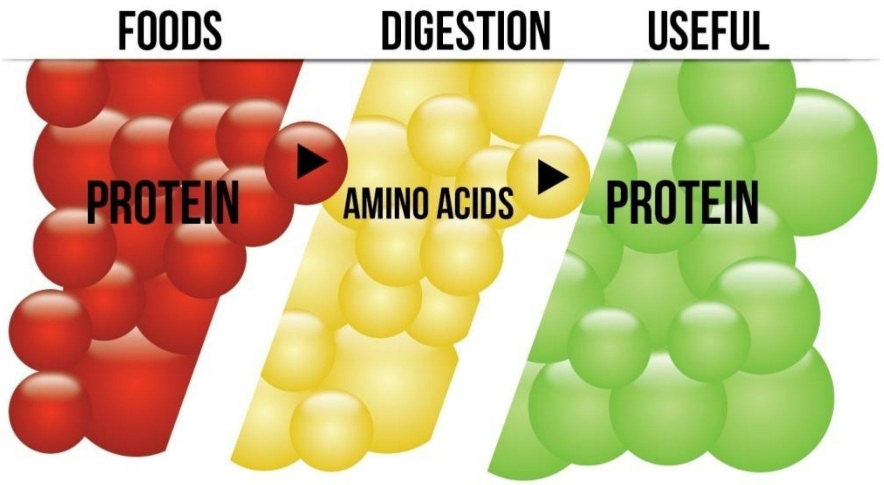
# *METABOLISM OF AMINO ACIDS*

**Lecture I**

# Dynamic state of body proteins

**Dynamic equilibrium between synthesis and breakdown of proteins.**




**Almost all of the body proteins are subject to incessant breakdown and synthesis.**

# Dynamic state of body proteins

**Adults break down 300–400 g of protein per day into amino acids (proteolysis). Approximately the same amount of amino acids is reincorporated into proteins (protein biosynthesis).**

# Dynamic state of body proteins

**This constant process of synthesis and degradation makes it possible for the cells to quickly adjust the quantities of important proteins in order to meet current requirements.**

# Dynamic state of body proteins

**Almost all cells are capable of carrying out biosynthesis of proteins.**

**Some intracellular proteolysis takes place in the lysosomes.**
**In addition, there are protein complexes in the cytoplasm, known as proteasomes, in which incorrectly folded or old proteins are degraded.**

# Dynamic state of body proteins

**The rate of body protein renewal is characterized by the half-life of the protein.**

**The body's high level of protein turnover is due to the fact that many proteins are relatively short-lived (hormones, enzymes).**

**By contrast, structural proteins such as the histones, hemoglobin, and the components of the cytoskeleton are particularly long-lived.**

# Dynamic state of body proteins

**Proteins are constantly being lost via the intestine and, to a lesser extent, via the kidneys.**
**To balance these losses, at least 30 g of protein have to be taken up with food every day.**

# Dynamic state of body proteins

**As it is not possible to store amino acids, up to100 g of excess amino acids per day are used for biosynthesis or degraded in the liver in this situation.**

**The nitrogen from this excess is converted into urea and excreted in the urine. The carbon skeletons are used to synthesize carbohydrates or lipids, or are used to form ATP.**

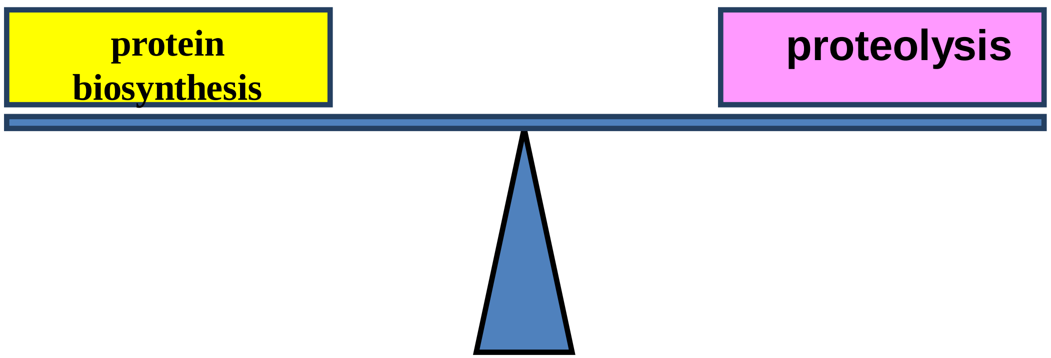
# Nitrogen balance

**Balance between nitrogen ingestion and secretion.**

# Nitrogen balance

## nitrogen equilibrium

**total dietary intake of nitrogen = total nitrogen loss**

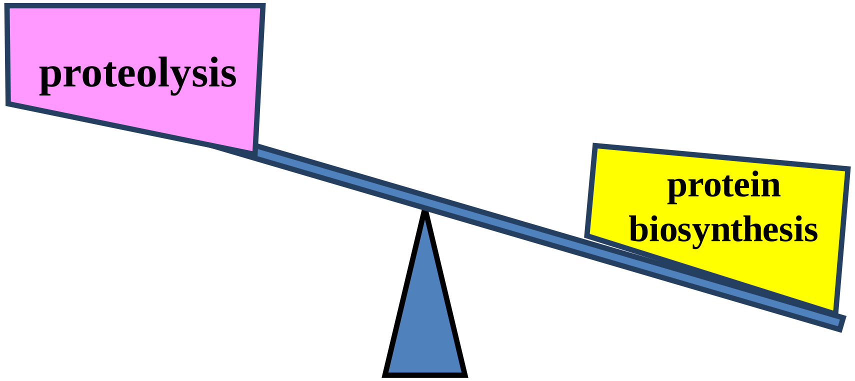



**In this state synthesis of body protein equals degradation.**
**This state takes place in a healthy adult on a balanced diet with the normal daily supply of proteins.**

# Nitrogen balance

## positive nitrogen balance

**total dietary intake of nitrogen > total nitrogen loss**

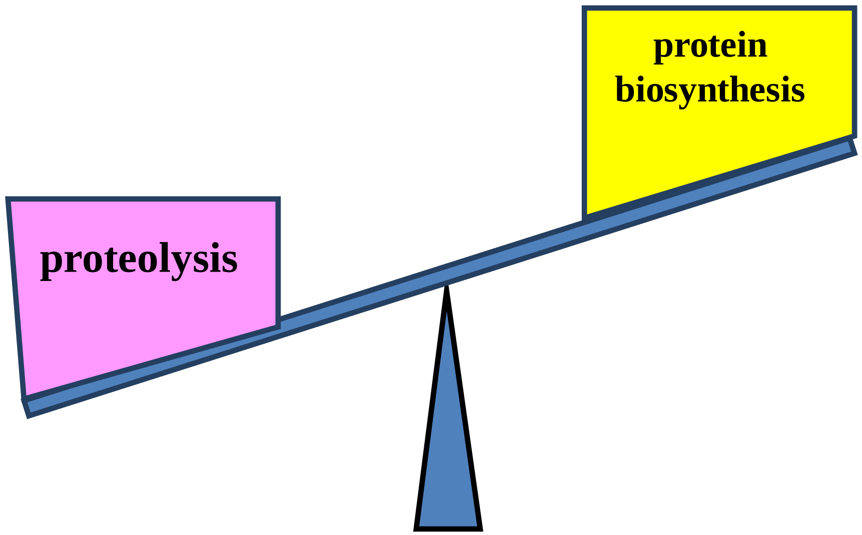



**Such a state takes place in a growing organism, recovering from trauma, pregnancy and lactation**

# Nitrogen balance

**negative nitrogen balance**

**total dietary intake of nitrogen < total nitrogen loss**




**takes place in starvation, protein deficiency, aged persons, grave infectious and chronic diseases, when the intensive breakdown of body proteins is not compensated for protein diet**

# Dietary proteins

**proteins which we take in our diet are either from animal source or vegetable source**

- ***Principal animal sources:***

**milk ,meat, fish, liver, eggs.**

- ***Principal vegetable sources:***

**cereals, pulses, peas, beans and nuts.**

**The minimum daily requirement of protein is 37 g for men and 29 g for women, but the recommended amounts 80-100 g.**
**Requirements in pregnant and breastfeeding women are higher.**


top
meatless
protein sources
neilarey.com
nut butters
8g / 2tbsp
oatmeal
6g / per cup
Greek yogurt
10g / per 100g
eggs
6g / per egg
beans
15g / per serving (180g)
nuts
6g / per handful
cauliflower
5g / per serving (180g)
broccoli
5g / per serving (180g)
seeds
6g / per handful
spinach
5g / per serving (180g)

# Dietary proteins

**Generally, proteins of animal origin are of higher biological value.**

**These proteins are called full-valued proteins because they contain essential amino acids which are not synthesized in the human body**

Nutritionally, amino acids are of two types: **Essential and Non-essential**.

