energy change of a reaction under conditions at which all substrates and products are at 1.0 M concentration, and the pH is at the physiological pH value, 7.4.

C. $\Delta G = \Delta G^\circ - RT \ln \{[\text{products}]/[\text{reactants}]\}$ relates the Gibbs free energy and the standard energy change of a reaction.

D. In the reaction $A + B \rightleftharpoons C + D$, if $\Delta G^\circ$ is a positive number, the overall $\Delta G$ can still be negative if, under physiological conditions, the concentration of $A$ or $B$ is very low.

E. $\Delta G$ can also be related to the redox potential, by the equation $\Delta G = -nF \Delta E^\circ$.

F. If the overall $\Delta G$ for a reaction is positive, then the reaction will proceed with simultaneous release of energy.

23. (2 points) Regulation of the TCA cycle is crucial for proper energy production. Which statements below are **INCORRECT** concerning TCA cycle regulation?

A. Both pyruvate dehydrogenase and pyruvate carboxylase are regulated by Protein Kinase B catalyzed phosphorylation/dephosphorylation.

B. ATP and NADH are frequently used as negative allosteric effectors of the key regulatory enzymes.

C. The concentration of oxaloacetate can sometimes be rate-limiting for the cycle.

D. Succinate thiokinase is a key regulated enzyme.

E. $\alpha$--ketoglutarate dehydrogenase and isocitrate dehydrogenase are key regulated enzymes.

F. The PDH kinase is activated by acetyl-CoA, NADH and ATP.

24. (2 points) Which of the following are consequences of Von Gierke’s disease?

A. Lactic acidemia

B. Lack of branches in glycogen

C. Enlarged liver

D. Fasting hypoglycemia

E. Defective liver phosphorylase activity

F. Constitutively activated insulin receptors.
25. (2 points) You have discovered a novel electron transfer chain in biochemistry professors which consists of five components with the terminal electron acceptor being oxygen. The five components have the following $\Delta E^\circ$ values:

- Component A: -0.157 volts
- Component B: +0.061 volts
- Component C: -0.032 volts
- Component D: +0.02 volts
- Component E: +0.105 volts

You then discover that a drug X blocks complex D from transferring its electrons to the next component of the chain. Thus, under conditions in which drug X has been added to this electron transfer chain, and in the presence of a substrate which can donate electrons to the first member of this chain, indicate which components of the chain will be in their reduced state.

A. Component A  
B. Component B  
C. Component C  
D. Component D  
E. Component E  

26. (1 point) The ATP synthase is necessary to synthesize ATP via oxidative phosphorylation. Which THREE of the following statements are CORRECT concerning this enzyme?

A. The enzyme consists both of a membrane spanning region, Fo, and a matrix facing “stalk” region, named F1.  
B. The energetics for ATP release from the enzyme comes from proton entry through the Fo and F1 components of the enzyme.  
C. Uncouplers block ATP synthesis by physically blocking protons from flowing through the enzyme complex.  
D. The enzyme also catalyzes the transfer of ADP from the cytoplasm into the matrix, in exchange for newly synthesized ATP.  
E. The enzyme is dependent on intramitochondrial ADP in order to be able to catalyze ATP synthesis.  
F. The enzyme, upon proton entry, catalyzes the formation of a high energy phosphate bond on a serine residue of the enzyme, which is then transferred to ADP to create ATP.
Questions 27 through 29 (1 point each) should be answered from the lettered list A-H. For each enzyme indicate the type of bond that it can cleave. A question may have more than one answer, and an answer may be used more than once.

27. Amylase
   A. Glu $\alpha$ 1,4 glu
   B. Glu $\alpha$ 1,6 glu
   C. Glu $\beta$ 1,4 glu

28. Isomaltase
   D. Gal $\beta$ 1,4 glu
   E. Fructose $\alpha$ 1,2 glu

29. Lactase
   F. Glu $\alpha$ 1,2 fructose
   G. Gal $\alpha$ 1,4 glu
   H. Glu $\alpha$ 1,1 glu

30. (2 points) A wide variety of transport systems have been discussed during the course. Which TWO of the following statements concerning the transport of biochemicals across biological membranes are INCORRECT?

