Ingestion, Digestion & Absorption of Dietary Proteins

Specific Learning Objectives

- Describe importance of dietary protein quality in maintenance of health, and consequences of protein-energy malnutrition (e.g. Marasmus and Kwashiorkor)
- Describe role of gastric hormone gastrin and paracrine hormone histamine in promoting secretion of HCl and pepsinogen, and activation of pepsinogen to pepsin.
- Describe pepsin action in digestion of peptides
- Describe roles of secretin, bicarbonate and cholecystokinin in neutralization of duodenal pH, and release of bile and pancreatic zymogens
- Describe activation of pancreatic zymogens and roles of active enzymes in protein digestion.
- Ingestion of Dietary Proteins
- Describe digestion of dietary proteins in stomach, duodenum and small intestine
- Describe uptake of peptides and aa from gastrointestinal tract
- Discuss absorption and transport of aa to liver
- Identify defects in uptake of aa (e.g. Hartnup disease) or peptides that lead to clinical symptoms (failure to thrive, edema, various vitamin deficiencies).

Introduction

Dietary Protein consists of long chains of aa

- In digestive process, enzymes in stomach and small intestine break down complex protein into polypeptides and further into individual aa.

- aa are absorbed through wall of small intestine, pass into blood and further to liver through portal vein.

Ingestion of Dietary Proteins

- Ingested dietary proteins is hydrolysed to aa

- Absorbed from intestine and utilization of these aa for synthesis of body proteins ex. structural proteins, plasma proteins, enzymes, milk proteins, and hormones

- Also synthesis of necessary non-protein nitrogen compounds includes urea, uric acid, creatine, creatinine, aa, and polypeptides

Cont-

- Recommended Dietary allowance (RDA) for both men and women: 0.8 g of protein/kg body weight/day
- Dietary proteins: Dietary proteins in our diet are either from animal source or vegetable source.
- Animal sources: Milk and dairy products, meat, fish and eggs.
- Vegetable sources: Cereals, pulses, peas, beans and nuts

Importance of Dietary Proteins

- For structural component of cells and tissues
- Without adequate protein in diet, body cells and tissues would not be able to function.
- Proteins are large, complex molecules made up of smaller aa compounds.

Cont-

- Some aa are made by body and are nonessential, but others are essential, meaning that we need to get them from diet
- Therefore, consume protein-rich foods each day, since body does not have a way to store amino acids

Cont--

- Essential aa: Cannot be synthesize in body so “essential” to eat them from dietary food.
- Non-essential: Body can synthesize them from other proteins so not essential to eat them

TABLE 27-1 Amino Acid Requirements of Humans

Nutritionally Essential	Nutritionally Nonessential
Arginine[a]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Hydroxyproline[b]
Tryptophan	Hydroxylysine[b]
Valine	Proline
	Serine
	Tyrosine

