

Study Guide – Lehninger Principles 5th Edition

Chapter Fifteen

By Frank Deis

Homework: 4,5,8,10,11. **15.1 Regulation of Metabolic Pathways.** One fundamental idea of this section is most easily visualized using *Atkinson's Energy Charge Function* ($[ATP]+0.5[ADP]÷([ATP]+[ADP]+[AMP])$). This number varies from zero to 1.0 and expresses the available "~P" (say "squiggle P") or energetic phosphate level in the cell. Nearly every pathway is regulated by levels of ATP, ADP, or AMP in some way. Class discussion – energy regulation is like a thermostat regulating temperature. Know about AMPK, AMP-Dependent Protein Kinase (576). Calculate the energy charge values for "before" and "after" in Table 15-4. Look at Fig 15-2. In bacteria, control of *transcription* is very important (repression and induction). Covalent modification is important for hormonal control of pathways, and allosteric regulation generally is used for local controls. "Irreversible" enzymes are likely to be control points for their pathways.

15.2 Analysis of Metabolic Control. Omit this section.

15.3 Coordinated Regulation of Glycolysis and Gluconeogenesis. Figure 15-11 contains three potential "cycles." These are prevented from cycling by regulation. In general catabolic pathways are inhibited by high ATP levels and stimulated by AMP, and anabolic pathways are affected oppositely (Fig 15-14, 15-15, 15-19). In addition Hexokinase has isozymes which are blocked by the product G6P, and liver Glucokinase can be sequestered in the nucleus (Fig 15-13). Fructose-2,6-BP (587) is a signal of abundant glucose which stimulates PFK-1 and inhibits FBPase. Acetyl CoA levels determine whether pyruvate goes "up" to oxaloacetate or "down" to produce more Acetyl CoA (Fig 15-20). cAMP and F-2,6-BP have opposite significances. In liver, Xylulose-5P enhances production of F-2,6-BP after a meal.

15.4 The Metabolism of Glycogen in Animals. One nutritional "Calorie" equals one biochemical "kilocalorie" (and about 4 kJ). An average person has about 280 Cal of liver glycogen and 480 Cal of muscle glycogen. What does that tell you about the purpose of glycogen in the body? Know the "simple" breakdown of glycogen – glycogen phosphorylase followed by the 2 activities of debranching enzyme, and phosphoglucomutase. In the liver at least some of the G6P produced will react with G6Pase (Fig 15-28). G6Pase is confined to the liver (and kidney) and also to the lumen of the ER. Lack of G6Pase causes von Gierke's disease, or Type I Glycogen Storage Disease (Box 15-4). Like many reactions of hexose sugars, glycogen synthesis requires UDP Glucose. Understand how G1P reacts to form UDP-Glu (Fig 15-29). Glycogen synthesis is catalyzed by glycogen synthase (Fig 15-30) followed by remodeling using branching enzyme (Fig 15-31). Every glycogen molecule has a molecule of glycogenin at its reducing end (601).

15.5 Coordinated Regulation of Glycogen Synthesis and Breakdown. Know the details of the Glycogen Breakdown Cascade (Fig 15-35). Chapter 12 has the initial events (Fig 12-4 p. 424). cAMP triggers activity of protein kinase A (see handout). Compare cartoons of glycogen phosphorylase a and b (Fig 15-34) to "Pima Paradox" handout online. Know PPI – we will do a "skimpy" treatment of insulin action.