

Study Guide – Lehninger Principles 5th Edition

Chapter Twenty two

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Homework: 4,7,8,9,13,16,17. **Introduction.** We will skip much of this chapter but two long pathways are covered, *Purine de novo* (884) and *Pyrimidine de novo* (886). There are **three** main ways in which **ammonia** nitrogen is incorporated into organic compounds. 1) *Glutamate DH* (reductive), 2) *Carbamoyl Phosphate Synthetase I* (not II), and 3) *Glutamine Synthetase*. The first two were described in Chapter 18, but the third will be discussed below. Then, once the nitrogen is attached, there are **three** major modes of nitrogen **transfer**: 1) *Transamination*, 2) *Aspartate donation*, and 3) *Glutamine donation*. Again, the first two were described in Ch. 18 but the third will be discussed here.

22.1 Overview of Nitrogen Metabolism. We won't be concerned with nitrogen fixation (834-6). *NOTE Box 22-1 is wonderful but not in the 4th ed.* The fact that *Glutamate DH* is reversible provides a ready pathway for incorporation of cellular NH_3 into amino acids. *Glutamine synthetase* allows a second NH_3 to be taken up. The reaction is simple but the allosteric feedback is rather complex in *E. coli* (Fig 22-6). Don't worry about covalent modification of Gln Syn. (Fig 22-7) but do know the allosteric inhibitors. Once formed, glutamine serves as a ready donor of its R group nitrogen via *glutamine amidotransferase* enzymes. You don't need to know the proposed mechanism of glutamine donation (Fig. 22-8).

22.2 Biosynthesis of Amino Acids. Students find this material intimidating. We are omitting most of it but retaining a few useful pathways. You should know the synthesis of *proline* (Fig 22-10), the synthesis of *ser/gly* (Fig 22-12), And know the conversion of ser to *cys* via *cystathionine* (Fig 22-14).

22.3 Molecules Derived from Amino Acids. Know that glycine is the starting material for *heme group* synthesis (but not the pathway) and know that *bilirubin* is a linear *tetrapyrrole*, and be able to sketch the structure (Fig. 22-25). Understand Box 22-2, about the disease *porphyria*. Know the pathway to *epinephrine*, mentioned already in Chapter 18 (Fig 22-29).

22.4 Biosynthesis and Degradation of Nucleotides. Start by learning the purine map (Fig 22-32). Then if you add in the sequence the *de novo* pathway is not difficult to master (Fig 22-23). Learn this "chant" – "N, Glycine, Formyl – N, cyclize, carboxyl – N, cleave, Formyl – Cyclize, N, cleave." The phrase "N, cleave" represents aspartate donation, whereas a simple "N" represents glutamine donation. The "chant" gets you all the way to AMP. Understand the branching pathway and mutual regulation between AMP and GMP (Fig 22-34 and Fig 22-35). Also learn the *de novo* pathway for pyrimidines (Fig 22-36). Nucleotide reactions are specific for mono, di, or triphosphates. Conversion to 2'-deoxy occurs at the diphosphate level. The enzyme is *ribonucleotide reductase* or "RNR" (888-890). This ancient enzyme proves that protein came before DNA. Know the *thymidylate synthase* reaction (Fig 22-44 & Fig 22-49), $\text{dUMP} \rightarrow \text{dTMP}$. Understand the *purine salvage pathway* and *gout* (893-4).