   A. Facilitated transport requires a membrane-bound carrier, and will transport the solute down its concentration gradient.
   B. Symport refers to the simultaneous transport of one molecule, which is energetically favorable due to its transport down its concentration gradient, coupled with the transport of a second solute, which may be actually transported against its concentration gradient.
   C. Both proton gradients and sodium gradients can be used to drive active transport.
   D. Glucose transport is exclusively symport with either protons or sodium ions in the absence of insulin. In the presence of insulin the transport system becomes facilitative.
   E. Sugar transport into the epithelial cells is totally dependant on the establishment of a sodium and proton gradient across the membrane.
   F. Establishment of a sodium gradient across the epithelial cell membrane is dependant on ATP hydrolysis.

31. (1 point) Starting with ribose-5-phosphate labeled in C3 with $^{14}$C, which position(s) of pyruvate would be labeled as ribose is converted to pyruvate? Assume all ribose-5-phosphate molecules are labeled with $^{14}$C. Choose only ONE answer for this question.

   A. Carbon 1   B. Carbon 2   C. Carbon 3   D. None, all are lost as carbon dioxide
   E. Carbons 1 and 2   F. Carbons 2 and 3   G. Carbons 1 and 3   H. All of the carbons
Questions 32-36 (1 point each) are matching, using the lettered list A-J below. Match the appropriate metabolite(s) with the statements. Choose the **ONE BEST** answer for each question. An answer may be used more than once.

32. Activated sugar required by glycogen synthase.  
   A. Acetyl-CoA  
   B. CDP-glucose  

33. Substrate for substrate-level phosphorylation reactions.  
   C. Erythrose phosphate  
   D. Fructose-1-phosphate  

34. The end product of fatty acid oxidation.  
   E. Fructose-6-phosphate  

35. An intermediate required for galactose entry into glycolysis.  
   F. Glyceraldehyde  
   G. Glucose-6-phosphate  

36. An early intermediate in fructose metabolism.  
   H. Succinyl-CoA  
   I. Sedoheptulose phosphate  
   J. UDP-glucose  

37. (2 points) Which of the following enzymes are required for the straightforward conversion of galactose to fructose 1,6 bisphosphate?  
   A. Phosphoglucomutase  
   B. Hexokinase  
   C. Glucokinase  
   D. Fructokinase  
   E. Galactokinase  
   F. Phosphohexoisomerase  
   G. PFK-1  
   H. Aldolase  

38. (2 points) Which of the following enzymes are **NOT** required for the complete conversion of fructose to ribose-5-phosphate in the absence of NADP⁺?  
   A. Phosphoglucomutase  
   B. Fructokinase  
   C. Aldolase  
   D. Fructose 1,6 bisphosphatase  
   E. Transketolase  
   F. PFK-1  
   G. C3 epimerase  
   H. Glucose-6-phosphate dehydrogenase
39. (1 point) Starting with ribose-5-phosphate labeled in C4 with $^{14}$C, indicate which positions of glucose would be labeled if the ribose were converted into glucose. Assume that all ribose-5-phosphate molecules used are labeled. Indicate all correct positions on the answer sheet. Note that since an answer cannot have more than four correct answers, if you believe that more than four of the carbons are labeled, choose the answer which indicates that all of the carbons are labeled.

A. Carbon 1
B. Carbon 2
C. Carbon 3
D. Carbon 4
E. Carbon 5
F. Carbon 6
G. All of the carbons
H. None of the carbons

40. (2 points) Citrate plays a major role in metabolism. Which statements below are **FALSE** concerning the role of citrate in intermediary metabolism?

A. Citrate is the carrier of acetyl-CoA equivalents into the cytoplasm from the mitochondria.
B. Citrate is the key activator of an enzyme of glycolysis.
C. Citrate is a key activator of the regulated step of fatty acid biosynthesis.
D. The synthesis of citrate within the mitochondria is regulated negatively by high energy levels.
E. In the presence of insulin, the anaplerotic reaction catalyzed by citrate lyase helps to maintain adequate levels of citrate within the mitochondria.
F. Citrate is a potent activator of the PDH kinase.
41. (1 point) Which **ONE** of the five fatty acids listed below would yield the greatest amount of ATP upon complete oxidation of the fatty acid to carbon dioxide and water, assuming that all of the oxidative steps occurred in the mitochondria?