There is also a third group of

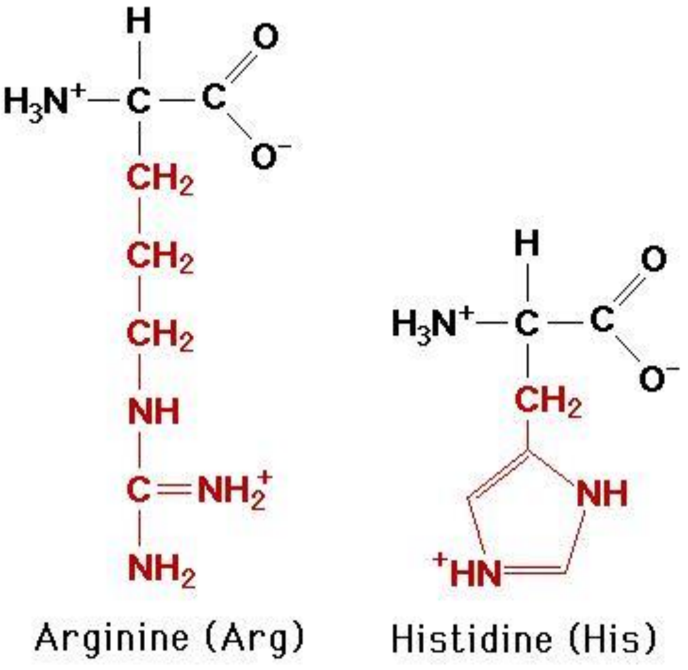
***semi-essential amino acids***

**Essential amino acids** are not synthesised by the body and must be taken in diet.

They include ***valine, leucine, isoleucine, phenylalanine, threonine, tryptophan, methionine and lysine*****.**

**Non-essential amino acids:** can be synthesised by the body and may not be the requisite components of the diet.

# Semi-essential amino acids



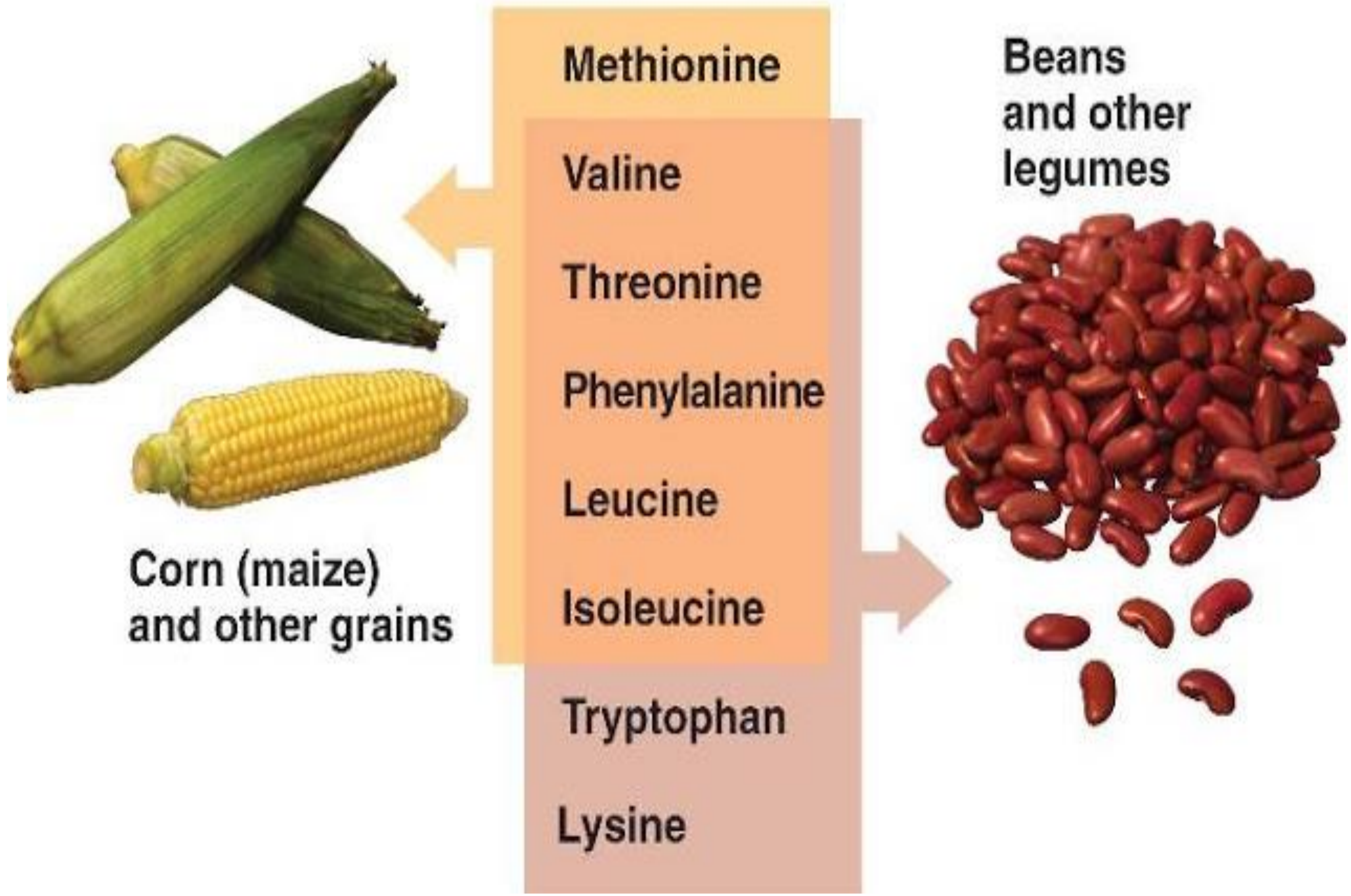

these are ***growth promoting factors*** since they are not synthesised in sufficient quantity during growth. They include ***arginine*** and ***histidine***

They ***become essential in growing children, pregnancy and lactating women.***

| Amino Acid | Main Food Sources |
|---|---|
| Histidine | soy protein, eggs, parmesan, sesame, peanuts |
| Isoleucine | eggs, soy protein & tofu, whitefish, pork, parmesan |
| Leucine | eggs, soy protein, whitefish, parmesan, sesame |
| Lysine | eggs, soy protein, whitefish, parmesan, smelts |
| Methionine | eggs, whitefish, sesame, smelts, soy protein |
| Cysteine | eggs, soy protein, sesame, mustard seeds, peanuts |
| Phenylalanine | eggs, soy protein, peanuts, sesame, whitefish |
| Tyrosine | soy protein, eggs, parmesan, peanuts, sesame |
| Threonine | eggs, soy protein, whitefish, smelts, sesame |
| Tryptophan | soy protein, sesame, eggs, winged beans, chia seeds |
| Valine | eggs, soy protein, parmesan, sesame, beef |


Essential Amino Acid Sources
operationvegan.tumblr.com
Histidine
Fennel
Isoleucine
Seaweed
Isoleucine
Peanuts
Lysine
Papaya
Methionine
Spinach
Cysteine
Oats
Phenylalanine
Sunflower Seeds
Tyrosine
Avocados
Threonine
Lentils
Tryptophan
Soy
Valine
Kidney Beans
All Plant Based!

# Essential amino acids for adults



# DID YOU KNOW?

**100 calories of steak**

**=**

**8.0 grams of protein**

**7.4 grams of fat**

Source: Eat to Live, Dr. Joel Furhman

**100 calories of broccoli**

**=**

**11.1 grams of protein**

**0.4 grams of fat**

**+**

phytochemicals, vitamins and essential nutrients that prevent disease and promote health

# Degradation of proteins

**combinations of several enzymes with different specificities are required for complete degradation of proteins into free amino acids.**

**Proteinases** and **peptidases** are found not only in the GIT, but also inside the cell.

The proteolytic enzymes are classified into **endopeptidases** and **exopeptidases.**

# Proteolytic enzymes are of two types

| Endopeptidase | Exopeptidase |
|---|---|
| Act in the interior of proteins | Act on the periphery of the protein molecule |
| Cleaves internal peptide bonds | Cleaves terminal peptide bonds |
| End product - Small peptides, | End product - free amino acids and dipeptides |
| Eg. Pepsin, Rennin, Trypsin, Chymotrypsin, Elastase | Eg. Carboxypeptidase, Aminopeptidase |

# Degradation of proteins

**The *endopeptidases* or *proteinases* cleave peptide bonds *inside* peptide chains. They "recognize" and bind to short sections of the substrate's sequence, and then hydrolyze bonds between particular amino acid residues.**

**The *exopeptidases* attack peptides from their *termini*.**

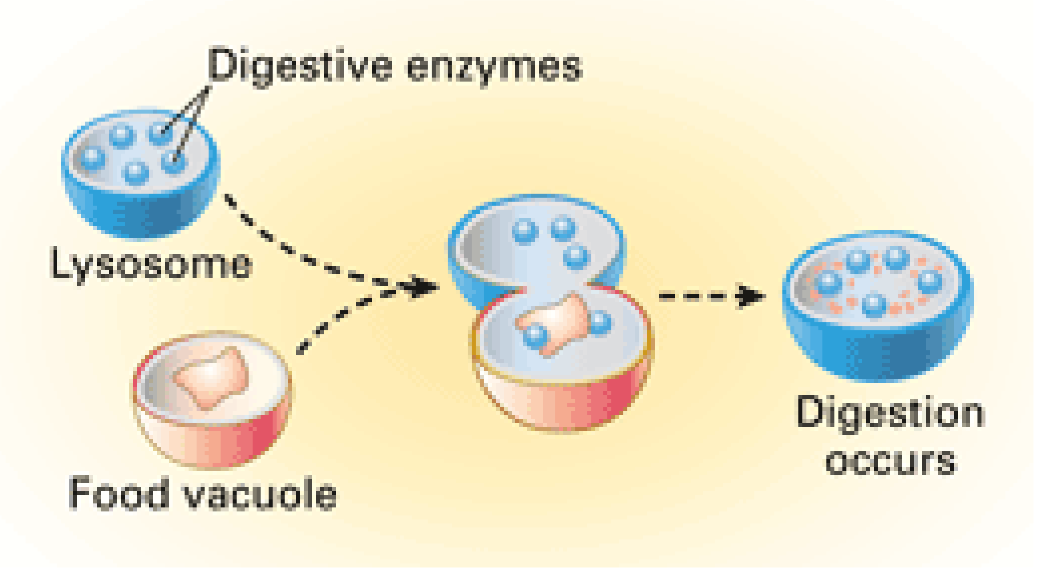
Peptidases that act at the N terminus are known as **aminopeptidases**, while those that recognize the C terminus are called **carboxypeptidases**.

