Multiple Choice (2 pts each) - Choose the single best answer.

1. You have a patient with a sluggish citric acid cycle. Which of the following would not account for this?
   A) Excessive consumption of raw eggs
   B) Thiamine deficiency
   C) Dehydration
   D) Excessive consumption of alcohol
   E) Excessive consumption of carbohydrates

2. During germination, plant seedlings that must thrive on fat reserves are highly dependent on which of the following pairs of enzymes?
   A) Glyoxylate synthase and citrate synthase
   B) Isocitrate lyase and malate synthase
   C) Rubisco and aldolase
   D) Aconitase and isocitrate dehydrogenase
   E) Pyruvate dehydrogenase complex and malate dehydrogenase

3. A new compound is isolated from mitochondria, and a claim is made that it is a previously unrecognized carrier in the electron transport chain; it is given the name coenzyme Z. Which line of evidence is the least conclusive in assigning the compound a position in the electron transport chain?
   A) When added to a mitochondrial suspension, coenzyme Z is taken up by the mitochondria very rapidly.
   B) Removal of coenzyme Z from the mitochondria results in a decreased rate of oxygen consumption.
   C) Alternate oxidation and reduction of the mitochondrion-bound coenzyme Z can be readily demonstrated.
   D) The rate of oxidation and reduction of mitochondrion-bound coenzyme Z is of the same order of magnitude as the overall rate of electron transport in mitochondria as measured by oxygen consumption.
   E) All lines of evidence are equally convincing.

4. Oligomycin inhibits the mitochondrial ATP synthase. Which of the following would not be an immediate effect of oligomycin in normal mitochondria?
   A) Decreased rate of oxygen consumption
   B) Decreased rate of electron transport
   C) Decreased rate of ATP synthesis
   D) Decreased proton gradient
   E) Decreased rate of ATP/ADP exchange
5. Which of the following statements about the mitochondrial ETC are correct?
   i) Electrons flow from carriers with high reduction potentials to ones with lower reduction potentials.
   ii) The proton gradient generated by the ETC is mainly used for ATP generation, but it may also power other processes such as transport.
   iii) Protons are exported from the matrix to the intermembrane space with the number of protons extruded greater than the number of electrons transported.
   iv) All of the electron carriers of the ETC are within four large protein complexes located in the inner mitochondrial membrane.
   A) All are correct.  
   B) All are incorrect. 
   C) Only i and iv are correct.  
   D) Only ii and iii are correct.  
   E) Only i, ii, and iii are correct.

6. Which of the following statements about the light reactions in photosynthetic plants is false?
   A) The light reactions do not occur in the dark.
   B) A membrane-bound ATP synthase uses a proton gradient to make ATP.
   C) There are two distinct photosystems, linked together by an electron transport chain.
   D) The ultimate source of electrons for the process is H$_2$O.
   E) The ultimate electron acceptor is O$_2$.

7. The Calvin cycle requires all of the following to operate except:
   A) glucose  
   B) CO$_2$  
   C) ribulose 1,5-bisphosphate  
   D) NADPH  
   E) light

8. Which of the following is true of glucagon and epinephrine in liver?
   A) They activate glycogen phosphorylase and inactivate glycogen synthase.
   B) They inactivate glycolysis and activate gluconeogenesis.
   C) They act by increasing the concentration of cAMP.
   D) They oppose the effects of insulin.
   E) All of the above are true.

9. Which of the following would not be a symptom of glycogen synthase deficiency?
   A) hypoglycemia between meals  
   B) hyperglycemia after meals  
   C) enlarged liver  
   D) muscle weakness  
   E) decreased glycogen stores

10. Which of the following is not true about gluconeogenesis?
   A) For starting materials, it can use the carbon skeletons from most amino acids.
   B) During exercise, it is activated in the muscles to process lactic acid.
   C) It is inhibited by the regulator fructose 2,6-bisphosphate.
   D) It is one of the ways that the liver maintains glucose homeostasis.
   E) It requires metabolic energy in the form of ATP, GTP, and NADH.
11. (12 pts) *Thiobacillus ferrooxidans* is a (non-photosynthetic) bacterium that lives on slag heaps (sites of coal mine waste) at pH 2. The bacterium uses the natural pH gradient provided by the environment to make ATP and NADPH to fix CO$_2$.

a) Calculate the $\Delta G$ for the transport of protons from the outside to the inside of *T. ferrooxidans* (pH 6.5; membrane potential is zero) on a hot summer day in Pennsylvania.

b) How many protons would have to enter through the ATP synthase to make an ATP under cellular conditions?

c) *T. ferrooxidans* oxidizes Fe$^{2+}$ from the environment to reduce NADP$^+$. The half reactions are

\[
\begin{align*}
    \text{Fe}^{3+} + e^- &\rightarrow \text{Fe}^{2+} & E^\circ = 0.77 \text{ V} \\
    \text{NADP}^+ + H^+ + 2 e^- &\rightarrow \text{NADPH} & E^\circ = -0.32 \text{ V}
\end{align*}
\]

What is the $\Delta G^\circ$ for this reaction? Comment on its favorability under standard conditions.