Table 27.1. Harper’s Illustrated Biochemistry 30th Edition

Overview of the Digestion of Dietary Proteins

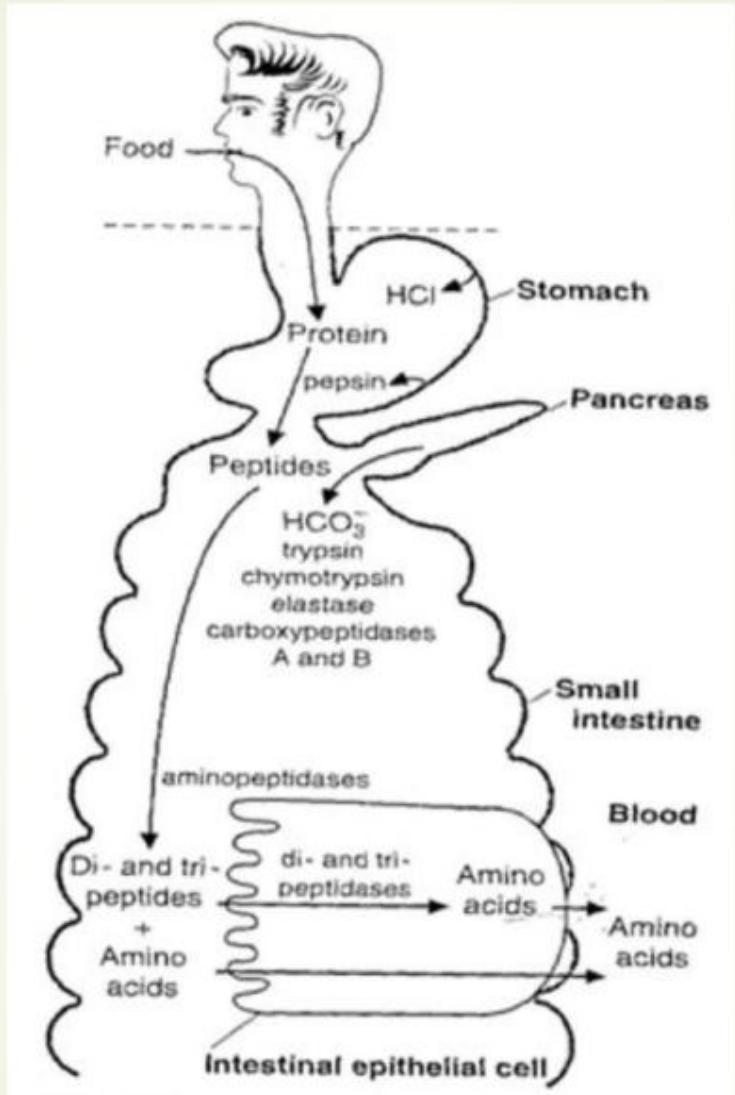


Fig. 37.3. Digestion of proteins. The proteolytic enzymes, pepsin, trypsin, chymotrypsin, elastase, and the carboxypeptidases, are produced as zymogens that are activated by cleavage after they enter the gastrointestinal lumen (see Fig. 37.4). Marks, Marks and Smith, Medical Biochemistry

Digestion of Dietary Proteins

- Proteins are too large to be absorbed by intestine, therefore, must be hydrolysed into di- and tripeptides as well as individual aa, which can be absorbed
- Proteolytic enzymes responsible for degrading proteins are produced by three different organs: stomach, pancreas, and small intestine

Activation of Gastric and Pancreatic zymogens

- Pepsinogen catalyzes its own cleavage at pH of stomach
- Trypsinogen is cleaved by enteropeptidase
- Active form of enzyme trypsin plays a key role by catalysing cleavage of other pancreatic zymogens

