



University of Fallujah
College of Medicine



Protein metabolism

Lecture : 1,2&3

Stage : 2nd Stage

Lecturer : Assia. Prof. Dr. Mustafa Saleam

Department: Chemistry and Biochemistry

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الرؤية

والرسالة

والاهداف

لكلية

طب

الفلوجة

الرؤية

تحقيق الريادة في التعليم الطبي وأن نكون شريكاً فعالاً في الإرتقاء بالمستوى الأكاديمي والصحي على مستوى القطر.

الرسالة

تعليم وتدريب الطلبة في بيئة تعليمية هادفة لتهيئة الخريجين لممارسة طبية متميزة وأمنة مع ترسيخ القيم الانسانية والعلمية والمبادئ والاجتماعية ومعايير الجودة. تخرج اطباء قادرين على الاستجابة للاحتياجات والتحديات الصحية وتوجيه البحث العلمي لحل المشكلات الصحية في المجتمع.

تجنيد وتطوير هيئة تدريسية بمواصفات عالية لتصبح الأفضل في مجال التعليم والبحوث العلمية

الاهداف

تخريج أطباء لديهم المعرفة والإرادة والمهارة التي تمكنهم من ممارسة الطب بشكل آمن مع تجسيد القيم الإنسانية والأخلاقية.

التحسين المستمر للعملية التعليمية وتطوير مهارات الهيئة التدريسية وفق معايير الجودة بواسطة التعليم والتدريب الطبي المستمر من خلال الورش والمؤتمرات العلمية.

تعزيز علاقات التعاون مع المؤسسات العلمية والطبية داخل وخارج العراق لتطوير المستوى الأكاديمي للهيئة التدريسية ولتعليم الممارسة الطبية الآمنة للطلبة الخريجين.

السعي في أن تكون الكلية مركزاً بحثياً علمياً رائداً في البحوث الصحية التطبيقية مع الاستغلال الأمثل لنتائج تلك البحوث في خدمة المجتمع وبالتعاون مع مختلف الجهات المستفيدة.

المساهمة في تحسين صحة المجتمع من خلال دعم وتطوير نظام الرعاية الصحية عبر علاقات تكامل وتعاون فعال.

Learn objectives:

- Identify the principle of protein digestion and absorption

- Know the digestion and absorption process

- Know , what are products of protein digestion

- know , What are aminotranferase reaction

- know , what are deamination reaction

Introduction

*Proteins, the primary constituents of the body.

*A regular & adequate supply of protein in the diet is essential for cell

integrity & function

*Dietary proteins serve three broad functions:

-Their constituent AAs are used for synthesis of body proteins.

-The carbon skeletons of AAs can be oxidized to yield energy

-Their “C” & “N” atoms may be used to synthesize other

nitrogenous and non-nitrogenous metabolites.

*Digestion is the disintegration of complex nutrients into simple form

*Proteolytic enzymes responsible for degrading proteins are produced

by three different organs; The stomach, pancreas and the small

intestine.

