Digestion and absorption of proteins

Most of nitrogen in the diet is consumed in the form of protein, Proteins are too large to be absorbed by the intestine. (Note: An example for an exception to this rule is that newborns can take up maternal antibodies in breast milk) They must, therefore, be hydrolyzed to yield their constituent amino acids, which can be absorbed. Proteolytic enzymes responsible for degradation proteins are produced by three different organs: the stomach, the pancreas, and the small intestine.

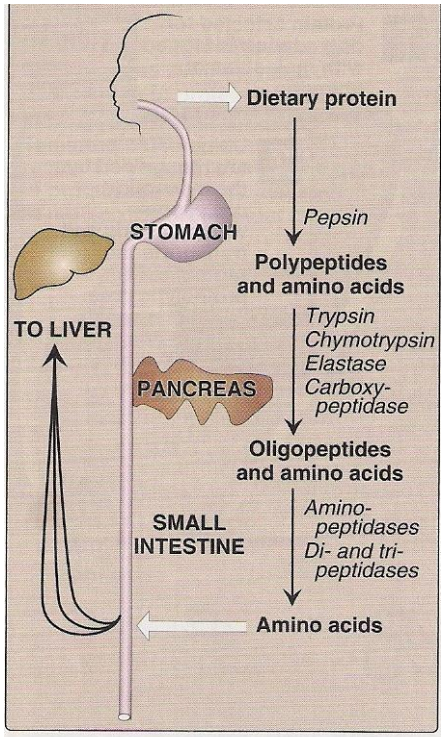

Figure 19.4
Digestion of dietary proteins by the proteolytic enzymes of the gastro-intestinal tract.

*A/ Digestion of proteins by gastric secretion

The digestion of proteins begins in the stomach, which secretes gastric juice, a unique solution containing hydrochloric acid and the proenzyme, pepsinogen.

1/ Hydrochloric acid: stomach acid is too dilute (pH 2-3) to hydrolyze proteins. The acid functions instead to kill some bacteria and to denature proteins, thus making the more susceptible to subsequent hydrolysis by proteases.

2/ Pepsin: This acid stable endopeptidase is secreted by serous cells of the stomach as an inactive proenzyme, pepsinogen. In general proenzymes contain extra amino acids in their sequences, which prevent them from being catalytically active. (Note: removal of these amino acids permits the proper folding required for an active enzyme.) Pepsinogen is activated to pepsin, either by HCL, or autocatalytically by other pepsin molecules that have already been activated. Pepsin releases peptides and a few free amino acids from dietary proteins.

*B/ Digestion of proteins by pancreatic enzymes

On entering the small intestine, large polypeptides produced in the stomach by the action of pepsin are further cleaved to oligopeptides and amino acids by a group of pancreatic proteases.

1/ specificity: Each of these enzymes has a different specificity for the amino acid R-groups adjacent to the susceptible peptide bond. For example, trypsin cleaves only when the carbonyl group of the peptide bond is contributed by arginine or lysine. These enzymes, like pepsin, are synthesized and secreted as inactive proenzymes.

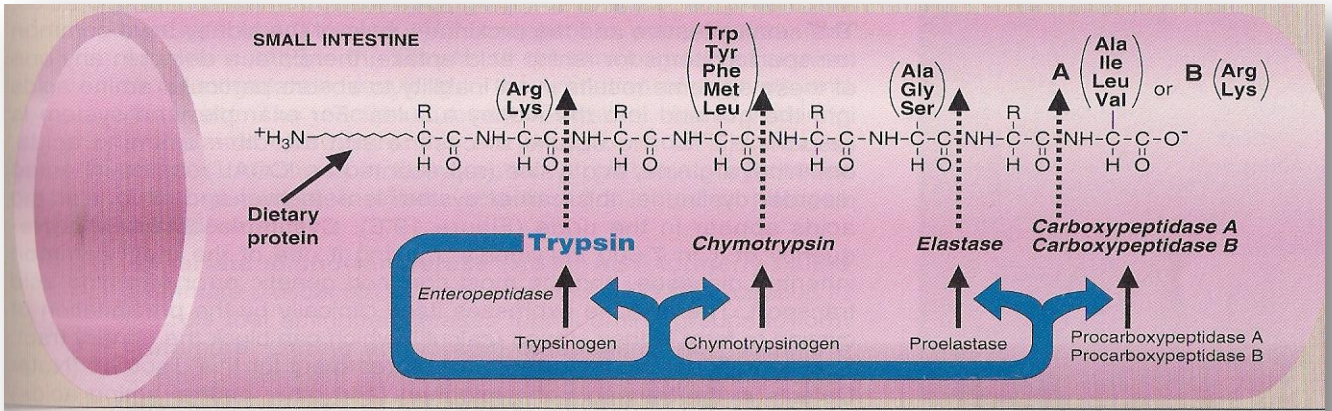

Figure 19.5
Cleavage of dietary protein by proteases from the pancreas. The peptide bonds susceptible to hydrolysis are shown for each of the five major pancreatic proteases. [Note: *Enteropeptidase* is synthesized in the intestine.]