The **dipeptidases** only hydrolyze dipeptides.

# Degradation of proteins

**The functional proteins in the cell have to be protected in order to prevent premature degradation.**

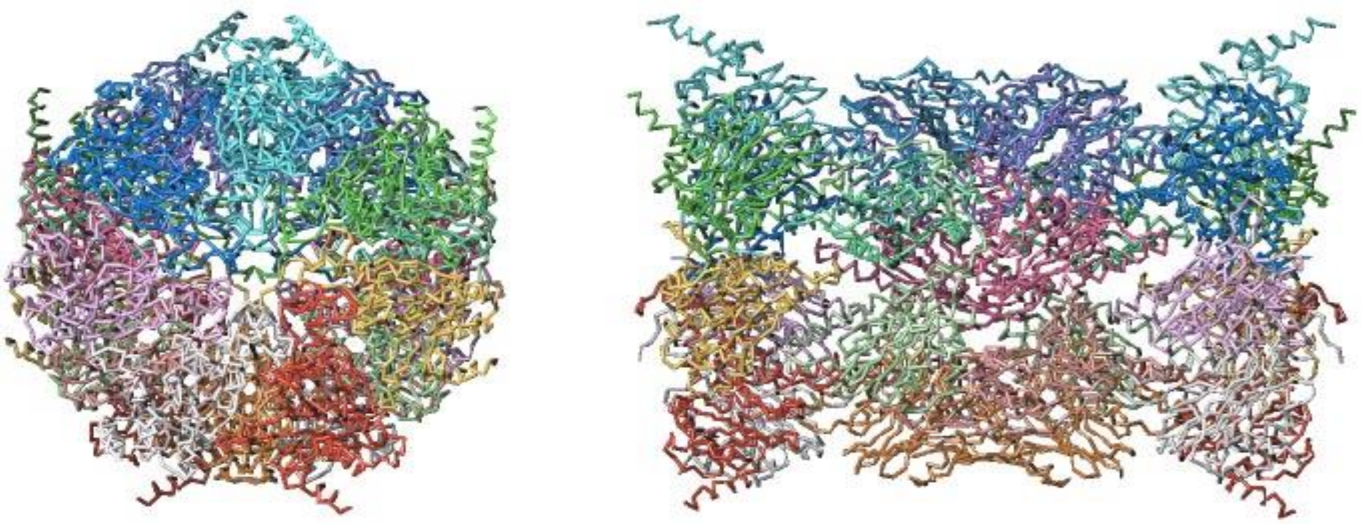
Some of the intracellularly active proteolytic enzymes are therefore enclosed in lysosomes.




The proteinases that act there are also known as **cathepsins**.

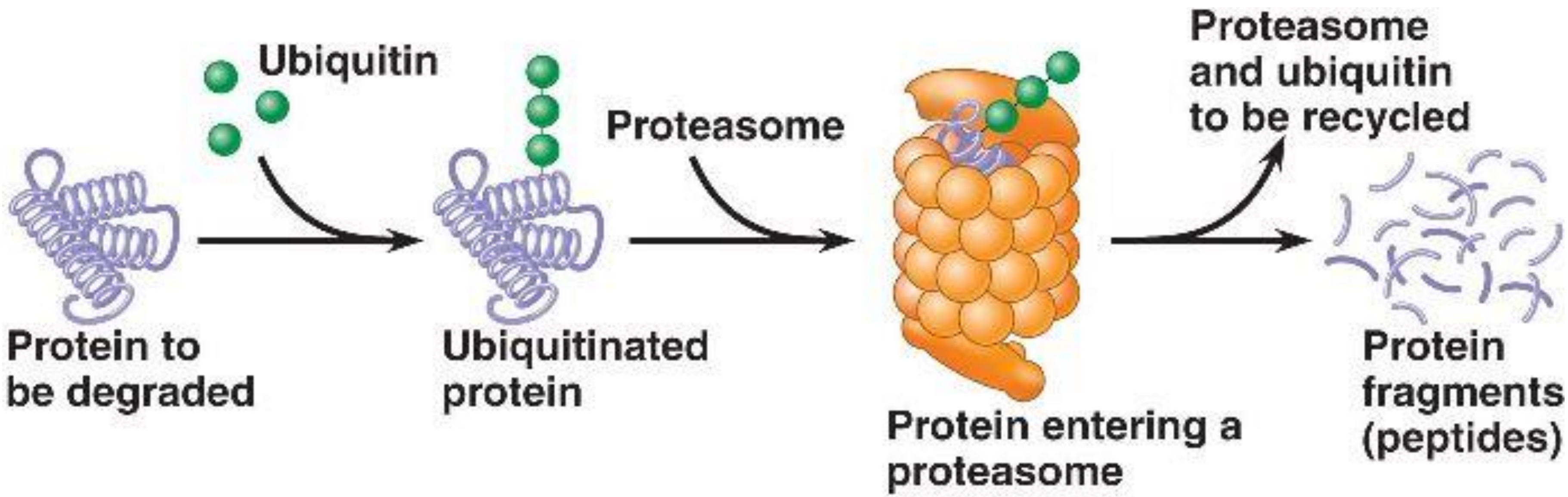
# Degradation of proteins

Another system for protein degradation is located in the cytoplasm. This consists of large protein complexes, the **proteasomes**.



Top view and side view of Cα drawings of the bovine 20S proteasome

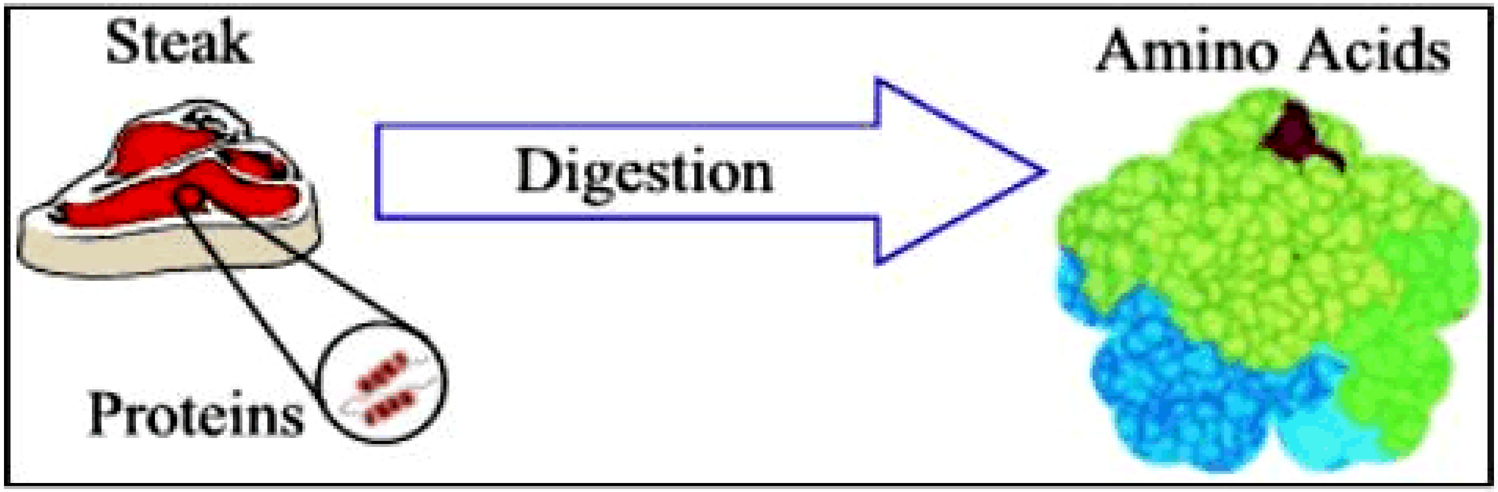
**Proteins destined for degradation in the proteasome are marked by covalent linkage with chains of the small protein ubiquitin**