Characteristics of Proteolytic enzymes

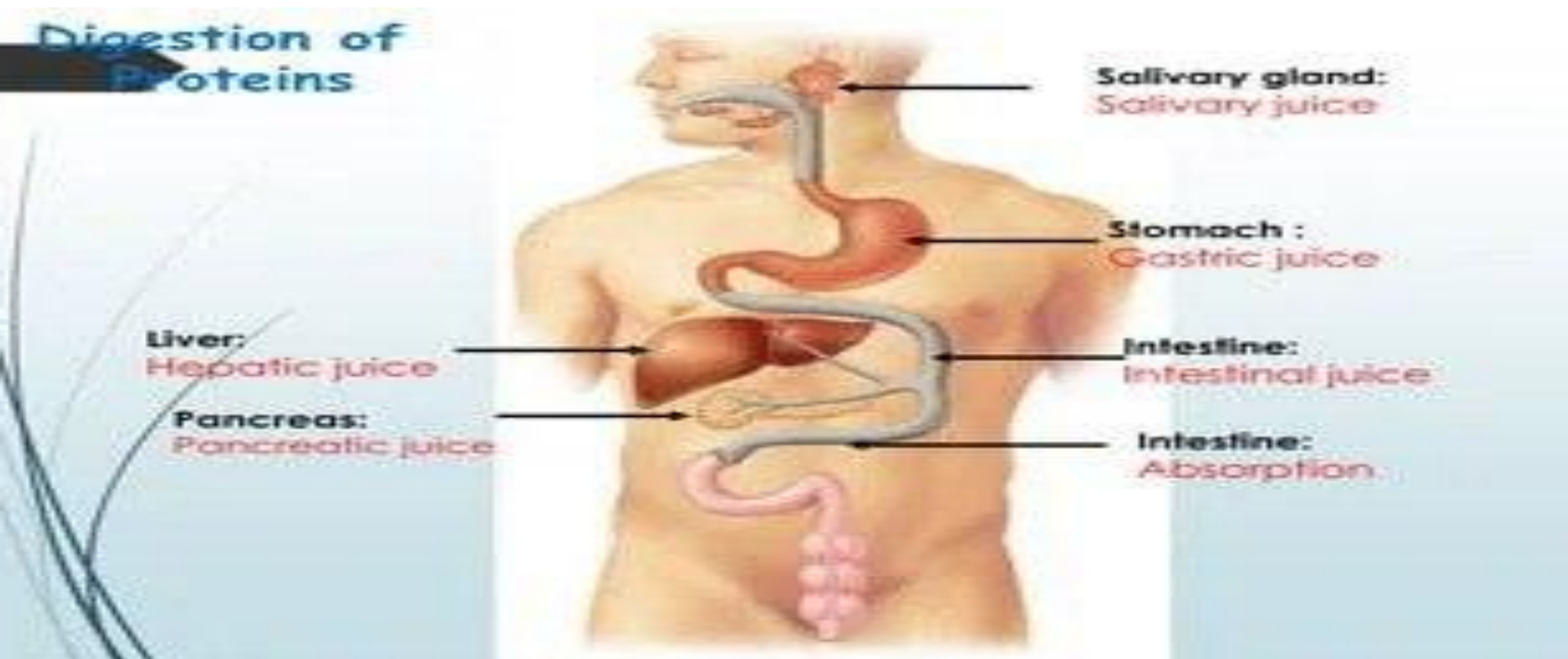
Peptidases :- *Endopeptidase : acts inside the core of protein, forms small peptide fragments

*Exopeptidase : acts from the amino terminal or carboxyl terminal ends of protein:-

*Aminopeptidase

*Carboxypeptidase Peptidases

Pro-enzymes (zymogens) :- Peptidases are secreted in the inactive form , when it reach the site of action they are activated



Digestion of Proteins (Overview)



Digestion in Mouth

No digestion of protein in mouth.

No proteolytic enzymes present in the saliva.