2/ Release of proenzymes: The release and activation of the pancreatic proenzymes is mediated by the secretion of cholecystokinin and secretin, tow polypeptide hormones of the digestive tract.

3/ Activation of proenzymes (zymogens): Enteropeptidase (formerly called enterokinase) an enzyme synthesized by and present on the luminal surface of intestinal mucosal cells of the brush border membrane converts the pancreatic zymogen trypsinogen to trypsin by removal of a hexapeptide from the NH2 terminus of trypsinogen. Trypsin subsequently converts other trypsinogen molecules to trypsin by cleaving a limited number of specific peptide bonds in the zymogen. Enteropeptidase, thus unleashes a cascade of proteolytic activity, because trypsin is the common activator of all pancreatic zymogenes.

4/ Abnormalities in protein digestion: In the individuals with a deficiency in pancreatic secretion (for example, due to chronic pancreatitis, cystic fibrosis, or surgical removal of the pancreas), the digestion and absorption of fat and protein is incomplete. This results in abnormal appearance of lipids (called steatorrhea) and undigested protein in the feces.

C/ Digestion of oligopeptides by enzymes of the small intestine

The luminal surface of the intestine contains aminopeptidase that repeatedly cleaves the N-terminal residue from oligopeptides to produce free amino acids and smaller peptides.

D/ Absorption of amino acids and dipeptides

Free amino acids are taken into the enterocytes up by a Na^+ linked secondary transport system. Di and tripeptides, however are taken up by a H^+ linked transport system. There the peptides are hydrolyzed in the cytosol to amino acids before being released into the portal system. Thus only free amino acids are found in the portal vein after a meal containing protein. These amino acids are either metabolized by the liver or released into the general circulation.

Transport of amino acids into the cells

The concentration of free amino acids in the extracellular fluids is significantly lower than that within the cells of the body. At least seven different transport systems are known that have overlapping specificities for different amino acids. The small intestine and the proximal tubule of the kidney have common transport systems for amino acids uptake; therefore, a defect in any one of these systems results in an inability to absorb particular amino acids into the gut and into the kidney tubules. For example, one system is responsible for the uptake of cystine and dibasic amino acids, ornithine, arginine, lysine, and (represented as COAL). In the inherited disorder cystinuria, this carrier system is defective, and all four amino acids appear in the urine. The disease expresses itself clinically by the precipitation of cystine to form kidney stone (calculi), which can block the urinary tract. Oral hydration is an important part of treatment of this disorder.

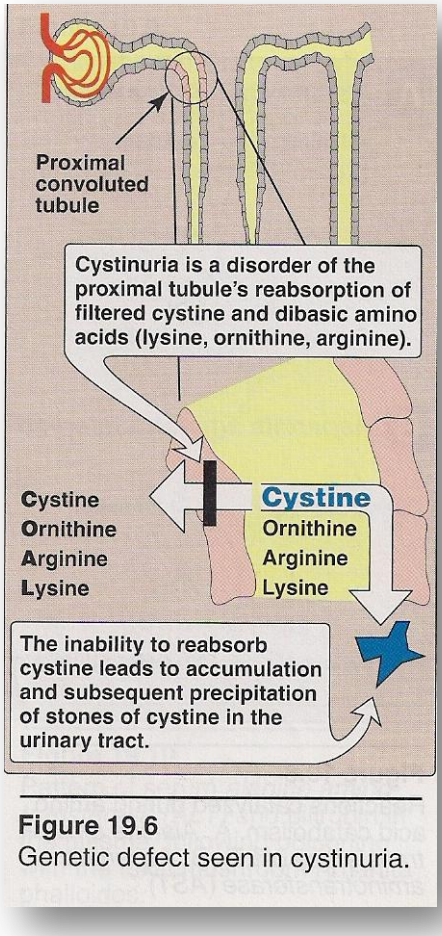

Figure 19.6
Genetic defect seen in cystinuria.