A. C 18:0  
B. C 17:0  
C. Cis $\Delta^9,12$ C 18:2  
D. Cis $\Delta^9,12,15$ C 20:3  
E. Cis $\Delta^6,9,12,15$ C 20:4

42. (2 points) Mitochondrial shuttle systems allow substrates to pass through the mitochondrial membrane. Which of the following molecules are **NOT** directly transported across the mitochondrial membrane?

A. Acetyl CoA  
B. ADP  
C. ATP  
D. Aspartate  
E. Citrate  
F. Malate  
G. NADH  
H. Oxaloacetate  
I. Phosphate ions  
J. Protons

43. (1 point) Which **TWO** of the statements below are **CORRECT** in comparing and contrasting the pathways of fatty acid synthesis and oxidation?

A. Both pathways generate NADPH.  
B. Both pathways utilize water; the process of oxidation generates water, whereas the process of biosynthesis consumes water.  
C. Both pathways occur in the same cellular compartment.  
D. Citrate inhibits MCAD, while activating fatty acid biosynthesis.  
E. Both pathways utilize acetyl-CoA as a nucleophile.  
F. Both pathways require activated intermediates, containing a high-energy thio-ester bond.
Questions 44-45 (1 point each) should be answered using the letter graphs to the right. Match the appropriate plot with the statement by the question. Choose the ONE best answer per question, but be advised that an answer may be used more than once.

44. This plot is used to determine the total number of receptors on the cell surface.

45. This plot is a modified version of the Lineweaver-Burk plot which offers less extrapolation for the determination of $K_m$ and $V_{max}$.

46. (2 points) Consider the following situation: an individual has gone on a starvation diet for 14 days, ingesting only 500 calories of fat/carbohydrates/protein per day. Which of the following statements are CORRECT concerning the individual’s enzyme status?

A. Malic enzyme has been transcriptionally up-regulated.
B. Acetyl-CoA carboxylase is phosphorylated and inactive.
C. Hormone-sensitive lipase is in its active, dephosphorylated state.
D. Liver pyruvate dehydrogenase is phosphorylated and inactive.
E. Carnitine acyl-transferase I is phosphorylated and active.
F. Pyruvate carboxylase is activated by allosteric means.

47. (1 point) Which TWO of the fatty acids listed below CANNOT be synthesized de novo in humans?

A. Cis $\Delta 9,12$ C 18:2
B. Cis $\Delta 9,12$ C 22:2
C. Cis $\Delta 9,12,15$ C 18:3
D. Cis $\Delta 9$ C 16:1
E. Cis $\Delta 11$ C 20:1
F. Cis $\Delta 4,13$ C 20:2
Questions 48-52 (1 point each) should be answered from the lettered list (A-H) below. Match the **ONE BEST** appropriate cofactor with the enzymes listed in the questions. An answer may be used more than once.

<table>
<thead>
<tr>
<th>Question</th>
<th>Enzyme</th>
<th>Cofactor</th>
</tr>
</thead>
<tbody>
<tr>
<td>48.</td>
<td>Transketolase</td>
<td>A. Vitamin B1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. Vitamin B2</td>
</tr>
<tr>
<td>49.</td>
<td>Complex II</td>
<td>C. Vitamin B6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D. Vitamin B12</td>
</tr>
<tr>
<td>50.</td>
<td>Glycogen phosphorylase</td>
<td>E. Niacin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F. Lipoic Acid</td>
</tr>
<tr>
<td>51.</td>
<td>Isocitrate dehydrogenase</td>
<td>G. Phosphopantothenic acid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H. Ubiquinone</td>
</tr>
<tr>
<td>52.</td>
<td>Methyl malonyl CoA mutase</td>
<td></td>
</tr>
</tbody>
</table>

Answer questions 53-59 (1.5 points each) from the lettered list to the right, A through M. Match the enzymes listed in the question with allosteric regulators (indicate both activators and inhibitors) listed in the column. A question may have more than one correct answer, and an answer may be used more than once.