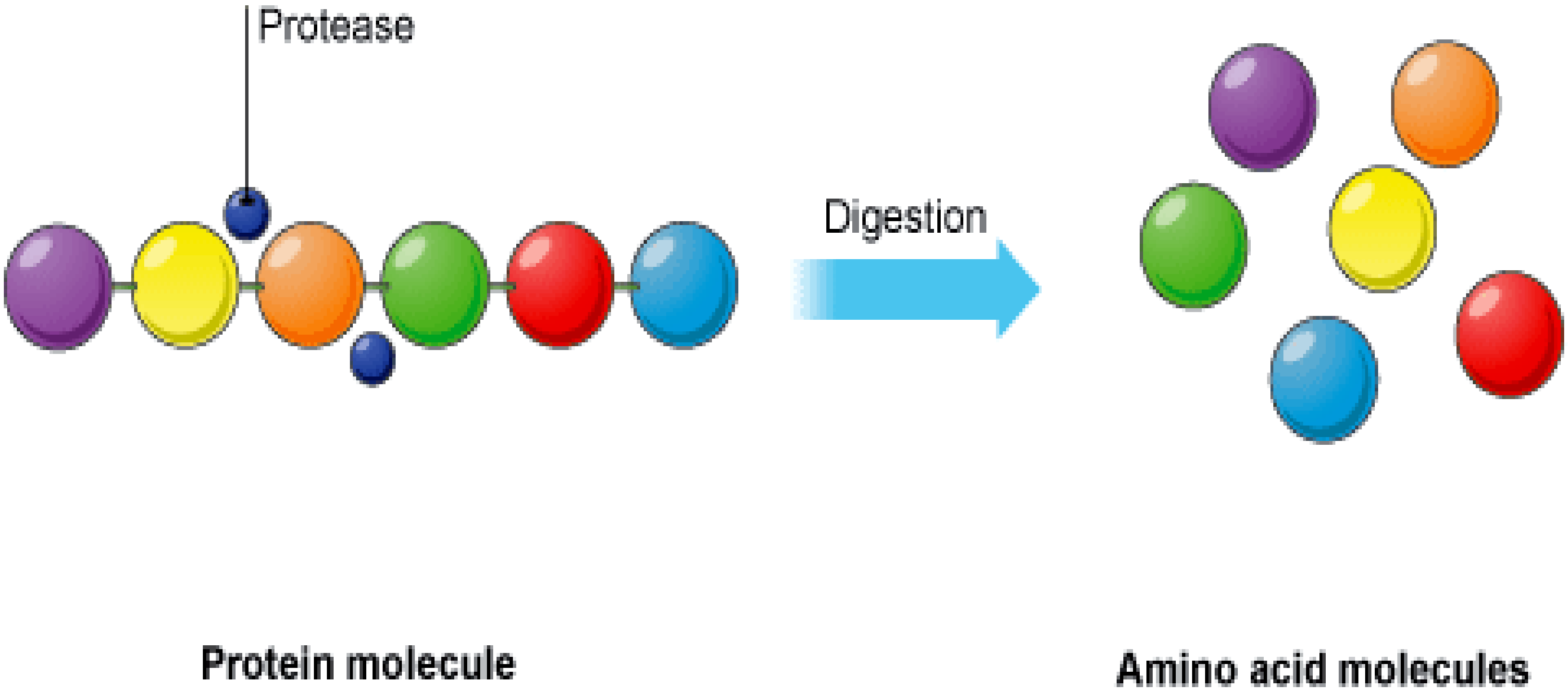


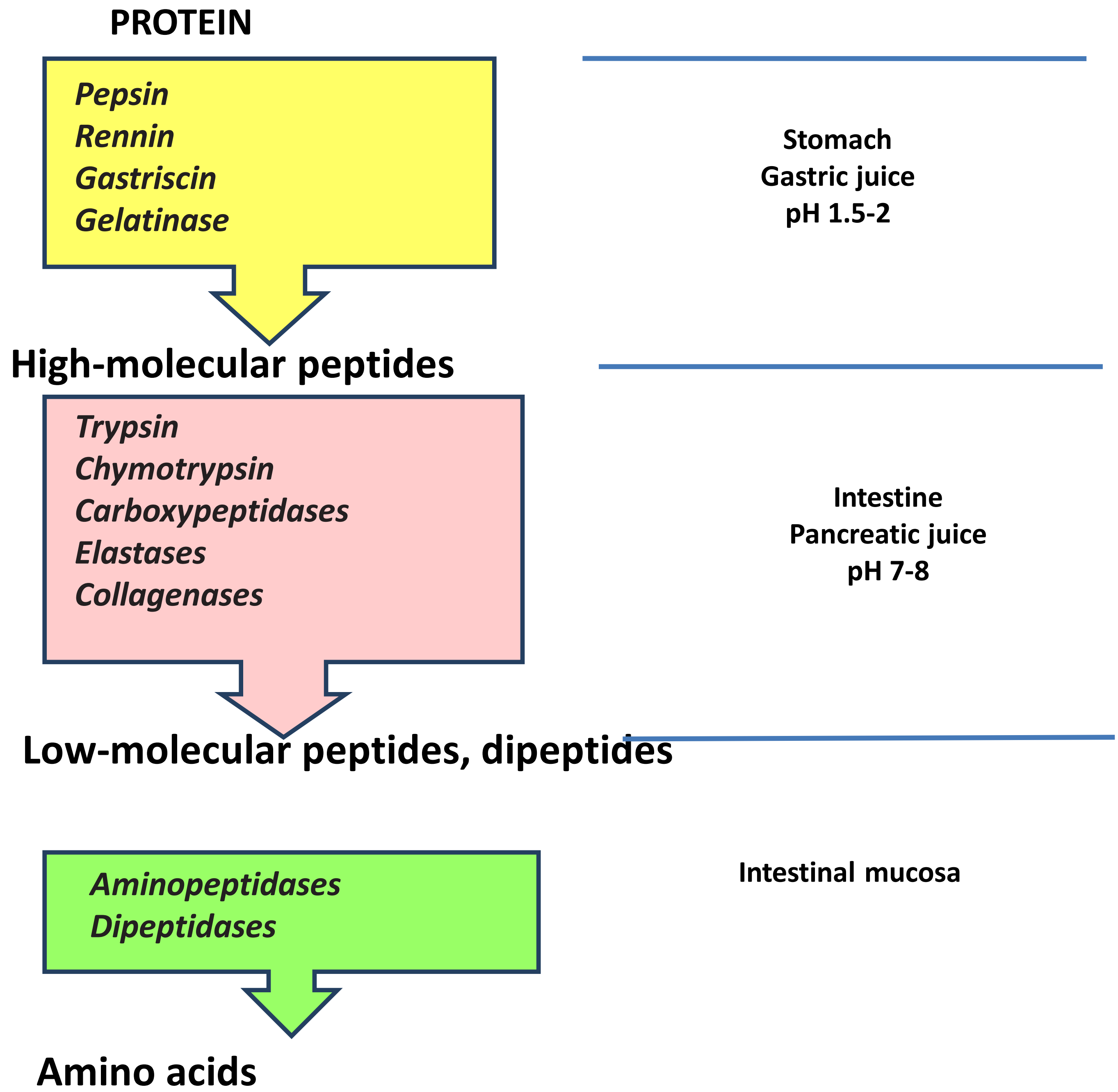

**Molecules marked with ubiquitin (“ubiquitinated”) are recognized and then shifted into the interior of the proteasome, where degradation takes place. Ubiquitin is not degraded, but is reused after renewed activation.**

# Digestion of proteins in the GIT

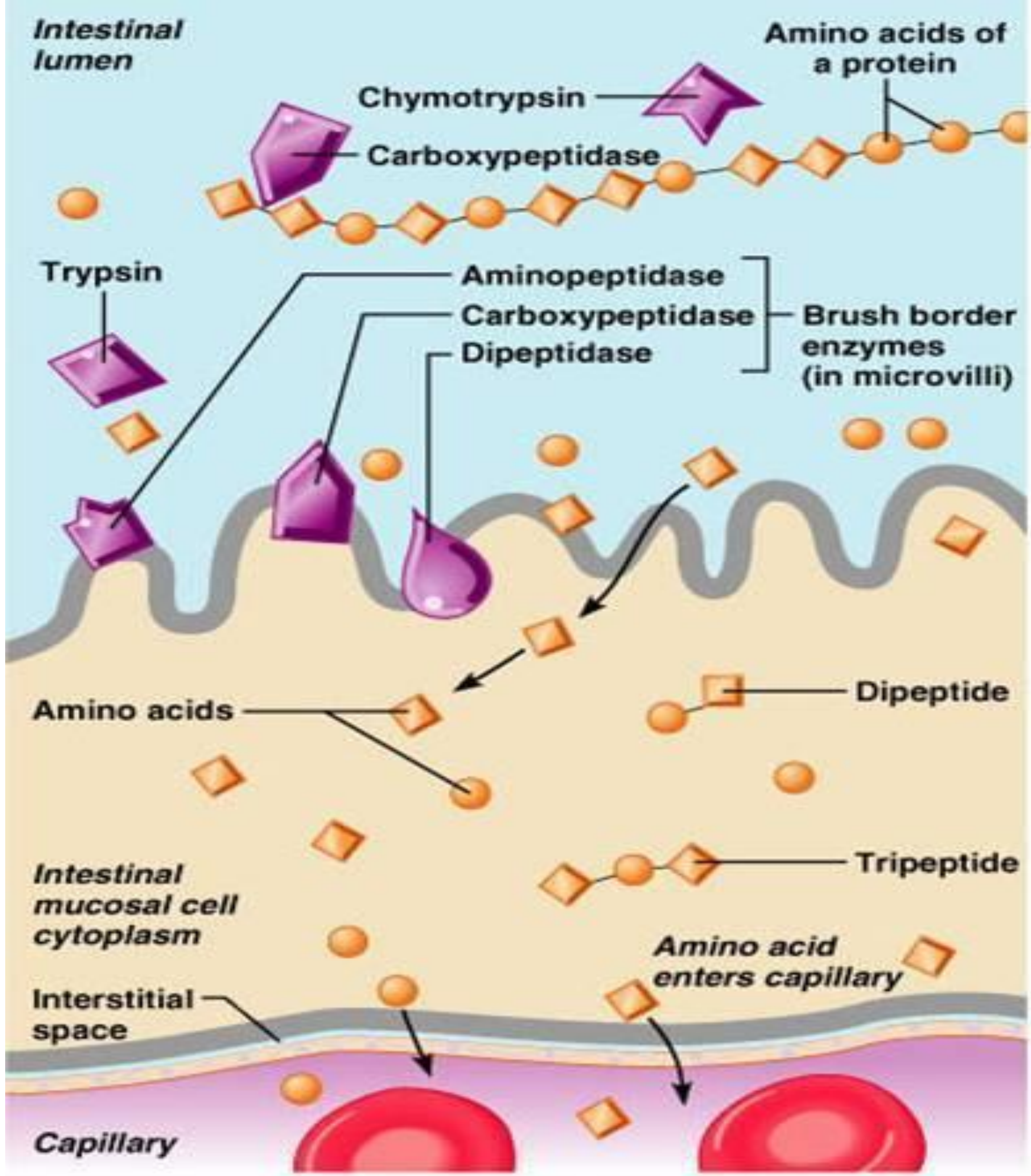
**Proteins taken up in food are initially broken down in the GIT into amino acids, which are resorbed and distributed in the organism via the blood.**