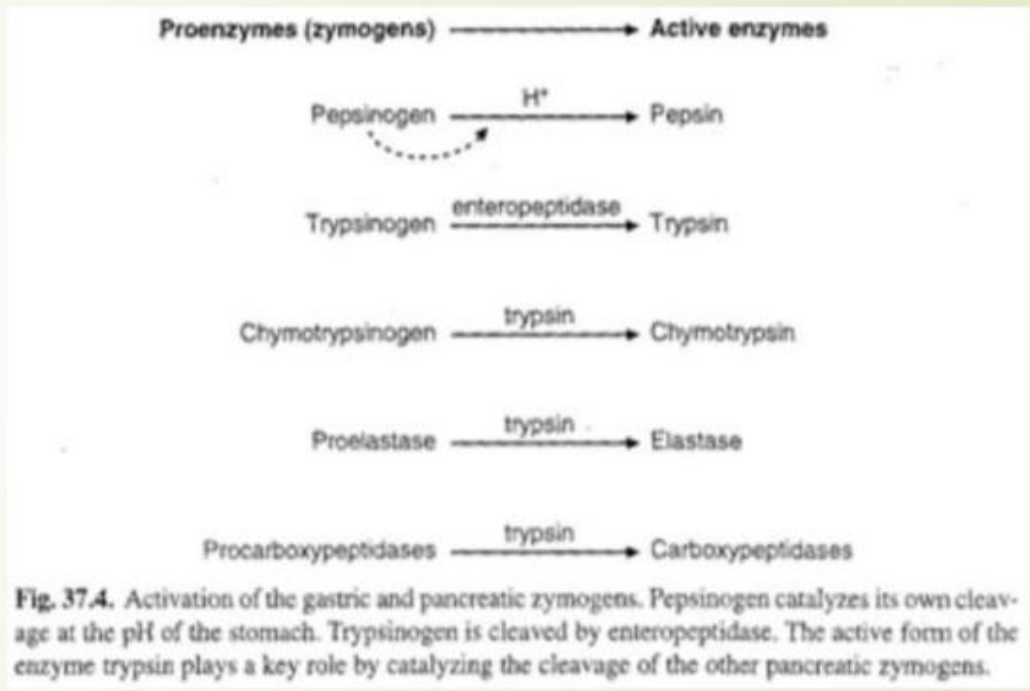


Fig. 37.4. Activation of the gastric and pancreatic zymogens. Pepsinogen catalyzes its own cleavage at the pH of the stomach. Trypsinogen is cleaved by enteropeptidase. The active form of the enzyme trypsin plays a key role by catalyzing the cleavage of the other pancreatic zymogens.

Marks, Marks and Smith, Medical Biochemistry

Cont--

Digestion by gastric secretion: Digestion of proteins begins in stomach, which secretes gastric juice, contains hydrochloric acid (HCl) and proteolytic enzyme

- Pepsin is a potent proteolytic enzyme and is present in gastric juices.
- It is secreted as inactive zymogen form, pepsinogen.

Cont--

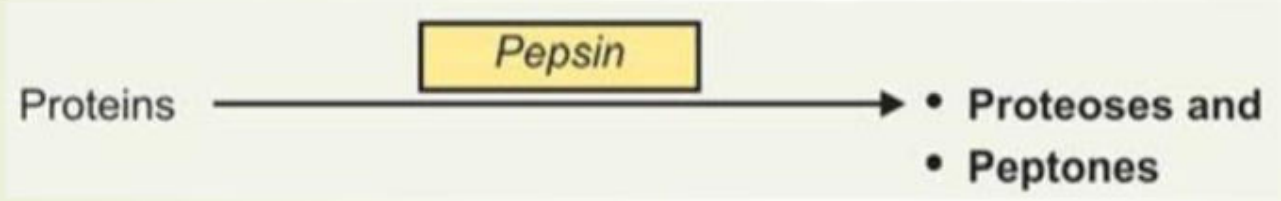
- It is synthesised in “chief cells” of stomach
- HCl maintains gastric pH at about 1 to 2 and ensures maximum pepsin activity.
- Optimum pH for pepsin is 1.6 to 2.5 and pepsin gets denatured if pH is greater than 5.

Cont--

- Pepsinogen is hydrolysed in stomach with help of HCl or pepsin itself (autocatalytically) to form “active” pepsin
- In process of activation (i) inactive peptide called as “pepsin inhibitor and (ii) 5 smaller peptides (inactive) are liberated.

Cont--

- Pepsin is a proteinase, a non-specific endopeptidase, and it hydrolyses peptide bonds well inside protein molecule and produces proteoses and peptones



- It is particularly active on a peptide bond, which connects -COOH group of an aromatic aa like Phe, Tyr, and Tryp with amino group of either a dicarboxylic acid or an aromatic a.a

Cont--

- Pepsin also hydrolyse peptide bonds of:
  - COOH group of methionine and leucine
  - Leucine and glutamic acid
  - Glutamic acid and asparagine
  - Leucine and valine
  - Valine and cysteine

- Pepsin cannot act on proteins like keratins, Silkfibroins, mucoproteins, mucoids and protamines

Digestion by pancreatic secretion

- Optimum pH for activity of pancreatic enzymes (pH 8) provided by alkaline bile and pancreatic juice
- Secretion of pancreatic juice is stimulated by peptide hormones, Cholecystokinin

Cont--

- On entering small intestine, large polypeptides produced in stomach by action of pepsin are cleaved to oligopeptides and aa by a group of pancreatic proteases
- Includes both endopeptidases (Trypsin, Chymotrypsin, Elastase) and exopeptidases (metalloenzyme, contains zinc).