<table>
<thead>
<tr>
<th>Question</th>
<th>Enzyme</th>
<th>Regulator</th>
</tr>
</thead>
<tbody>
<tr>
<td>53.</td>
<td>PFK-1</td>
<td>A. Acetyl-CoA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. Citrate</td>
</tr>
<tr>
<td>54.</td>
<td>Acetyl-CoA carboxylase</td>
<td>C. Creatine-phosphate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D. Fructose-6-phosphate</td>
</tr>
<tr>
<td>55.</td>
<td>Glucose-6-phosphate dehydrogenase</td>
<td>E. Glucose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F. Glucose-6-phosphate</td>
</tr>
<tr>
<td>56.</td>
<td>Acyl-carnitine transferase I</td>
<td>G. Fructose 1,6 bisphosphate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H. Fructose 2,6 bisphosphate</td>
</tr>
<tr>
<td>57.</td>
<td>Pyruvate kinase</td>
<td>I. Malonyl-CoA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>J. NADH</td>
</tr>
<tr>
<td>58.</td>
<td>Pyruvate carboxylase</td>
<td>K. NADPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L. Oxaloacetate</td>
</tr>
<tr>
<td>59.</td>
<td>Isocitrate dehydrogenase</td>
<td>M. Pyruvate</td>
</tr>
</tbody>
</table>
60. (2 points) Futile cycles are energetically wasteful. Reciprocal regulation is often used to keep one pathway active, while the opposing pathway is inactive. Which ONE of the following statements concerning reciprocal regulation is INCORRECT?

A. Glycolysis and gluconeogenesis exhibit reciprocal regulation at the PFK-1 and Fructose 1,6 bisphosphatase steps.
B. Glycogen synthesis and glycogenolysis are reciprocally regulated by the action of the cAMP dependant protein kinase.
C. The fate of pyruvate can be reciprocally regulated by acetyl CoA.
D. The enzymes of fatty acid synthesis and triglyceride degradation are reciprocally regulated by phosphorylation.
E. The enzymes of the HMP shunt pathway and glycolysis are reciprocally regulated by the levels of NAD and NADPH.

61. (1 point) Oxygen radicals can cause major damage to lipids and proteins. Fortunately, cells can protect themselves from such oxidative stress by all of the statements below except for which ONE?

A. Superoxide dismutase will convert 2 superoxide radicals into 2 water molecules and an oxygen molecule.
B. Glutathione peroxidase will convert the peroxide radical to oxygen, using reduced glutathione as an electron donor, and generating oxidized glutathione.
C. Vitamin E can act as a radical chain terminator and as an electron sink, thereby protecting nearby molecules from oxidation.
D. Catalase will convert hydrogen peroxide into water and oxygen, in order to reduce peroxide levels.
E. Glutathione can often be preferentially oxidized by oxidizing agents in the red cell membrane, requiring NADPH to regenerate the reduced form.

62. (2 points) Consider the situation of a sprinter running the last 50 meters of a 200 meter run. Under these conditions, which of the following statements are INCORRECT?

A. Fat oxidation is mobilized and maximal, leading to significant acetyl-CoA production and ketone body synthesis.
B. Epinephrine has been released, which activates the muscle adenylate cyclase through the action of a Gs protein.
C. The insulin receptor is phosphorylated and inactivated.
D. Phosphorylase kinase in muscle and liver is phosphorylated and active.
E. Muscle energy production is accomplished primarily through anaerobic glycolysis.
F. Hypoglycemia results due to the uptake of blood glucose by the working muscle.
63. (1 point) All of the following statements concerning cytochrome P450 systems are INCORRECT except for which ONE?

A. Cytochrome P450 systems contain iron-sulfur complexes to aid in electron transfer to oxygen.
B. Cytochrome P450 systems are constitutively active, and are only used when the appropriate substrate is available.
C. NADH supplies the electrons which will eventually be used to reduce oxygen.
D. Cytochrome P450 contains a heme iron group, and is complexed with cytochrome P450 reductase, which aids in the electron transfers to oxygen.
E. Cytochrome P450 complexes are grouped into the di-oxygenase type of enzyme.

64. (1 point) The transfer of reducing equivalents to the electron transfer chain can occur through a variety of mechanisms. Which of the following statements are INCORRECT concerning such transfers?

A. FADH₂ generated during fatty acid oxidation within the mitochondrial matrix transfer their electrons to ETF, which then transfers the electrons to Coenzyme Q.
B. NADH generated in the cytoplasm can be directly transported into the mitochondria by an active symporter with citrate.
C. The malate/aspartate shuttle operates primarily in muscle cells.
D. The glycerol-3-phosphate shuttle requires the participation of dihydroxyacetone phosphate.
E. Transaminations are required for the malate/aspartate shuttle to work properly.
F. The mitochondrial enzyme transhydrogenase can convert NADH + NAD⁺ to NAD⁺ + NADPH.