Protease
Digestion
Protein molecule
Amino acid molecules


PROTEIN
Pepsin
Rennin
Gastriscin
Gelatinase
Stomach
Gastric juice
pH 1.5-2
High-molecular peptides
Trypsin
Chymotrypsin
Carboxypeptidases
Elastases
Collagenases
Intestine
Pancreatic juice
pH 7-8
Low-molecular peptides, dipeptides
Aminopeptidases
Dipeptidases
Intestinal mucosa
Amino acids

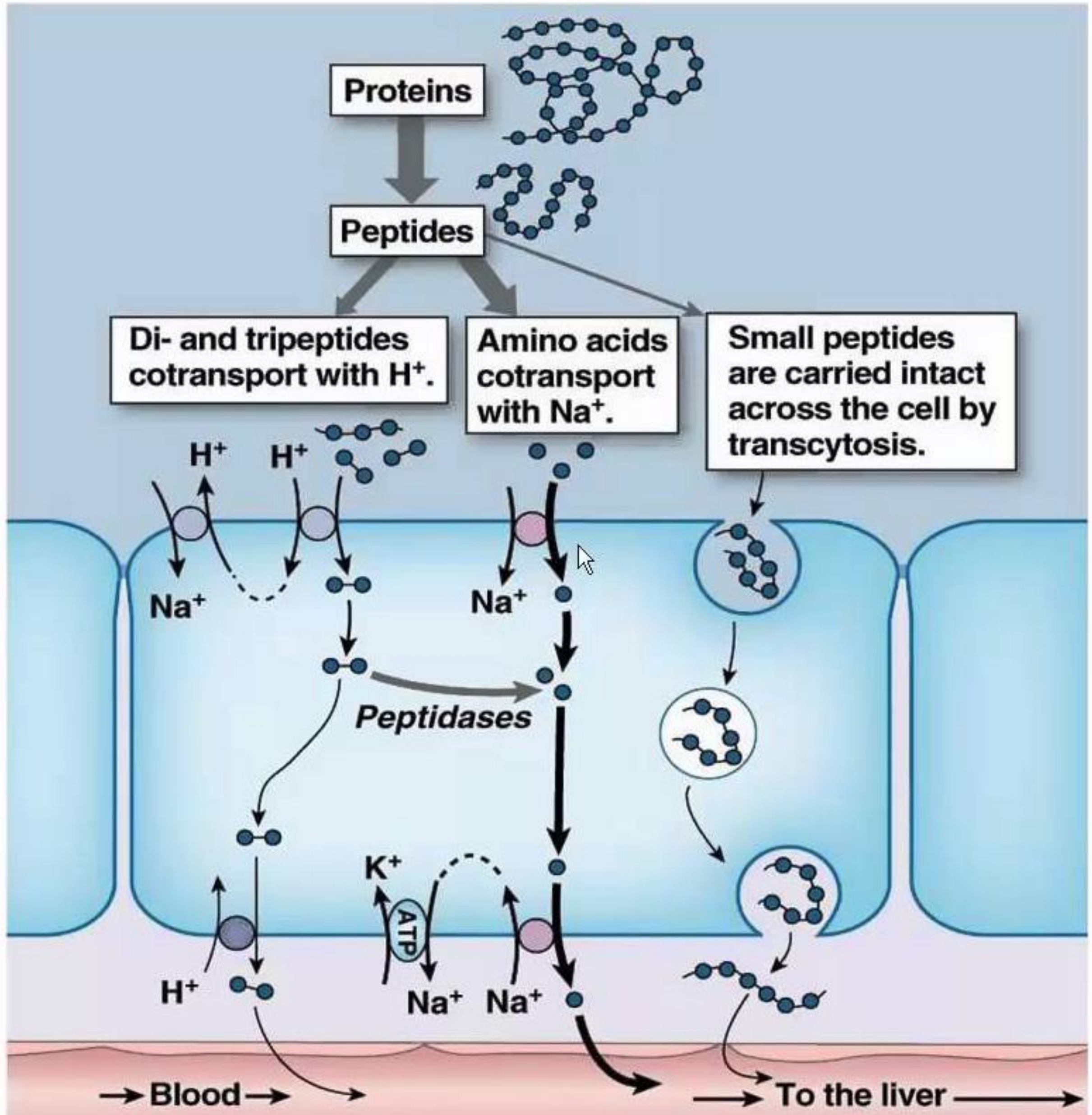
# Protein digestion in the small intestine



# Some intestinal proteolytic enzymes (Proteases)

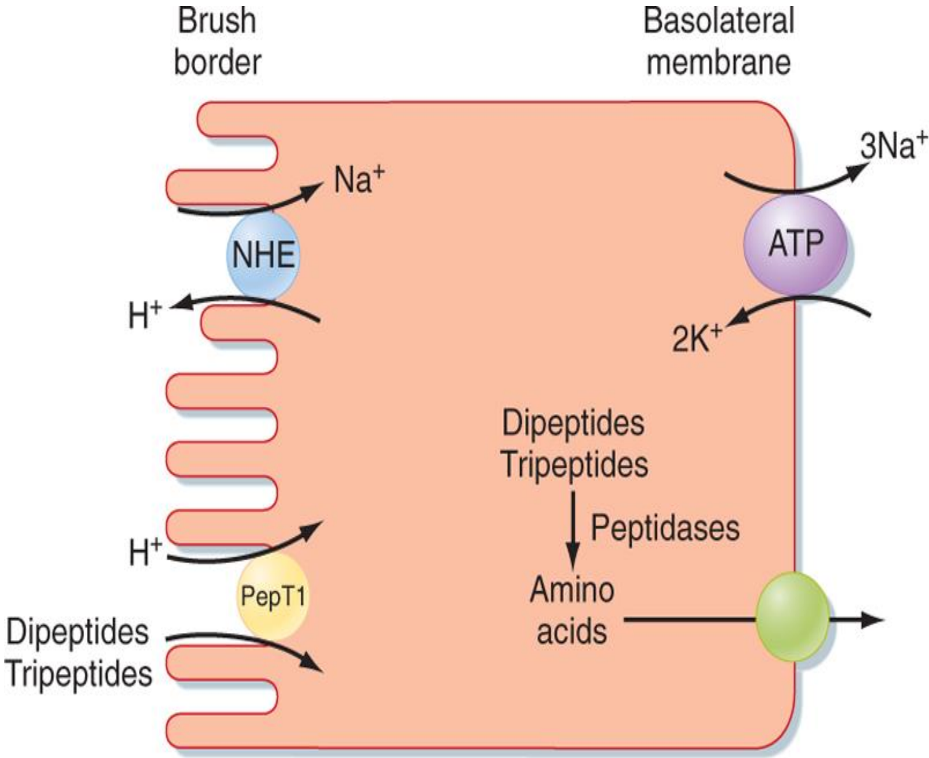
| Intestinal proteases | Sources | Zymogen form | End product of digestion | Types of enzymes |
|---|---|---|---|---|
| Trypsin | Pancreas | Trypsionogen | Shorter chain peptide | Endopeptidase |
| Chymotripsin | Pancreas | Chymotripsinogen | Shorter chain peptide | Endopeptidase |
| Carboxypeptidase | Pancreas | Procarboxypeptid ase | Single amino acid | Exopeptidase |
| Aminopeptidase | Epithelium cells of intestine | Proaminopeptidase | Splits off individual A.A. from amino terminal end of peptide chain | Exopeptidease |
| Dipeptidase | Epithelium cells of intestine | | Breakdown dipeptides into constituent AA | Exopeptidease |

# Absorption of peptides and amino acids



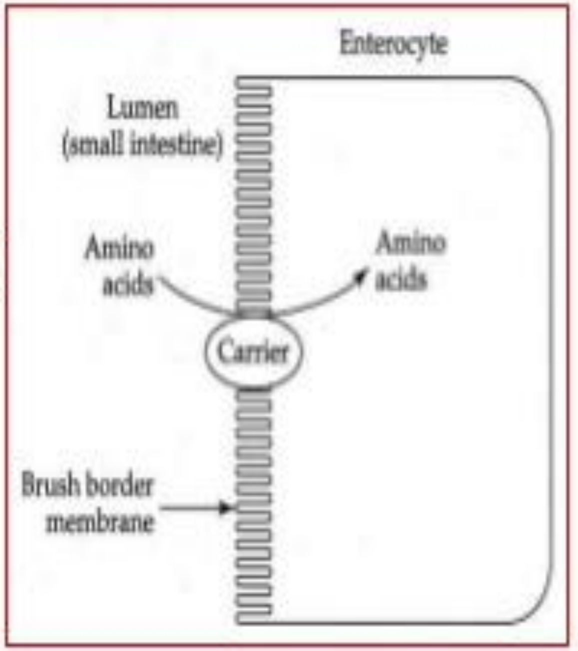
# Absorption of di- and tri-peptides:

- Di- and tri-peptides are absorbed across the enterocyte membrane by **$H^+$-dependent transporters** (unlike glucose).
- Di- and tri-peptides are further hydrolyzed to amino acids inside the intestinal mucosa.
- The final transfer of amino acids into blood by facilitated diffusion
- So, Only free amino acids appear in blood.