Digestion by proteolytic enzymes in intestinal juice

Amino-peptidases: Luminal surface of intestinal epithelial cells contains aminopeptidase, an exopeptidase that repeatedly cleaves N-terminal residue from oligopeptides to produce even smaller peptides and free aa.

- Requires presence of Zn++, Mn++ and Mg++ which help in formation of a metal-enz-substrate coordination complex for catalysis

Cont--

- Hydrolyse a terminal peptide bond connected to an end a.a bearing a free-α NH2 group, splits off end a.a. from N-terminal end of a peptide, changing latter gradually stepwise to a “tripeptide”

Tri and Di-peptidases: hydrolyse peptides at either of two places

- In microvillus membrane of intestinal epithelial cells, or inside epithelial cells after peptides absorbed inside cell

Cont--

- Tri-peptidase acts on a tri-peptide and produces a di-peptide and free a.a
- Di-peptidase hydrolyses a di-peptide to produce two molecules of aa
- They require presence of Mn++, Co++ or Zn++ as cofactors for their activity.

Cleavage of dietary protein in small intestine by pancreatic proteases

- Peptide bonds susceptible to hydrolysis for each of five major pancreatic proteases
- First three are serine endopeptidases, whereas the last two are exopeptidases
- Each is produced from an inactive zymogen

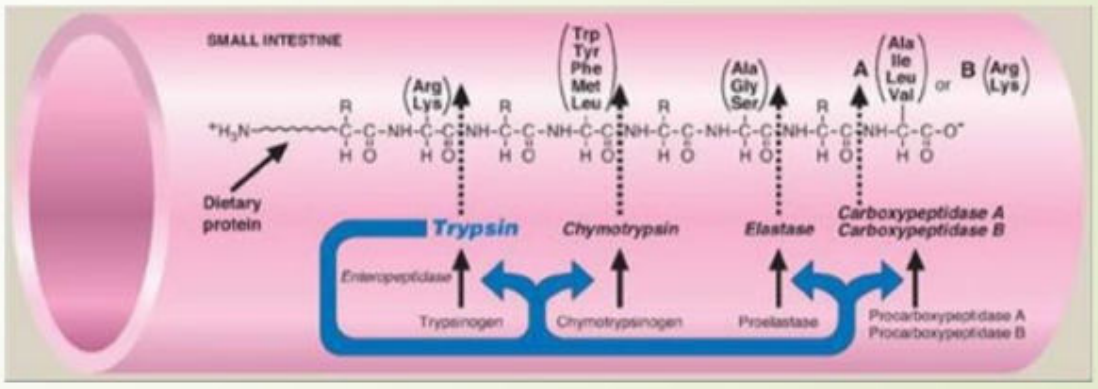


Fig 19.5. Lippincott's Illustrated Reviews, Biochemistry, 6th Ed

Absorption of Amino Acids

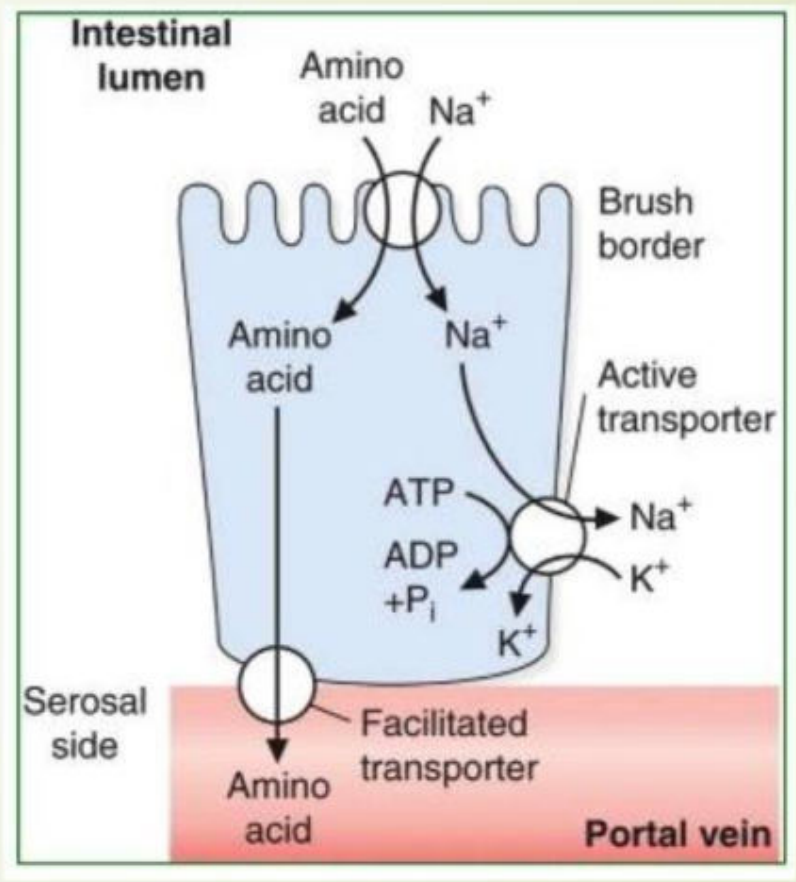
- Free aa are taken into enterocytes by a sodium-linked secondary transport system of apical membrane.
- Di- and tripeptides, are taken up by a proton-linked transport system.
- Peptides are hydrolyzed in cytosol to aa that are released into portal system by facilitated diffusion.

