CHAPTER 22

1. Homework 3, 4, 6. Look carefully at Fig. 22.2 on page 618 (and online handout). The similarity of fatty acid beta oxidation (in red, on left) to the way succinate is handled in the Citric Acid Cycle (487, 425) makes this pathway an easy one to learn. Fatty acids are stored as triglycerides, and hydrolyzed by lipase enzymes. Lipases are under the control of Protein Kinase A and hormones etc. Free fatty acids are ionophores which could uncouple mitochondria, so they are rapidly attached to Coenzyme A by acyl CoA synthetase (or fatty acid thiokinase) via acyl-AMP. Cytoplasmic acyl CoA cannot enter the mitochondrion without the help of carnitine acyltransferase (Fig 22.8). The steps of beta oxidation are shown in Fig 22.9, and the enzymes are named in Table 22.1. Acyl CoA dehydrogenases feed electrons in through complex II directly to the mitochondrial ETC. Complete breakdown of palmitoyl CoA affords 108 ATP, and oxidation of palmitate gives 106 (because 2 must be subtracted for the thiokinase step). Know how to deal with "delta even" and "delta odd" unsaturated chains, using reductase and isomerase enzymes as required.

2. Odd-chain fatty acids (C-17 etc.) make up about 5% of the fatty acids in seafood. Beta oxidation takes them down to C-3, leaving propionyl CoA. To be metabolized this must be carboxylated, racemized, and remodeled with the aid of Cobalamin (or vitamin B-12). Know the reactions in Fig 22.12 (627). Know what ketone bodies are, and how they are formed (Fig 22.20, 631). Ketone bodies are exported from the liver, especially when "fat metabolism predominates" – in starvation, diabetes, or low carbohydrate "fad" diets. The condition is called ketosis, and can lead to severe acidosis and even the death of kidneys. (633). The article, "The Pima Paradox" from the New Yorker is relevant to this discussion (see below).

3. Know the basics of fatty acid synthesis – it is cytoplasmic, and mainly based on malonyl ACP (635). The process is driven by decarboxylation of malonate. Eukaryotes have "one big enzyme" with all the various activities (Fig 22.26) but other organisms have an enzyme complex. The reactions in Fig 22.27 are sometimes called the "Citrate Lyase Cycle." This explains how Acetyl CoA gets out into the cytoplasm to serve as starting material for fatty acid synthesis. Know that aspirin and celebrex both inhibit prostaglandin synthesis via cyclo-oxygenase (cox-2) (339, 644). GENERAL LESSON – if a fatty acid enters the mitochondrion, it will be destroyed, i.e. oxidized as fuel. Any synthetic process, whether fatty acid synthesis of membrane lipid synthesis etc., must thus occur in the cytoplasm.