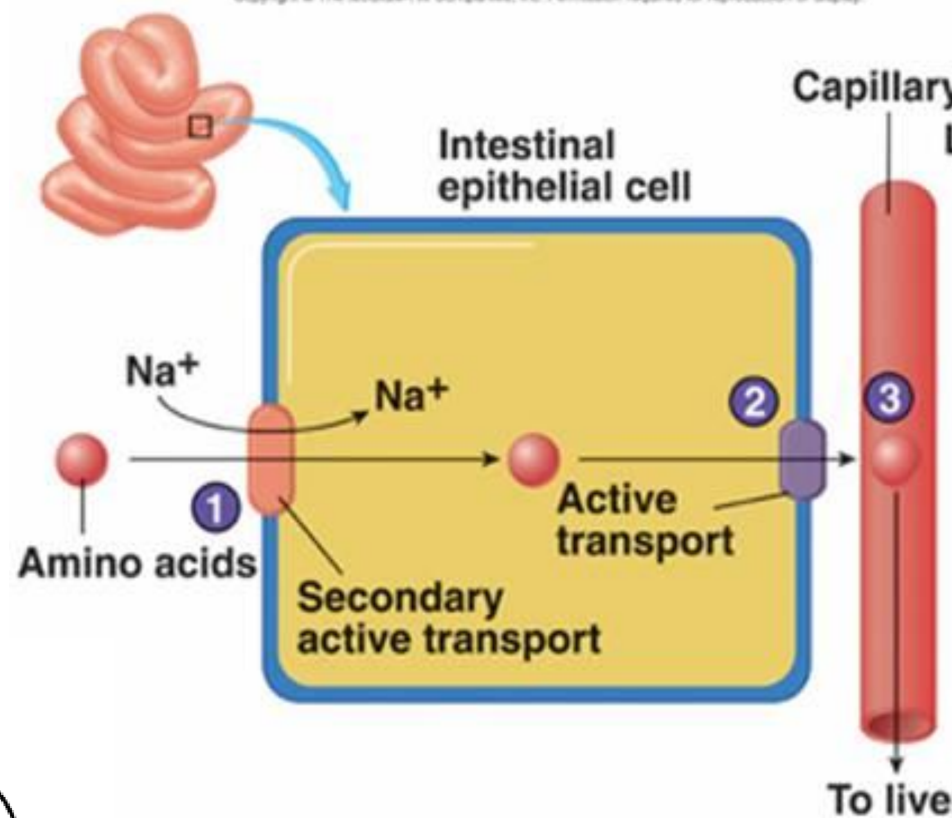


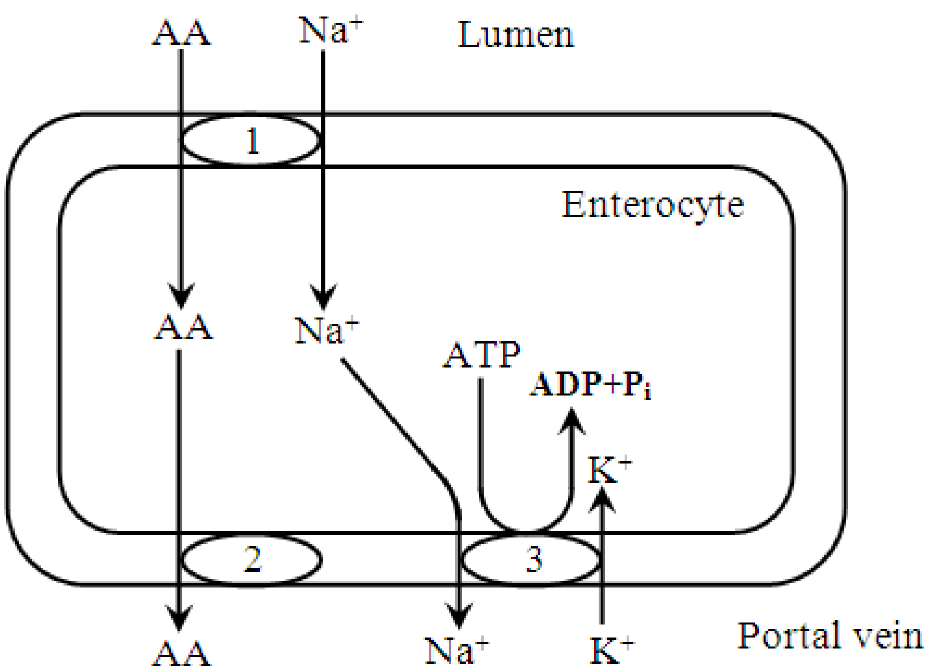
# ABSORPTION OF AMINO ACIDS

- The absorption of amino acids occurs mainly in the small intestine
- It is an energy requiring process
- Transport systems are carrier mediated and/or ATP-$Na^+$ dependent symport systems
- 5 different carriers for amino acids:
  - Neutral amino acids (Ala, Val, Leu, Met, Phe, Tyr, Ile)
  - Basic amino acids (Lys, Arg) and Cys
  - Imino acids and Glycine
  - Acidic amino acids (Asp, Glu)
  - Beta amino acids ( beta Ala)