Cont--

- Therefore, only free aa are found in portal vein after a meal containing protein.
- These aa are either metabolized by liver or released into general circulation

Absorption of products of protein digestion by carrier protein transport system

- AA are absorbed into epithelial cells by Na_+-linked secondary transport via symporter
- Various aa are transported by carriers specific for them
- AA exit cell at basal membrane via various passive carriers by facilitated transporter
- AA enter blood by simple diffusion



Marks, Marks and Smith, Medical Biochemistry

Role of Glutathione in Amino Acid Absorption

- Meister proposed that glutathione participates in an active group translocation of L-amino acids (except L-Pro) into cells of small intestine, kidneys, seminal vesicles, and brain.
- He proposed a “cyclic” pathway/γ-glutamyl cycle in which Glutathione is regenerated again
- γ-glutamyl transferases (GGT) plays a key role in this cycle, a pathway for synthesis and degradation of glutathione and drug and xenobiotic detoxification

γ-glutamyl/Meister cycle

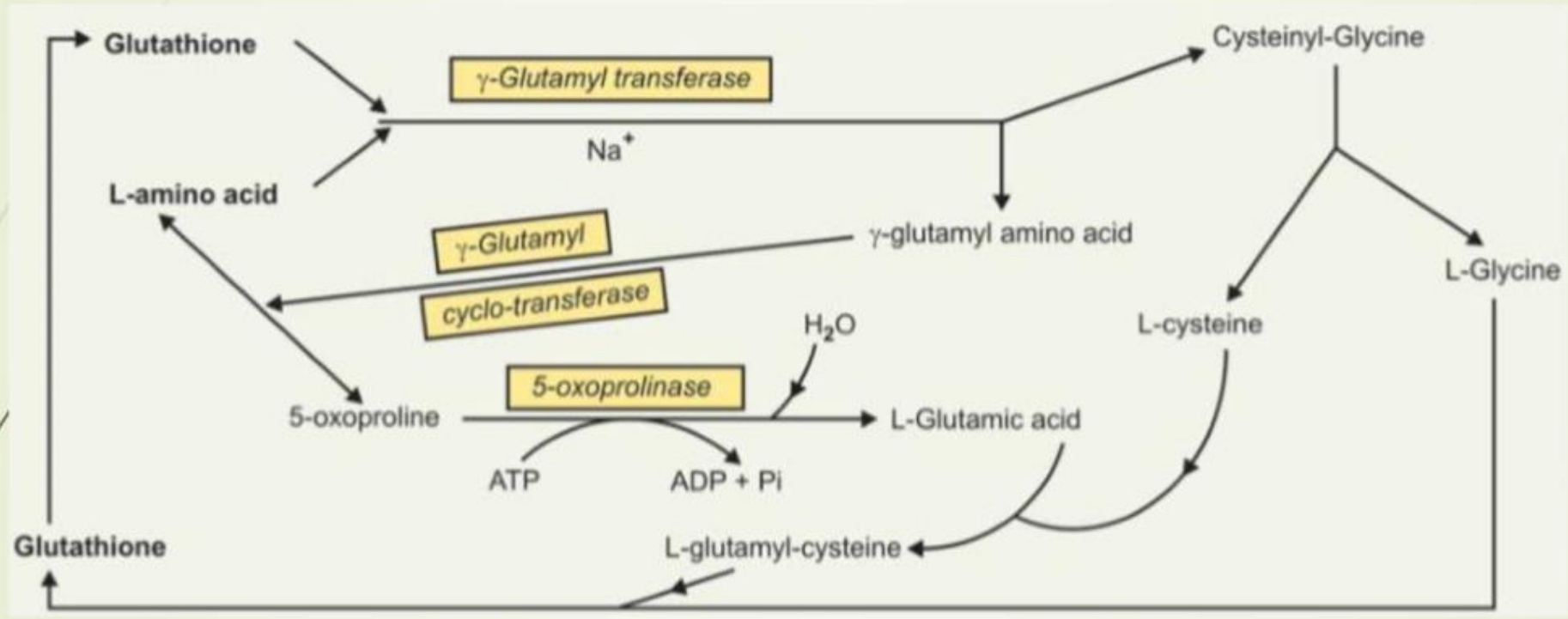


Fig.26.1: Text Book of Medical Biochemistry by Chatterjee & Rana Shinde, 8th Ed

Disorder related to aa transporter

Hartnup disease: Defect in SCL6A19 gene, it is a sodium-dependent and chloride independent neutral aa transporter, expressed in kidneys and intestine

- This gene controls absorption of certain aa from intestine and reabsorption of those aa in kidneys
- Person with Hartnup disease cannot absorb aa properly from intestine and cannot reabsorb them from tubules in kidneys

Cont--

- Resulting excessive amount of aa such as Trp excreted in urine
- Due to inadequate amount of Trp, body not able to make sufficient amount of niacin (vit B3), which is necessary component of NAD^+
