PROTEIN METHABOLISM

Unlike fats and carbohydrates, amino acids are not stored by the body. Therefore, amino acids must be obtained from the diet, synthesized *de novo*, or produced from normal protein degradation. Any amino acids in excess of the biosynthetic needs of the cell are rapidly degraded.

The first phase of catabolism involves the removal of the α-amino groups (usually by transamination and subsequent oxidative deamination), forming ammonia and the corresponding α-keto acid—the "carbon skeletons" of amino acids. A portion of the free ammonia is excreted in the urine, but most is used in the synthesis of urea.

In the second phase of amino acid catabolism the carbon skeletons of the α-ketoacids are converted to common intermediates of metabolic pathways. These compounds can be metabolized to CO_2 and water, glucose, fatty acids, or ketone bodies by the general pathways of metabolism described in the beginning of this lecture.

The amino acid pool is supplied by three sources:

1) amino acids provided by the degradation of body proteins,

2) amino acids derived from dietary protein, and

3) synthesis of nonessential amino acids from simple intermediates of metabolism

Conversely, the amino acid pool is depleted by three routes:

1) synthesis of body protein,

2) amino acids consumed as precursors of essential nitrogen-containing small molecules,

3) conversion of amino acids to glucose, glycogen, fatty acids, ketone bodies, or $CO_2 + H_2O$.

But the amino acid pool is small, about 90–100 g of amino acids, while the protein in the body is about 12 kg in a 70-kg man. When the amino acid pool is in a steady state, the individual is said to be in nitrogen balance. In healthy adults, the

total amount of protein in the body remains constant, because the rate of protein synthesis is sufficient to replace the protein that is degraded. This process, called protein turnover, leads to the hydrolysis and resynthesis of 300–400 g of body protein each day.

DIGESTION OF PROTEINS

Dietary protein makes up approximately 70–100 g/day. These proteins must be hydrolyzed to yield di- and tripeptides as well as individual amino acids, which can be absorbed. Proteins are digested by proteolytic enzymes.

The **digestion of proteins begins in the stomach**, which secretes gastric juice containing hydrochloric acid and the proenzyme, pepsinogen. This endopeptidase is secreted by the chief cells of the stomach as an inactive proenzyme, pepsinogen. Pepsinogen is activated to pepsin, either by HCl, or autocatalytically by other pepsin molecules that have already been activated. Pepsin releases peptides called peptones and albumoses, and a few free amino acids from dietary proteins.

Digestion of proteins by pancreatic enzymes

The release of the pancreatic zymogens is mediated by the secretion of *cholecystokinin and secretin*, two polypeptide hormones of the digestive tract. Trypsin, chymotrypsin, elastase, carboxypeptidases, aminopeptidases are secreted from pancreas in the form of zymogens. Enteropeptidase (formerly called enterokinase) synthesized by the luminal surface of intestinal mucosal cells converts trypsinogen to trypsin by removal of a hexapeptide from the N-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 activation, because trypsin is the common activator of all rest pancreatic zymogens.

Trypsin cleaves in peptides carbonyl group formed by *arginine or lysine*.

Chymotrypsinogen breaks the bonds formed by the carboxy groups of *aromatic amino acids*, methionine and leucine.

Elastase breaks the bonds formed by the carboxyl groups of glycine, alanine and serine.

The luminal surface of the intestine contains exopeptidases: aminopeptidases and carboxypeptidases.

Each carboxypeptidase contain one zinc atom.

Carboxypeptidase B cleaves arginine and lysine from the C-end. Carboxypeptidase A cleaves from the C-terminus all amino acids except arginine, lysine, proline and hydroxyproline. Aminopeptidases repeatedly cleaves the N-terminal residue from oligopeptides to produce smaller peptides and free amino acids.

There are also dipeptidases and tripeptidases of intestinal juice, e.g. prolinease, prolidase, glycyl-glycine dipeptidase.

Normally most amino acids are absorbed in the small intestine and enter blood, however some of them post-digest to the large intestine. Fermentation and decay of amino acids takes place here. The conversion of amino acids to acetate, lactate and butyrate is called fermentation. Deamination and decarboxylation of amino acids is called decay. Rotting produces CO_2, ammonia, methane, indole, scatol. During decarboxylation are formed ptomains namely cadaveric poisons. During decarboxylation, lysine is converted into cadaverine, tyrosine - to tyramine, histidine - to histamine. Normally, these compounds are not absorbed through the intestinal wall. However, when inflamed, colitis, cholera appears, their absorption is accelerated. The part of the ptomaines absorbed in the intestine with the portal vein, enters the liver and is neutralized there.

Tyrosine both by decarboxylation and deamination is converted to cresol and phenol. Tryptophan in both ways is converted to scatol and indole. Sulphur-containing amino acids turn into mercaptans.

TRANSPORT OF AMINO ACIDS INTO CELLS

Free amino acids are taken into the enterocytes by a Na^+-linked secondary transport system of the apical membrane. 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.
Branched-chain amino acids are important examples of amino acids that are not metaboized by the liver, but instead are sent from the liver primarily to muscle via the blood.

In Hartnup disorder defects in the transport of tryptophan, when absorption and reabsorption are failed.This can result pellagra-like dermatologic and neurologic symptoms.