PRACTICE FOR EXAM 2
1. There is a cis-Δ⁹ 17 carbon fatty acid (a 17:1 heptadecenoic acid) found in the fish and blubber eaten by Inuit people.
   a. Estimate how many ATPs could be obtained from this fatty acid. Show/explain your reasoning.

   ![Fatty Acid Structure]

   98.5 ATP incl. activation (lose 1 FADH2)

   The fatty acid above is an exception to the rule that glucose cannot be made from fatty acids. EXPLAIN WHY. The final product is propionyl CoA which is converted to succinyl CoA. This increase of a TCA cycle intermediate would lead to a net production of oxaloacetate which could be drawn off for glucose synthesis by gluconeogenesis.
2. PGI₂, a prostaglandin, is an inhibitor of blood clotting which is secreted by endothelial cells while thromboxane TXA₂ produced by blood platelets is a strong promotor of blood clotting. (12)

a. Explain why aspirin in small doses taken every few days inhibits TXA₂ production while the concentration of PGI₂ does not change too much.
b. Explain how EPA (eicosapentaenoic acid) from fish oil might have the same overall effect as a “blood thinner” as aspirin. Do you think that high doses would reverse the anticoagulant properties as in aspirin? Explain why or why not.

a. Thromboxane $A_2$, which promotes platelet aggregation and blood clotting, is produced in anucleate blood platelets whereas $PGL_2$ is derived from nucleated endothelial cells and is a vasodilator and inhibitor of platelet aggregation. Both are derived in part by action of cyclooxygenase. The small dose of aspirin irreversibly inhibits both cyclooxygenases, but endothelia can quickly recover and synthesize more while the platelets, being anucleate, cannot and are inhibited for the lifespan of a platelet (several days). Hence the overall effect is to shut down clot-promoting $TXA_2$ synthesis while leaving clot-inhibiting $PGI_2$ levels practically unchanged.

b. EPA, an $\omega-3$ fatty acid, with 5 double bonds instead of arachidonic acid’s 4, leads to the synthesis of $PGI_3$ instead of $PGI_2$ from endothelia and can block production or lead to the synthesis of $TXA_3$ instead of $TXA_2$. $PGI_3$ is at least as good as $PGI_2$ at inhibiting platelet aggregation while $TXA_3$ is much less effective than $TXA_2$ at promoting aggregation. Hence a blood thinning effect as with aspiring occurs, though by a different mechanism. Aspirin at high continuous doses would continually inhibit production of both $TXA_2$ and $PGI_2$, neutralizing the “blood thinning” effect described above. On the other hand, high doses of EPA would still have the anticoagulant effect since selective permanent inhibition of a platelet enzyme is not involved.

4. Type VIII glycogen storage disease is caused by a deficiency in phosphorylase kinase in the liver. Explain these clinical symptoms. Don’t forget to describe what the enzyme does!: (8)

a. “increased amount and normal glycogen structure in the liver”

b. “hypoglycemia”

“increased amount and normal glycogen structure in the liver”

Phophorylase kinase is a regulatory enzyme which activates glycogen phosphorylase by phosphorylation. The liver is a main repository of glycogen since it is responsible for glucose homeostasis. Lack of this enzyme would reduce the ability to release glucose, but not to synthesize glycogen. Hence glycogen would accumulate but should have a normal structure since no branching enzymes are involved.

“hypoglycemia”

Again, because of the role of the liver in glucose homeostasis, any problems with glucose release from glycogen would impair one’s ability to release sufficient amounts of glucose into the blood.

5.a. Why is water excluded from the active site of the phosphorylase enzyme? (8)
Phosphorolysis is a process by which phosphate attack is used to release glucose from glycogen rather than hydrolysis. This process effectively saves an ATP since a glucose phosphate is generated. Hydrolysis is a more favorable reaction and water at the site of this process would promote hydrolysis. The glucose released would then need to be phosphorylated with ATP to enter glycolysis making the glycogen storage process much more costly.

b. Predict the effect of a mutation expressed in the protein that allows a water molecule to occasionally enter. Would this have a bigger effect on the liver or muscle phosphorylase? Explain.

As explained above, hydrolysis might occur instead and free glucose would be released. Muscle tissue could arguably be more affected by this defect since the role of muscle is to use glucose, not secrete it. In fact, liver has the enzyme glucose-6-phosphatase, unlike muscle, so that free glucose can be released. Hence the results of this sort of defect in liver would be similar to what already happens, except that the efficiency of glucose storage would be compromised. However, since the liver is so heavily involved in biosyntheses requiring NADPH (from pentose phosphate) this could be a more serious defect since it would reduce the amount of glucose phosphates available.

6. a. Dichlorophenyldimethylurea (DCMU), a herbicide, interferes with photophosphorylation and O₂ evolution. However, it does not block O₂ evolution in the presence of an artificial electron acceptor such as ferricyanide. Propose a site for the inhibitory action of DCMU. Draw a schematic diagram of PS I and II to help. DCMU blocks O₂ production, so it must somehow interfere with PSII and electron transfer. It seems most likely that it would inhibit transfer to plastoquinone, Q. This would block any further oxidation of water and hence, no oxygen. When a route is supplied for electrons to be passed on (like ferricyanide) oxygen production can continue. It is also possible that DCMU could block at the level of electron transfer to cyt bf and QH₂ could get “backed-up” and stop water oxidation.

b. In light of the previous answer, predict the effect of DCMU on a plant's ability to perform cyclic photophosphorylation.
If a site on PSII is blocked, then cyclic phosphorylation, which does not depend on water electrons, should not be affected. If you proposed that a site in cyt bf or PSI is blocked (causing electron back-up) then cyclic photophosphorylation would be inhibited. Your answers should be consistent.
7. a) Glycogen Storage Disease 0 involves a deficiency of liver glycogen synthase. Describe the symptoms you might expect (specifically what would blood sugar levels be like under conditions of fasting and feeding). How could this disease be treated (assume that a large enzyme like glycogen synthase could not be injected and taken up by the liver)?

Since the liver controls blood glucose levels to a large extent, this could be serious. One would expect, since less glycogen synthesis would occur, that after fasting (or sleeping) that blood glucose levels would drop (hypoglycemia). The could only be maintained by gluconeogenesis. One would also expect that liver glycogen levels would also be reduced. On the other hand after a carb-rich meal, one would expect hyperglycemia (high blood glucose), since blood glucose could not be stored efficiently as liver glycogen. Treatment could possibly be through diet, eating a little bit very often to keep blood sugar steady (no fasting and no big pasta meals). Maybe insulin and glucagon when needed could keep blood sugar regulated.


b) Glycogen Storage Disease I (Von Gierke Disease) involves a deficiency of liver and kidney glucose-6-phosphatase. Describe the symptoms you might expect (specifically what would blood sugar levels be like under conditions of fasting and feeding). How could this disease be treated?

Once again, since the liver controls blood glucose levels to a large extent, this could be serious. Glucose 6-phosphatase is that last step in releasing glucose into the blood. Without it neither glucose from gluconeogenesis or glycogen breakdown could be released. This would severely alter the liver’s ability to regulate glucose and hypoglycemia would be a BIG problem. One might expect high concentrations of glycogen in the liver due to excess G-6-P → G-1-P. The only possible treatment other than gene therapy would be to eat constant small meals of glucose to keep blood sugar up (but not too high!!). One might expect rapid exhaustion, like the first case study problem due to inability to maintain blood glucose high enough.

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