- Pellagra, a similar condition, is also caused by low nicotinamide; this disorder results in dermatitis, diarrhea, and dementia

Cont--

- Cystinuria: Dibasic (diamino aa) transporter Lys, Arg, Ornithine and Cys. If there is any defect in this transport system, it leads to Cystinuria
- In medicine, Garrod's tetrad is a term named for British physician Archibald Garrod, who introduced phrase “inborn errors of metabolism" in a lecture in 1908
- Tetrad comprises four inherited metabolic diseases: albinism, alkaptonuria, Cystinuria and pentosuria

Intestinal aa transport systems and their disorders

Transport Systems

Intestinal Amino Acid Transport Systems and Their Disorders	Transport system	Amino acids transported	Inherited defects
	Neutral amino acids (Monoamino, Moncarboxylic)	Ala, Gly, Ser, Thr, Val, Leu, Ile, Phe, Tyr, Trp, Asp, His, Cys, Met, citrulline	Hartnup disease
	Dibasic (diamino) amino acids*	Lys, Arg, ornithine, and cystine	Cystinuria or dibasic aminoaciduria
	Dicarboxylic (acidic) amino acids	Glu, Asp	Dicarboxylic aminoaciduria
	Glycine and imino acids	Gly, Pro, Hyp	Joseph's syndrome (iminoglycinuria)

*There appear to be two distinct pathways for transport of dibasic amino acids. One transports lysine, arginine, ornithine, and cystine, and the other transports lysine, arginine, and ornithine but not cystine. An inherited defect in the former pathway leads to cystinuria with malabsorption of all four amino acids and appearance of all four amino acids in the urine. If the second pathway is affected, dibasic aminoaciduria results, with normal cystine transport.

Clinical-cases discussed

Reference Books

1) Biochemistry, Lippincott's Illustrated Reviews, 6th Ed
2) Harper's Illustrated Biochemistry-30th Ed
3) Lehninger Principles of Biochemistry, 6th Ed
4) Marks, Marks and Smith, Medical Biochemistry
5) Netter's Essential Biochemistry, 1st Ed

Thank you