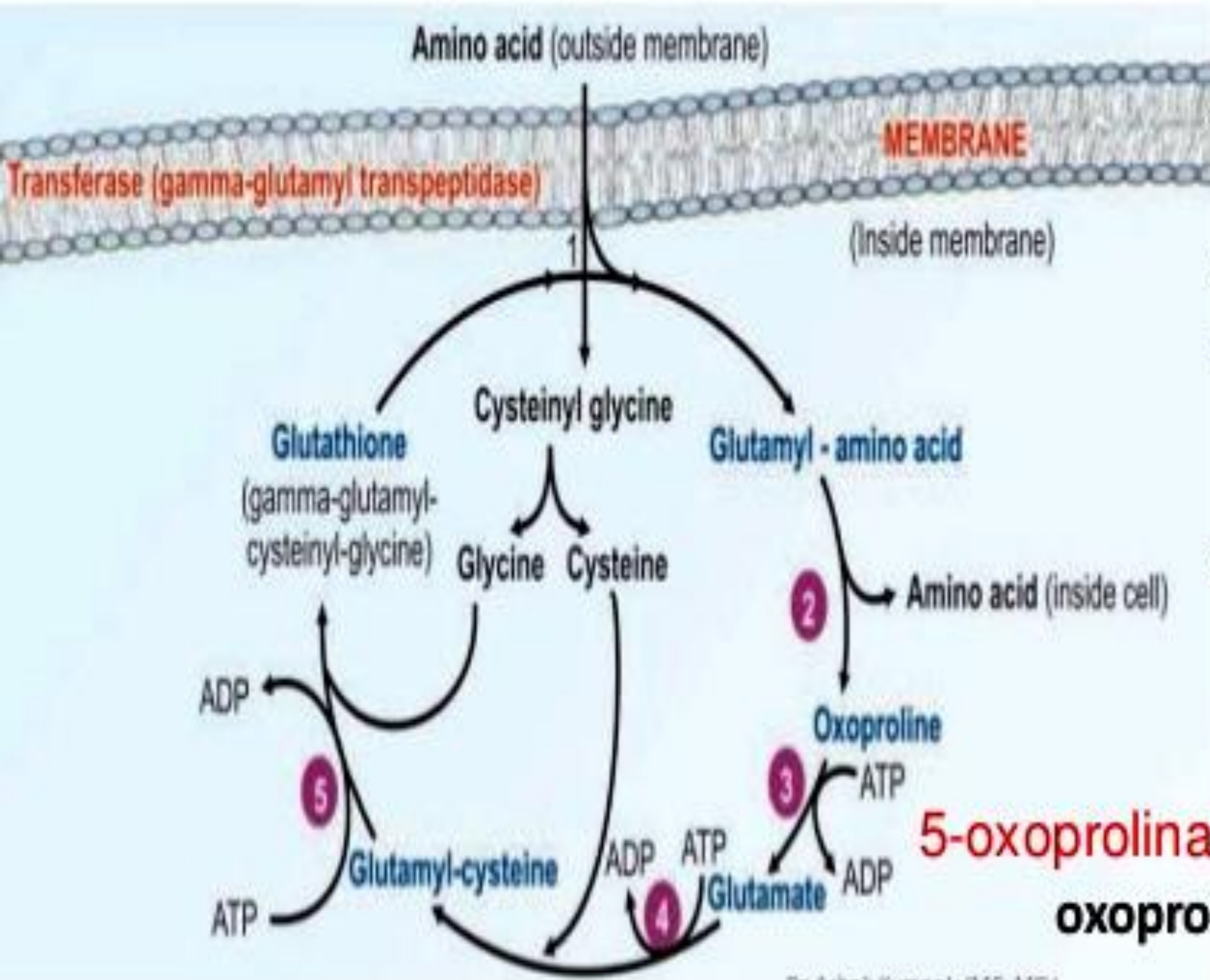


# Absorption of amino acids



# γ - glutamyl cycle



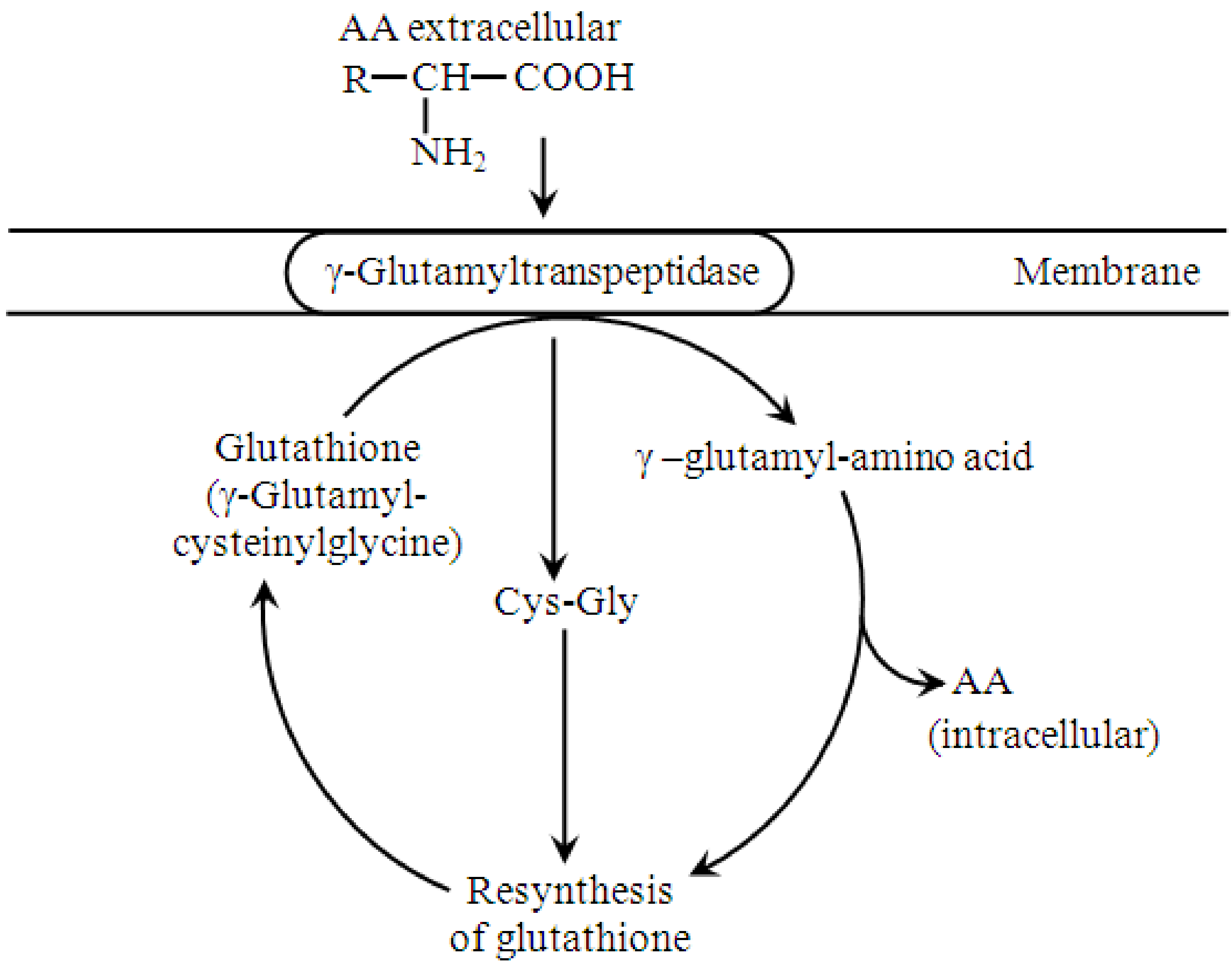

- Intestines, kidney tubules and brain
- Absorption of neutral amino acids
- Also called Miester cycle
- Requires the tripeptide glutathione (GSH) and energy
- Catalysed by gamma glutamyl transferase

5-oxoprolinase deficiency leads to **oxoprolinuria**



1 = gamma-glutamyl transferase; 2 = gamma-glutamyl cyclotransferase; 3 = 5-oxoprolinase; 4 = gamma-glutamyl cysteine synthetase; 5 = glutathione synthetase

# Gamma-glutamyl cycle



# CONVERSION OF AMINO ACIDS BY INTESTINAL BACTERIA

1. Putrefaction of sulfur-containing amino acids produces hydrogen sulfide ($H_2S$) and methylmercaptan ($CH_3–SH$), the products which are removed from the intestine with intestinal gas.
2. Putrefaction of diaminomonocarboxylic acids:

Ornithine → Putrescine

Lysine → Cadaverine

putrescine and cadaverine are detoxified in enterocytes by diaminoxidases

## CONVERSION OF AMINO ACIDS BY INTESTINAL BACTERIA

3) **Putrefaction of aromatic amino acids:**

**Tyrosine → Cresol → Phenol**

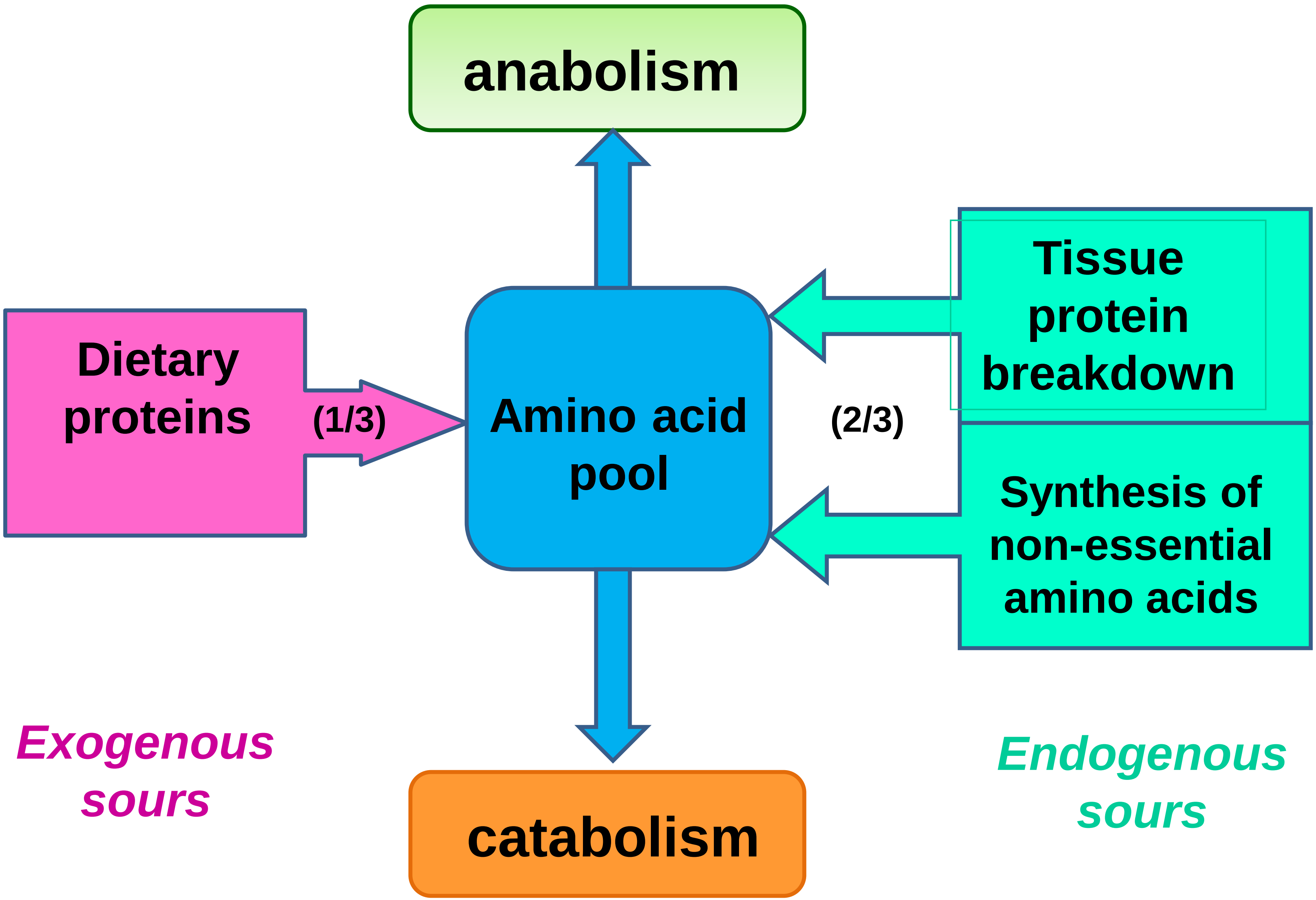
**Tryptophan → Scatol → Indole**

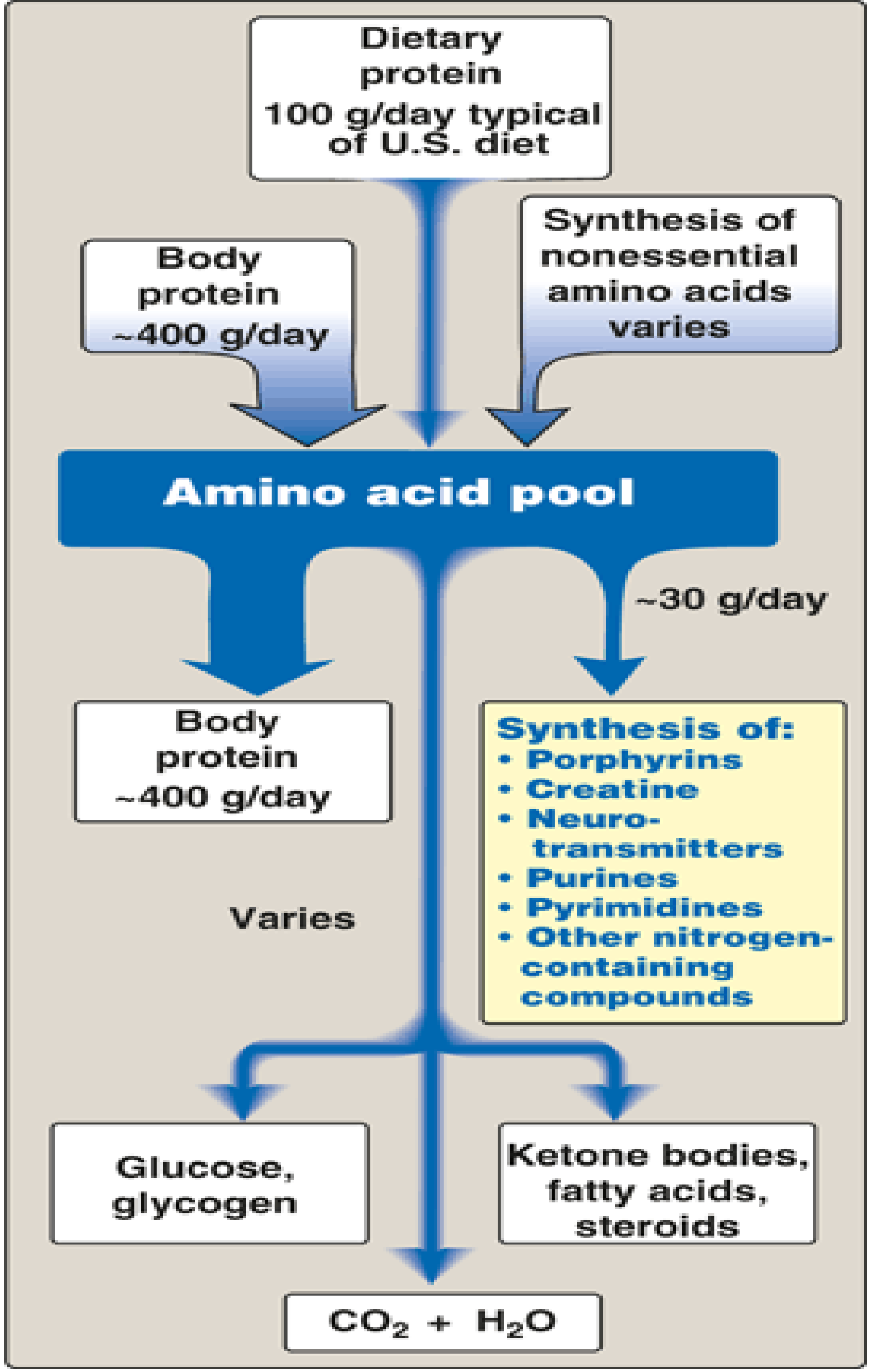
**Skatole is excreted in the feces.**

**Some portion of skatole is converted to indole.**

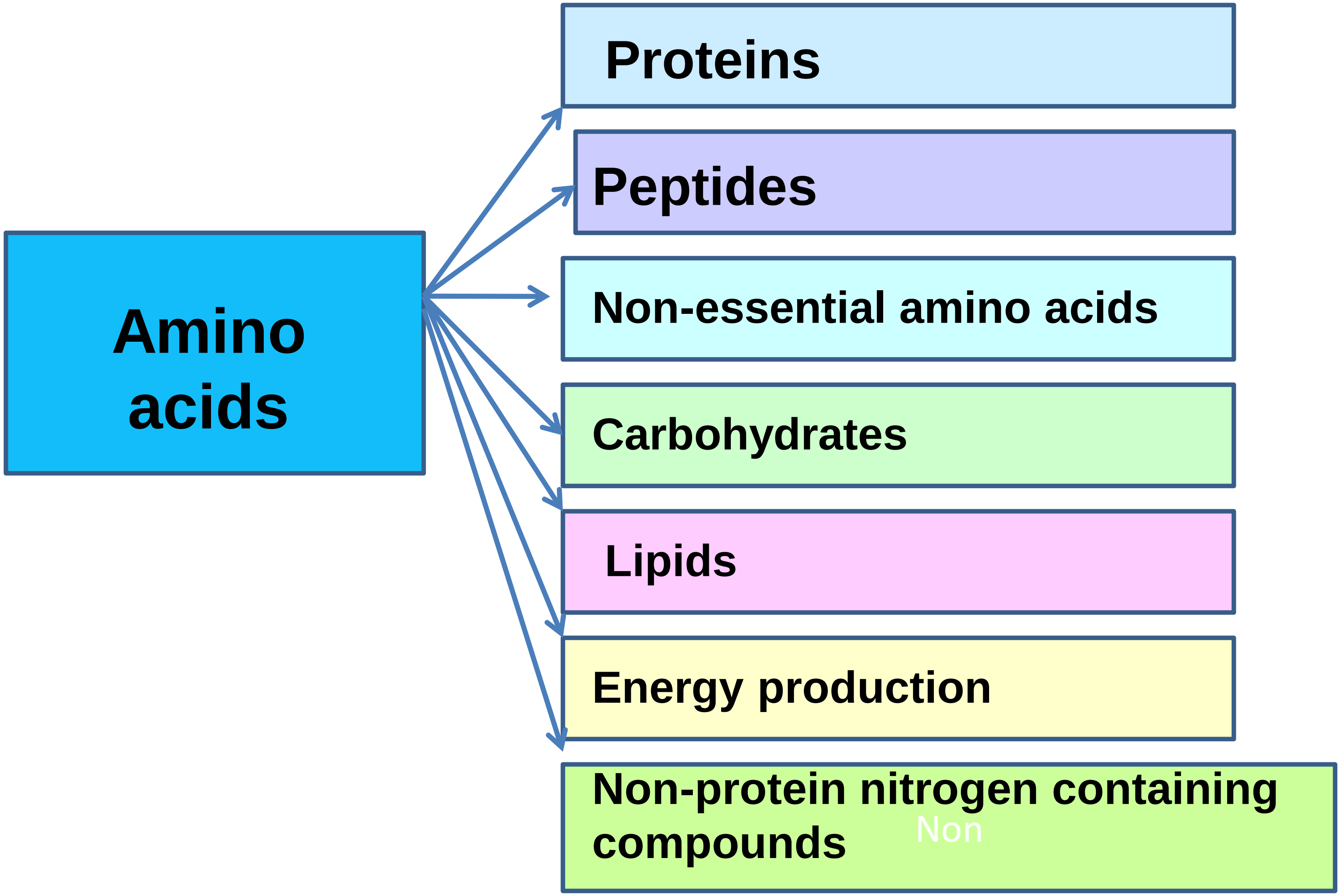
**Potassium salt of indoxyl sulfate, known as indican, is excreted in the urine.**

# Sources of amino acids in the body




Dietary protein
100 g/day typical of U.S. diet
Body protein
~400 g/day
Synthesis of nonessential amino acids
varies
Amino acid pool
~30 g/day
Body protein
~400 g/day
Synthesis of:
• Porphyrins
• Creatine
• Neuro-transmitters
• Purines
• Pyrimidines
• Other nitrogen-containing compounds
Varies
Glucose, glycogen
Ketone bodies, fatty acids, steroids
$CO_2$ + $H_2O$

# Ways of amino acid use



# GENERAL PATHWAYS OF AMINO ACID METABOLISM

- **deamination** (removal of the amino group from an amino acid with the release of ammonia);
- **transamination** (the transfer of amino group from an amino acid to an α-keto acid, without the intermediary formation of ammonia);
- **decarboxylation** (removal of the carboxyl group from an amino acid with the release of $CO_2$);
- **polymerization** (synthesis of protein);
- **modification** of side chain.

# GENERAL PATHWAYS OF AMINO ACID METABOLISM