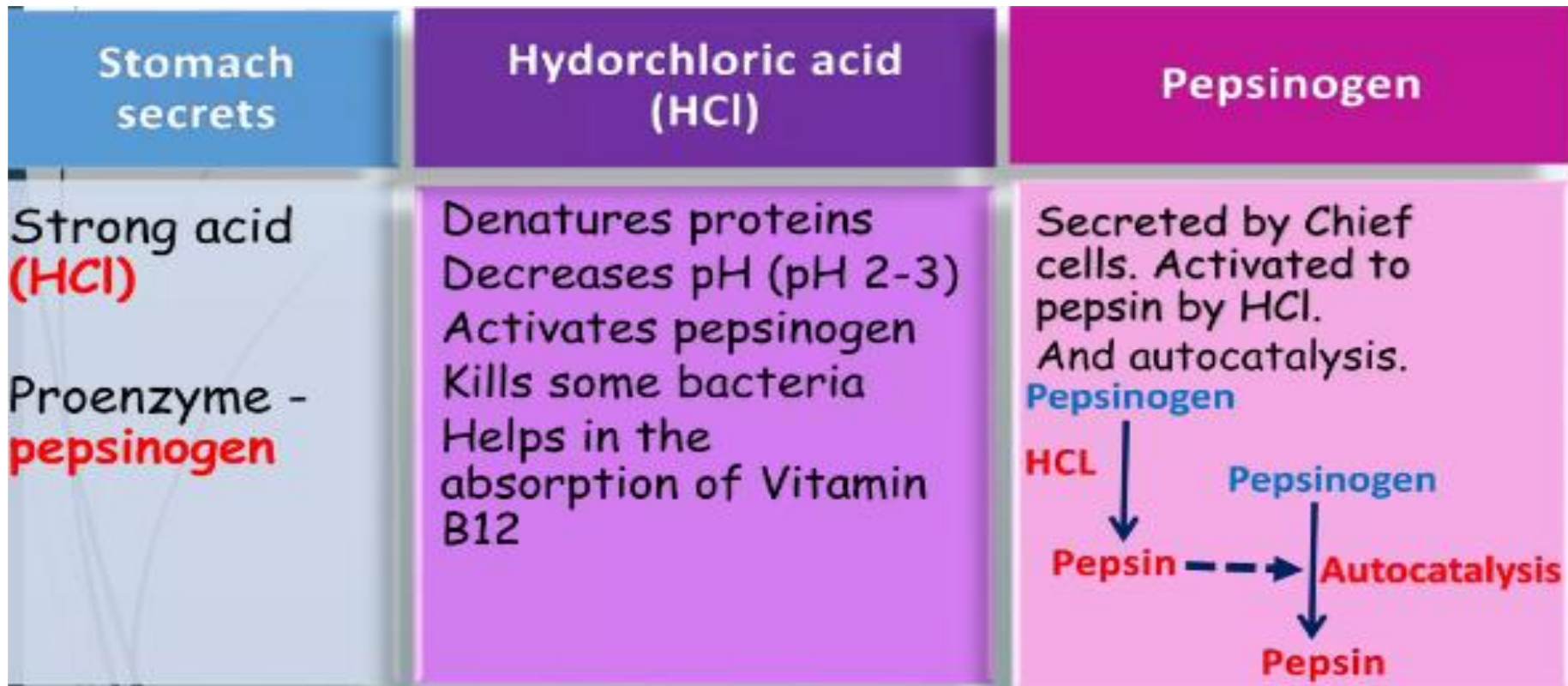
Function of the saliva - lubricate the food, this helps in making food soluble for the action of proteolytic enzymes.

After mastication and chewing, the bolus of food enters stomach where it is acted upon by gastric juice

Digestion in Stomach

Digestion of protein starts in stomach.

The pH of gastric juice is 1.5-2.5.



Pepsin acts on

Peptide bond formed by carboxyl group of Phenylalanine, Tyrosine, Tryptophan, methionine

Converts proteins into proteases and peptones

RENNIN

Also called chymosin
Active in infants
curdling of milk
Absent in adult stomach

Converts Casein of milk into paracasein
It combines with calcium to form calcium paracaseinate

Digestion of proteins in the Intestine By Pancreatic Enzymes

As the acidic stomach contents pass into duodenum, the low pH triggers the secretion of the hormones...

- Secretin – stimulate pancreas to secrete bicarbonate. It neutralizes HCL and rises the pH from 1.5-2.5 to 7.0
- Cholecystokinin - stimulate secretion of pancreatic
- Endopeptidase – Trypsin, Chymotrypsin, Elastase
- Exopeptidase – Carboxypeptidases, Aminopeptidases

Endopeptidase

Endopeptidase

- Cleave internal peptide bonds.
- Results into formation of smaller peptides.

Endopeptidase secreted by pancreas are...