12. (8 pts) Aspirin is widely used to reduce fever, pain, and inflammation, but in high doses, a side effect is hyperthermia. You perform several experiments in order to elucidate how aspirin causes hyperthermia.

a) In one promising experiment, you treat isolated mitochondria with high dose aspirin (or not, in the control) while measuring the oxygen concentration, with the results shown here. Briefly propose a mechanism for aspirin’s hyperthermic effect.

b) Another side effect of high-dose aspirin is lactic acidosis. Explain.
13. (12 pts) Not all plants operate exactly according to the Z scheme discussed in class and in the text. An investigation was carried out to characterize photophosphorylation in the Bird’s-nest orchid (*Neottia nidus-avis*). This plant contains chlorophyll, carotenoids, both photosystems, and the electron transport chain components.

a) Orchid chloroplasts were isolated and illuminated in the presence of an oxygen electrode and P-32. Oxygen was not evolved, but P-32 was incorporated into ATP. What can you conclude about orchid photophosphorylation from this experiment?

b) The absorbance (solid line) and fluorescence (the energy emitted; dotted line) spectra of antenna carotenoids from orchid and sweet pea (a control for normal photosynthesis) were compared (see below). What is the most notable difference, and how can you account for this difference given that the pigments are the same?

c) Chlorophyll molecules in photosystem II absorb at about 460 nm. How effective are the antenna carotenoids of orchid at transferring energy to these chlorophylls? Explain.

d) Propose a mechanism for photophosphorylation in the Bird’s-nest orchid, citing specific experimental evidence given in this problem to support your mechanism.
14. (10 pts) These questions are based on the following stages of glucose oxidation:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Name</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>glycolysis</td>
</tr>
<tr>
<td>II</td>
<td>oxidation of pyruvate to acetyl-CoA</td>
</tr>
<tr>
<td>III</td>
<td>Krebs cycle</td>
</tr>
<tr>
<td>IV</td>
<td>oxidative phosphorylation</td>
</tr>
</tbody>
</table>

a) Which stage produces the most ATP when glucose is oxidized to CO$_2$ and H$_2$O? (circle)

I    II    III    IV

b) Where in the cell does each stage occur? (put an X in the correct column)

<table>
<thead>
<tr>
<th>Stage</th>
<th>cytosol?</th>
<th>mitochondrion?</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
<td></td>
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<tr>
<td>III</td>
<td></td>
<td></td>
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<tr>
<td>IV</td>
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</tbody>
</table>

c) Which stage(s) release(s) CO$_2$? (circle)

I    II    III    IV

d) Which stage(s) release(s) H$_2$O? (circle)

I    II    III    IV

15. (6 pts) Insufficient intake of key nutrients can compromise metabolism and give rise to a range of human diseases. Provide specific metabolic explanations for the following observations, including the affected protein and pathway.

a) Hypoallergenic baby formulas given to infants with milk allergies in Japan contain no biotin. Seizures, hypotonia, and lactic acidosis can result.

b) Copper deficiency leads to impairment of mitochondrial energy production and structural changes in cardiac mitochondria.

16. (12 pts) Glucose 6-phosphate is a “branch-point” molecule that can proceed down multiple possible metabolic pathways, depending on the tissue type and conditions.

a) Identify three direct metabolic transformations of glucose 6-phosphate in a liver cell and describe the conditions that would favor each transformation.

<table>
<thead>
<tr>
<th>Resulting Molecule</th>
<th>Conditions</th>
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<tbody>
<tr>
<td>1</td>
<td></td>
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<tr>
<td>2</td>
<td></td>
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<td>3</td>
<td></td>
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</table>

b) How does this differ in skeletal muscle? Explain.
17. (12 pts) A 22-yr-old Swedish man presents with lifelong exercise intolerance marked by intermittent episodes of increased muscle pain, fatigue, and weakness. Testing reveals a low VO2\text{max} (maximal oxygen uptake) of 12 mL/min per kg (healthy sedentary men = 39 ± 5). At rest, his serum lactate and pyruvate are normal, but they increase excessively relative to workload during exercise. He does not have hypoglycemia.

a) Based only on this information, name two pathways that could be defective in this patient, briefly explaining how your answer accounts for the observed symptoms.

b) Further testing reveals that the patient has a low lactate/pyruvate ratio (L/P) during maximal exercise (L/P for patient = 36; normal is 48 ± 8). Does this exclude either of your proposed pathways as the site of the defect? Explain briefly.

c) Further testing reveals that the patient has elevated succinate in the urine. Mitochondrial enzymes were tested for activity, and one was found to be deficient, with most others more active than normal. Given this new information, what single enzyme is the best candidate for the defect? Explain.

18. (8 pts) The proton motive force is responsible for ATP production in bacteria, mitochondria, and chloroplasts. You are testing the hypothesis that the pmf may also power bacteria movement via a flagellar motor. Your test subject is a motile strain of Streptococcus. These bacteria swim when glucose is available for oxidation, but they do not swim when glucose is absent. Explain how each of the following experimental observations supports the hypothesis that the flagellar motor is driven by protons moving back into the cell, down their electrochemical gradient.

a) Bacteria that are swimming in the presence of glucose stop swimming upon addition of DNP.

b) Bacteria that are motionless in the absence of glucose in a medium containing low K\textsuperscript{+} (relative to inside the cell) swim briefly after addition of valinomycin and then stop.