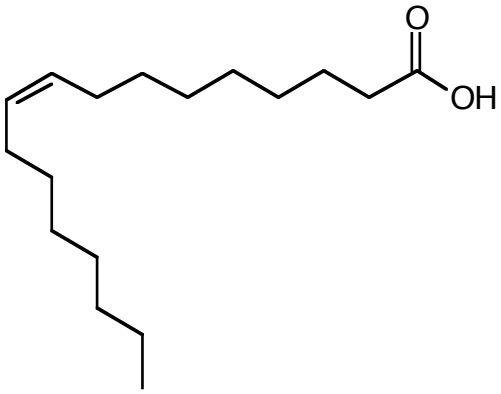
PRACTICE FOR EXAM 2

1. There is a cis-Δ^9 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.



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.

KETONE STRIPS
LARGE 100 CT SIZE
CHECK YOUR KETONE LEVELS WHILE ON YOUR DR. ATKINS LOW CARB DIET.
ESPECIALLY HELPFUL DURING THE DR. ATKINS DIET TWO WEEK INDUCTION PHASE. A MUST FOR ANY LOW CARBER!

2. Above is a web ad for Uriscan strips ($11.95) to detect ketones in one's urine.

a. Explain in as much detail as you can why the presence of ketones signals the "success" of Atkins low carb diets.

Low carbohydrates causes a depletion of OAA for glucose maintenance. This means there is less TCA activity and since more fats are being used, an excess of acetyl CoA. This excess appears as ketone bodies and is excreted - success!

What effect on urine <u>ketones</u> in an Atkins dieter would you expect from the following:

b. Eating a big beef jerky (all protein essentially). Explain your answer.

Depending on the balance of gluco-genic + keto genic amino acids, it would probably reduce ketone out put by leading to synthesis of TCA int.

c. Eating a big chunk of butter (yechh!). Explain your answer.

Increase ketone bodies

d. Eating a bag of candy. Explain your answer

decrease!

3. PGI_2 , a prostaglandin , is an inhibitor of blood clotting which is secreted by endothelial cells while thromboxane TXA_2 produced by blood platelets is a strong promotor of blood clotting. (12)

a. Explain why aspirin in small doses taken every few days inhibits TXA_2 production while the concentration of PGI_2 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 PGI_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 oveall effect is to shut down clot-promoting TXA_2 synthesis while leaving clot-inhibiting PGI_2 levels practically unchanged.

b. EPA , an ω-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 glucoses homeostasis, any problems with glucose release from glycogen would impair one's ability to release sufficient amounts of glucose into the blood.

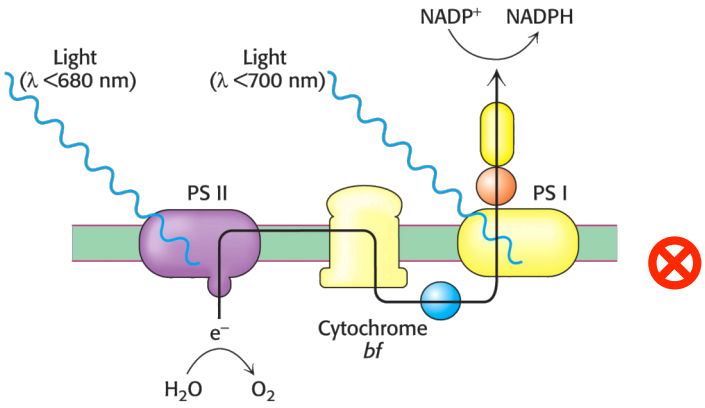
5.a. Why is water excluded from the active site of the phosphorylase enzyme? (8)

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.

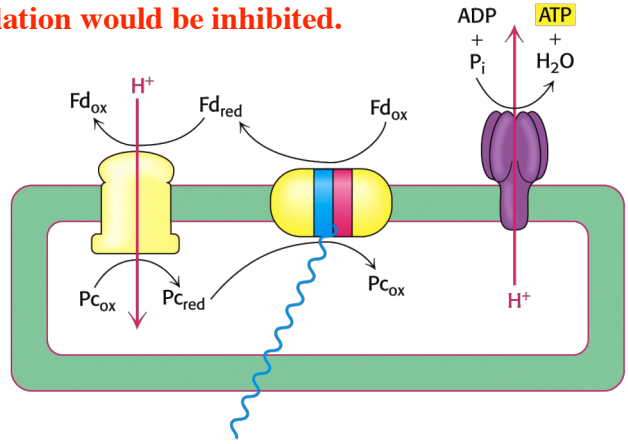
As explained above, hydrolysis might occur instead and free glucose would be released. Muscle tissue could arguably be more affected by this defect since the role of muscle is to use glucose, not secrete it. In fact, liver has the enzyme glucoses-6-phosphatase , unlike muscle, so that free glucose can 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 glucoses phosphates available.

6. a. Dichlorophenyldimethylurea (DCMU), a herbicide, interferes with photophosphorylation and O_2 evolution. However, it does not block O_2 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 O_2 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 QH_2 could get "backed-up" and stop water oxidation.**



b. In light of the previous answer, predict the effect of DCMU on a plants 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 (causeing electron back-up) then cyclic photophosphorylation would be inhibited. Yopur answers should be consistent



a.

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 *hyper*glycemia (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.

Find out *real* details here: http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=240600

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 big 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.

Find out *real* details here:
http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=232200