- Trypsin (Trypsinogen)
- Chymotrypsin (Chymotrypsinogen),
- Elastase (Proelastase)

Exopeptidase

Exopeptidase

- Cleave off 1 AA at time from either the C or N end of the polypeptide

Exopeptidase secreted by pancreas are...

- Carboxypeptidase (Procarboxypeptidase)
- Aminopeptidase

Pancreatic Peptidases

Secreted as pro-enzymes



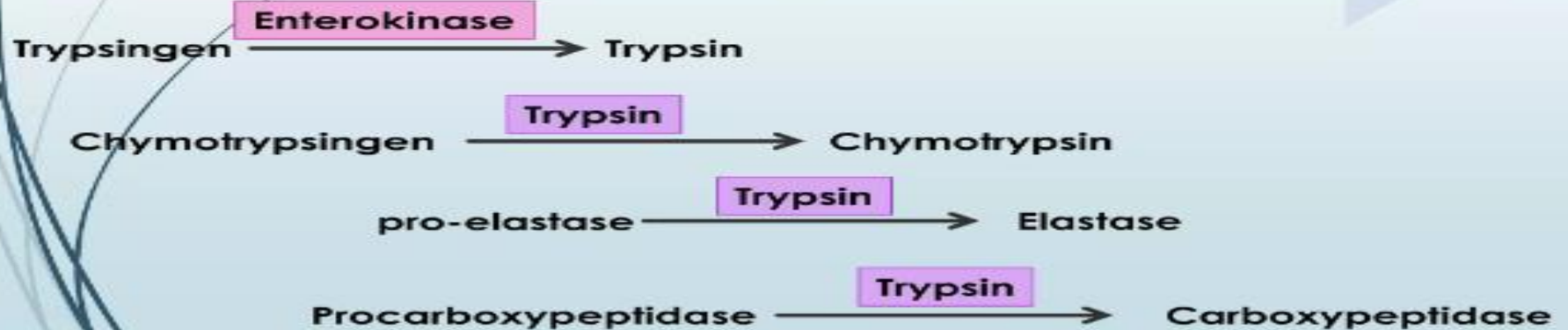
(Endopeptidases)
Trypsin
Chymotrypsin
Elastase

(Exopeptidase)
Carboxypeptidase A
Carboxypeptidase B

Trypsin

Trypsin

- Secreted in the zymogen form (Trypsinogen)
- **activated by Enterokinase and trypsin itself.**
- specific for cleaving peptide bonds contributed by lysine, arginine (basic amino acids)
- Acts on the zymogen forms of other pancreatic enzymes and activates them
- It has weak action on casein



CHYMOTRYPSIN (Endopeptidase)

- Zymogen form – Chymotrypsinogen
- activated to chymotrypsin by trypsin
- Hydrolyzes the peptide bond formed by the carboxyl group of aromatic amino acids

ELASTASE (Endopeptidase)

- Zymogen form – Proelastase
- activated to elastase by trypsin
- Acts on peptide bonds formed by the amino acids like glycine, alanine, serine

CARBOXYPEPTIDASE

Carboxypeptidase

- Zinc containing
- Exopeptidase
- Zymogen form is procarboxypeptidase
- Activated by trypsin
- Cannot act on dipeptides

