Study Guide – Lehninger Principles 4th Edition

Chapter Eighteen

By Frank Deis

Homework: 1,3,4,6,8,10,11,14,15. **Introduction.** The amount of amino acid catabolism varies widely from species to species. Amino acids have to be broken down after 1) normal protein turnover, 2) a high protein meal or 3) in diabetes or starvation when the carbon is used for gluconeogenesis.

18.1 **Metabolic Fates of Amino Groups**. Amino acid catabolism involves removing nitrogen from the carbon chains, and then metabolizing the carbon. *Glutamate* and *glutamine* play an important role in this removal (Fig. 18-2). The removed nitrogen is simply excreted in *ammonotelic* organisms, and is excreted as a solid in *uricotelic* organisms. We are *ureotelic* and thus make urea. *Pyridoxal phosphate* (PLP) is very important in nitrogen metabolism, and you should be able to draw it (as in class) and understand mechanisms. See Fig 18-6 and online handout. In general most amino acids can transaminate, giving their nitrogens to α-KG and becoming α-keto-acids (Fig 18-4) with PLP as cofactor. Then glutamate DH can oxidatively remove the NH_3 (Fig 18-7). Thus α-KG can carry one nitrogen (as Glu) or two nitrogens (as GlN) (Fig 18-8). Know the reactions of *glutamine synthetase* and *L-glutaminase*. Why does the body respond to *metabolic acidosis* (low level *ketosis*) with enhanced glutamine metabolism? (p. 663) Know the enzymes in Box 18-1 (mentioned in *"Supersize Me"*). Know the *glucose-alanine cycle* (Fig 18-9). Know that ammonia is toxic (p. 665).

18.2 **Nitrogen Excretion and the Urea Cycle**. Know everything about the Urea Cycle, including structures, enzymes, and cofactors. Know how *carbamoyl phosphate* is produced. Understand the *"bicycle"* that links the urea cycle to the citric acid cycle (Fig 18-12). Know the reactions of *N-acetyl-glutamate synthetase* and that the product, N-acetyl glutamate, stimulates *CPS-I* (Fig 18-13). Understand that the *"urea bicycle"* reduces the overall cost of urea synthesis from 4 ~P to 1.5 ~P (p. 669). Know the "ten" *essential amino acids* taught in class (refer to Table 18-1) and know the treatments for urea cycle deficiencies (p. 670).

18.3 **Pathways of Amino Acid Degradation**. Understand the concept of *glucogenic* and *ketogenic* amino acids (Fig 18-15). All amino acids with 6 or more contiguous carbons are at least partly ketogenic. *One carbon metabolism* (672-677) is extremely important and should be studied carefully. Be able to recognize *THF* structures, see Fig 18-17 and online handouts. Know structure and synthesis of *SAM* (Fig 18-18). Homocysteine is bad (not in book). Be able to draw *biotin* and know that *B-12* or *cobalamin* is also a "one carbon cofactor." **Pyruvate Family**: Know the lower four enzymes in Fig 18-19. **Acetyl CoA Family**: Know the first reaction in Fig 18-23 and the online handout about *epinephrine synthesis(860)*. Understand *PKU* and *mixed function oxidases* (679-680). **α-Ketoglutarate Family**: Know reactions in Fig 18-26 except His pathway. **Succinyl CoA Family**: Know how Thr and homocysteine go to Succinyl CoA. **Branched Chain Family**: Understand that these are metabolized in muscle, adipose, etc. by enzymes that resemble fatty acid beta oxidation enzymes. Lack of DH Complex leads to *Maple Syrup Urine Disease*. Read *Box 18-2*. Know AsN and Asp go to OAA.