Questions 65-73 (1 point each) are TRUE/FALSE questions. Answer T or F on the answer sheet. There is only one correct answer for each of these questions.

65. Upon glucagon release, protein inhibitor I is phosphorylated in the muscle.
66. The sequence of the cycling events in fatty acid biosynthesis consist of condensation, reduction, dehydration, and reduction.
67. The sequence of events in fatty acid degradation (saturated fatty acids) consist of oxidation, generating FADH₂, hydration, a second oxidation (generating NADPH), and thiolytic cleavage.
68. The tetrameric insulin receptor consists of four identical subunits.
69. Glycerol kinase is found in both the liver and adipocyte.
70. Mutations in pancreatic glucokinase can lead to a form of type II diabetes.
71. Fatty acids represent the most abundant energy supply in humans.
72. Liver lactate formation is favored when the NAD⁺/NADH ratio is high.
73. During exercise, the rate of formation of ATP via anaerobic glycolysis is greater than the rate of ATP formation via aerobic fatty acid oxidation.
74. (9 points) Compare and contrast the onset of hypoglycemia under the following three conditions. Discuss the biochemical reasons as to why hypoglycemia results, and indicate if the mechanism of hypoglycemia is the same or different as from the other situations asked.

A. Chronic alcoholic on a binge, where the only caloric intake for the past twelve days has been alcohol. **Lack of gluconeogenic substrates due to a lack of NAD⁺, due to the metabolism of alcohol.**

```
\[ \text{alcohol} \xrightarrow{\text{NAD}^+} \text{CH}_2-C=O \xrightarrow{\text{NAD}^+} \text{CH}_3-C-OH \]
```

So when make pyruvate, pyr → lactate to generate NAD⁺

If make OAA, OAA → malate to generate NAD⁺

So gluconeogenic precursors lacking, gluconeogenesis slow, results in hypoglycemia.

B. An individual deficient in MCAD activity who does not eat for 15 hours.

MCAD deficiency results in inefficient fatty acid oxidation, and a reduction in available energy from fatty acids. FAs can be oxidized from 16→10C’s long, but no more. Insufficient energy is produced to allow gluconeogenesis to proceed at a rapid pace (2 lactate→glucose requires 6 molecules of ATP), so the liver can’t keep up for the demand. Liver glycogen has been depleted at 12 hours after eating, so all glucose must come from gluconeogenesis.

C. A patient with type 1 glycogen storage disease who has not eaten for 15 hours.

Lack of G6Pase: no glucose can come from glycogen or gluconeogenesis since G6P→glucose cannot occur. Only way to keep blood glucose levels is by eating frequently. When dietary glucose levels drop, blood glucose drops, and hypoglycemia results.

The 3 situations are all different in terms of the causes of hypoglycemia, but they all have the same end result.
75. (9 points) Compare and contrast the causes for lactic acidosis under the following conditions. Explain for each situation why lactic acidosis occurs (the biochemical mechanism), and whether the mechanism is the same or different for the three situations being asked.

A. High infusion of fructose into the bloodstream.

Fructose is rapidly coverted to F1P by fructokinase, which is split into DHAP + glyceraldehyde. The glyceraldehyde is also phosphorylated to form G3P: the whole process is incredibly rapid, and G3P accumulates. This pushes glycolysis forward (bypassing the first 2 regulated steps) and generates pyruvate. However, now NAD+ levels are limiting for glycolysis (due to the amount of substrate available), such that pyr→lactate, NADH→NAD+, to allow glycolysis to continue. This leads to a buildup of lactate, and lactic acidosis.

B. Muscles working under anaerobic conditions.

Under anaerobic conditions (no oxygen) glycolysis generates NADH, but then cannot continue due to a lack of NAD+. If O2 were present, the NADH could be used to donate electrons to the ETC, to regenerate NAD+. But since this cannot occur without oxygen, pyr→lactate, NADH→NAD+, and glycolysis can continue.