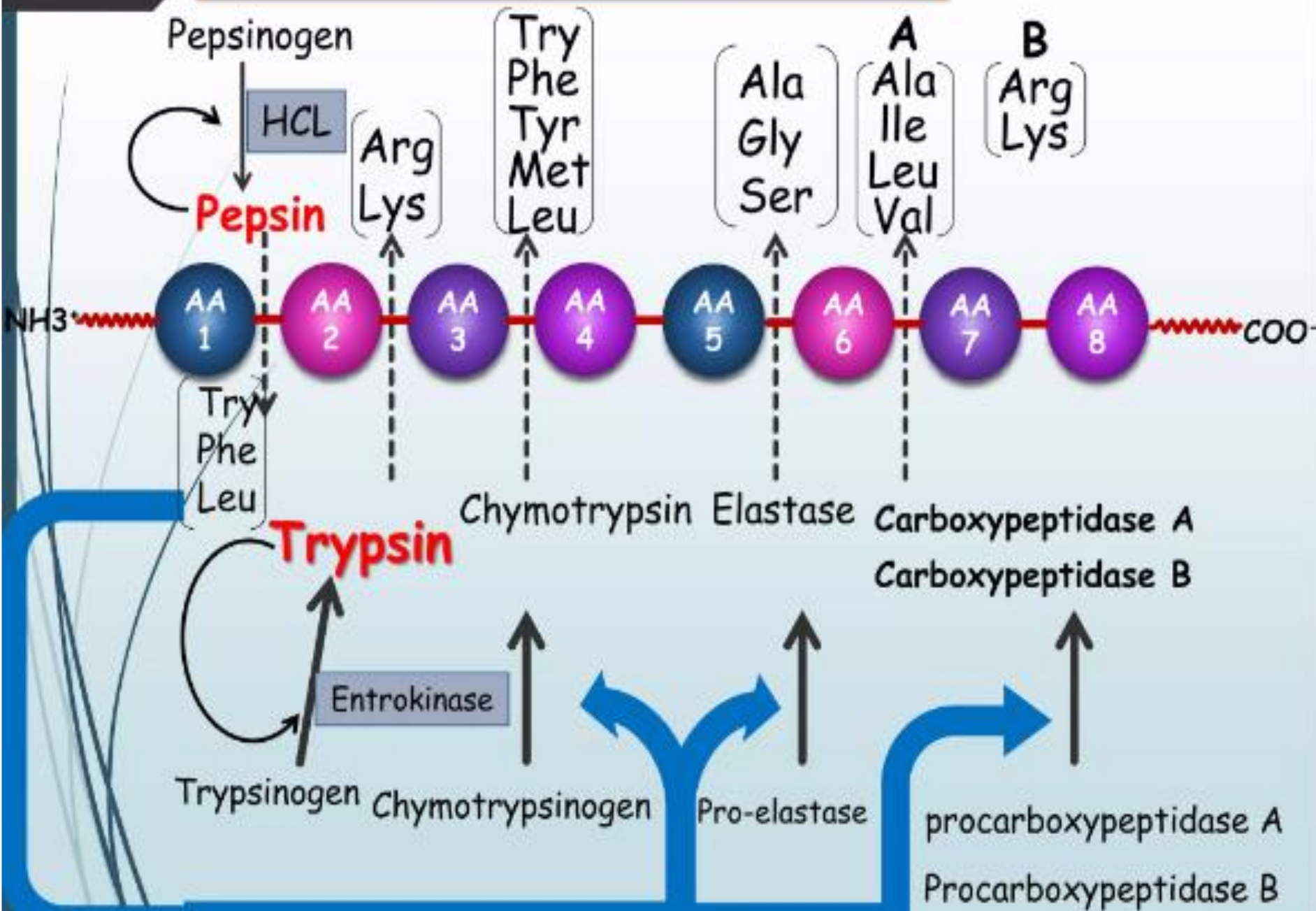
Carboxypeptidase A

acts on the Carboxy terminal peptide bond connected to Tyrosine, Phenylalanine or tryptophan

Carboxypeptidase B

acts on the carboxy terminal peptide bond connected to Arginine, lysine

Overview of Digestion of proteins



Digestion of protein in intestine

Amino peptidase

- Present on the luminal surface of the intestinal mucosa
- Is an exopeptidase.
- Acts on the amino terminal peptide bond
- Release free amino acid

