METABOLISM

I. Introduction.

- metabolism: all chemical reactions necessary to maintain life; these processes are either anabolic or catabolic.

A. Anabolism: reactions that build large molecules from smaller ones (i.e., aa form proteins)

B. Catabolism: reactions in which complex molecules are broken down into simpler ones (i.e., events of cellular respiration).

II. Carbohydrate metabolism.

A. General comments.

- all food carbohydrates eventually are converted to glucose; glucose breakdown is oxidation of glucose

- recall that oxidation is a loss of electrons, reduction is a gain of electrons.

- oxidation of glucose involves a stepwise removal of pairs of hydrogen atoms from substrate molecules, passing them on to electron acceptors.

- two major electron acceptors are NAD+ and FAD.

- the bulk of energy (ATP) from glucose oxidation results from use of NADH+H+/$FADH_2$ to set up a hydrogen ion gradient used to drive ATP synthesis.

- glucose oxidation: $C_2H_{12}O_6 + 6O_2$ -------> $6H_2O + 6CO_2$ + 38ATP + heat

- this process involves glycolysis, Krebs Cycle, and electron transport chain (ETC).

-there are two means of ATP production throughout glucose oxidation: substrate level phosphorylation where high energy phosphate groups are transferred directly from phosphorylated molecules to ADP; oxidative phosphorylation which is carried out by ETC proteins; uses NADH+H+/FADH2 to set up a hydrogen ion gradient, the dissipation of which leads to ATP synthesis.

B. Glycolysis.

- series of 10 chemical steps where one glucose molecule is converted into two pyruvate molecules; net yield is 2 ATP/glucose molecule.

- this process is anaerobic (doesn't need oxygen).

1. Sugar activation: glucose committed to glycolysis; 2 ATP molecules are used.

2. Sugar cleavage: a six-carbon sugar converted to two three-carbon sugars.

3. Sugar oxidation and formation of ATP: begin stepwise removal of pairs of hydrogen atoms passing them onto electron acceptors; net yield is 2 pyruvate, 2 NADH+H+, and 2 ATP.

    - in aerobic conditions, pyruvate is moved in the direction of the Krebs cycle; in anaerobic conditions pyruvate is converted into lactic acid.

C. Krebs cycle.

- occurs in the mitochondrial matrix; fueled by the pyruvate from glycolysis.

1. Pyruvate converted to acetyl CoA: step that links glycolysis to the Krebs cycle; it involves three reactions all catalyzed by one enzyme, pyruvate dehydrogenase:

    a. decarboxylation: pyruvate has one carbon removed, released as CO_2.

    b. oxidation: removal a pair of hydrogen atoms.

        - as a result of the decarboxylation and the oxidation, acetic acid is produced.

    c. acetic acid reacts with coenzyme A to form acetyl CoA.

2. Acetyl CoA enters the Krebs: series of events take place as cycle moves through 8 consecutive steps.

-2 decarboxylations; account for the 2 Cs that came into Krebs; produce carbon dioxide.

- 4 oxidations: four transfers of hydrogen atom pairs from Krebs intermediates to electron acceptors

- 1 substrate level phosphorylation: 1 ATP produced.

- Summary:

per pyruvate	per glucose
3 CO_2	6 CO_2
4 NADH + H^+	8 NADA + H^+
1 $FADH_2$	2 $FADH_2$
1 ATP	2 ATP

D. Electron transport chain (ETC) and oxidative phosphorylation:

- at this point we have electron acceptors loaded down with electrons; they are "worth" a lot of energy

- a group of proteins in the inner mitochondrial membrane are arranged in a sequence of decreasing energy states.

- the electron acceptors (from glycolysis and Krebs) deliver electrons and protons at the "top" level of the chain to one of the protein electron acceptors; the protons (H+) escape into the matrix and electrons are passed down the chain into successively lower energy levels, with a release of energy in every step.

- the final electron acceptor (at lowest point in chain) is oxygen; it accepts electrons and combines with hydrogen to form water.

- electrons are delivered at a high energy level in the chain to molecules with lower affinity (desire) for electrons than oxygen (which has the highest affinity for electrons); thus as electrons are passed on each successive carrier has greater affinity for electrons than the one preceding it; oxygen therefore helps to "pull" the electrons down the chain ; if there is no oxygen present, then there would be no final acceptor for electrons and no gradient of energy levels would be maintained.

- the stepwise release of energy is used to pump the protons from the matrix, across the membrane into the intermembranous space.

- therefore a proton gradient is established across the inner mitochondrial membrane, an electrochemical gradient.

- this dissipation of the electrochemical gradient (as protons move from area of high concentration to area of low concentration) releases energy used in the production of ATP.

- the protein channel, ATP synthase, allows the protons to move down the electrochemical gradient and drive the process by which ATP is synthesized from ADP and P.

- for every NADH+H+ there are 3 ATP formed; for every $FADH_2$, there are 2 ATP formed; why?

E. Glycogenesis / Glycolysis.

1. Glycogenesis:

- if more glucose is available than can be immediately oxidized, then glycogen is produced.

- under hormonal control.

2. Glycolysis:

- when blood glucose levels drop below the amount needed to maintain the body's needs, glycogen is broken down and glucose is produced.

- tight hormonal control.