C. A patient with pyruvate carboxylase deficiency.

In the absence of pyruvate carboxylase, pyruvate has one less potential fate (others are to alanine or acetyl CoA, by PDH). Thus, under high energy conditions, or conditions in which pyruvate DH is inhibited by acetyl CoA (fatty acid oxidation, for example), pyruvate will accumulate (it should go to OAA under those conditions, but it is not possible). Thus, as [pyr]↑, since pyruvate is in equilibrium with lactate, [lactate]↑, and lactic acidosis will occur.

The first two conditions are similar in that lactate formation occurs to allow glycolysis to continue; the third situation is different in that mass action, a buildup of pyr→lactate, leads to the lactic acidosis.
76. (6 points) Dichapetalum toxicanium, a shrub that grows in Sierra Leone, produces ω-flouro-oleic acid, which is highly toxic to warm blooded animals. This substance has been used as an arrow poison, and powdered fruit from the plant is sometimes used as a rat poison. Explain, at the biochemical level, why this compound is so toxic (indicate the target enzyme as well).

When this fatty acid is degraded, one gets out fluoro-acetyl CoA, which upon condensation with OAA, gives fluorocitrate. Fluorocitrate inhibits aconitase, and blocks the TCA cycle from functioning. In addition, the aconitase block will lead to an accumulation of fluorocitrate, which will diffuse out of the mitochondria and inhibit PFK-1, which leads to an accumulation of F6P, then G6P. The toxicity results from the blockage of the TCA cycle (even very high concentrations of citrate cannot overcome the block) and the loss of energy, which is exacerbated by the inhibition of glycolysis by fluorocitrate.
77. (2 points) Indicate on the graph below what the oxygen consumption curve would look like if at time = 1 succinate was added to a carefully prepared suspension of mitochondria, at time = 2, rotenone was added, at time = 3 DCCD was added, at time = 4 dinitrophenol was added, and at time = 5 carbon monoxide was added.

78. (3 points) From the data below, determine the type of inhibition exhibited by the inhibitor I, the Km in the presence and absence of inhibitor, and the Vmax in the presence and absence of inhibitor. Indicate your answers below. Partial credit can be awarded if the work is shown (on one of the extra sheets of paper), although it is not required that your work be shown (in which case this will be an all or none question).

<table>
<thead>
<tr>
<th>[S], mM</th>
<th>V (nmol/min/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-I</td>
</tr>
<tr>
<td>.083</td>
<td>.0465</td>
</tr>
<tr>
<td>.125</td>
<td>.0625</td>
</tr>
<tr>
<td>.2</td>
<td>.083</td>
</tr>
<tr>
<td>.5</td>
<td>.125</td>
</tr>
</tbody>
</table>

The type of inhibition is: **non-competitive**

The Km in the presence of inhibitor is: ~ **0.30 mM**

The Km in the absence of inhibitor is: ~ **0.30 mM**

The Vmax in the presence of inhibitor is: ~ **0.1**

The Vmax in the absence of inhibitor is: ~ **0.2**
ANSWER KEY for Exam 2

1. A, F  
2. D  
3. A, F  
4. A, D  
5. A, B, D  
6. A, C  
7. C, F, L  
8. A, C, H, L  
9. J  
10. L  
11. E  
12. D  
13. F  
14. J  
15. I or H  
16. H  
17. A  
18. A, E  
19. A, D  
20. E, G, H  
21. A, B, K  
22. A, E  
23. A, D  
24. A, C, D  
25. A, C, D  
26. A, B, E  
27. A  
28. A, B  
29. D  
30. D, E  
31. A  
32. J  
33. H  
34. A  
35. J or G  
36. D  
37. A, E, F, G  
38. A, F, H  
39. B, E  
40. B, E, F  
41. D  
42. A, G, H  
43. E, F  
44. A  
45. D  
46. B, D, F  
47. A, C  
48. A  
49. B  
50. C  
51. E  
52. D  
53. B, H  
54. B  
55. K  
56. I  
57. G  
58. A  
59. J  
60. E  
61. A or B  
62. A, C, F  
63. D  
64. B, C  
65. F  
66. T  
67. F  
68. F  
69. F  
70. T  
71. T  
72. F  
73. T  
74. Answer in exam booklet  
75. Answer in exam booklet  
76. Answer in exam booklet  
77. Answer in exam booklet  
78. Answer in exam booklet