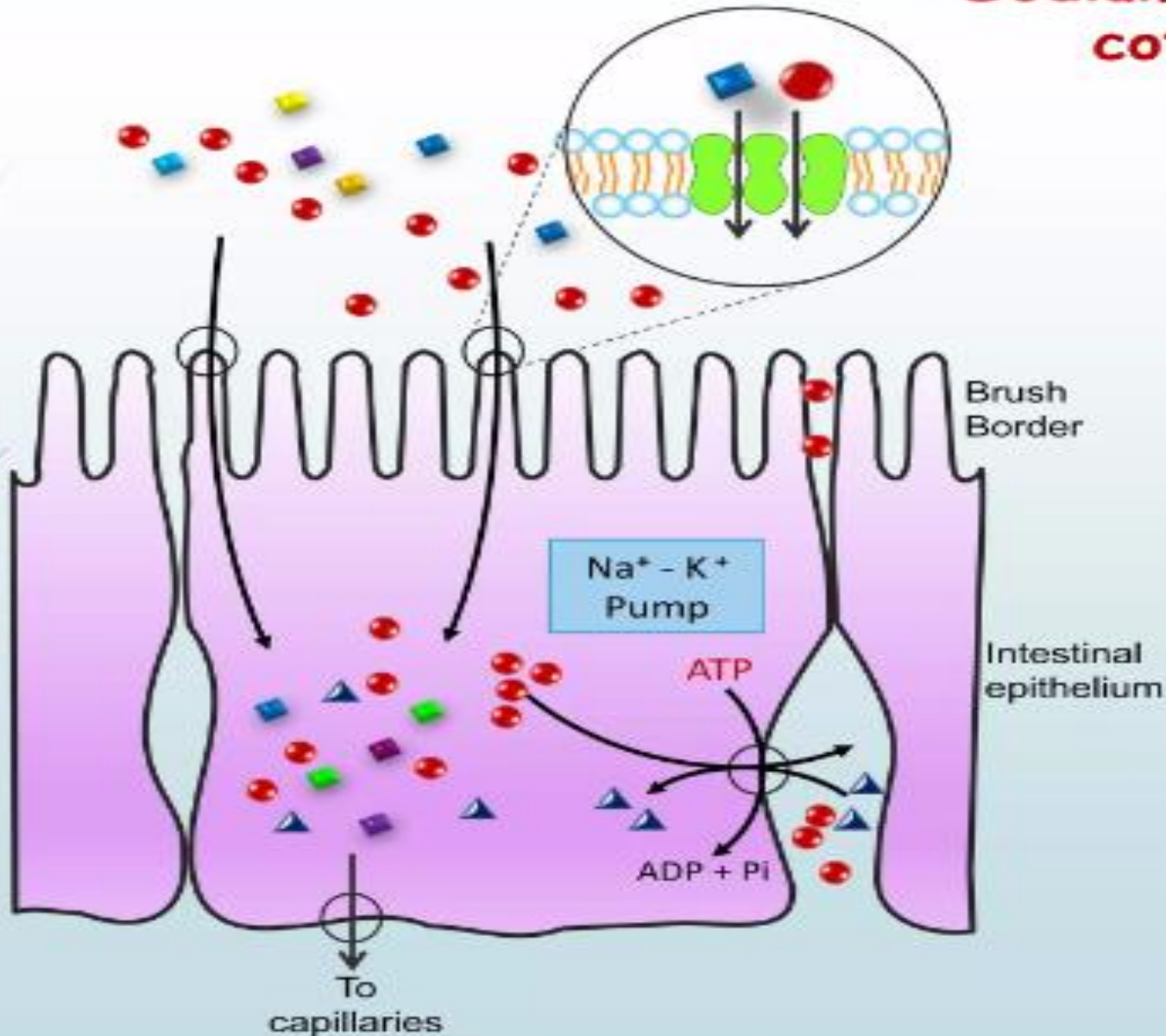
Di and Tri peptidases

- Present on the surface of the intestinal mucosal They act on **dipeptides** and release free amino acids
- Enterocytes take up some di and tripeptides
- These peptides are hydrolyzed to amino acids by **intracellular dipeptidase**

Amino acids absorption

- Active transport
- Na-amino acids co-transportal

Sodium-amino acid cotransport

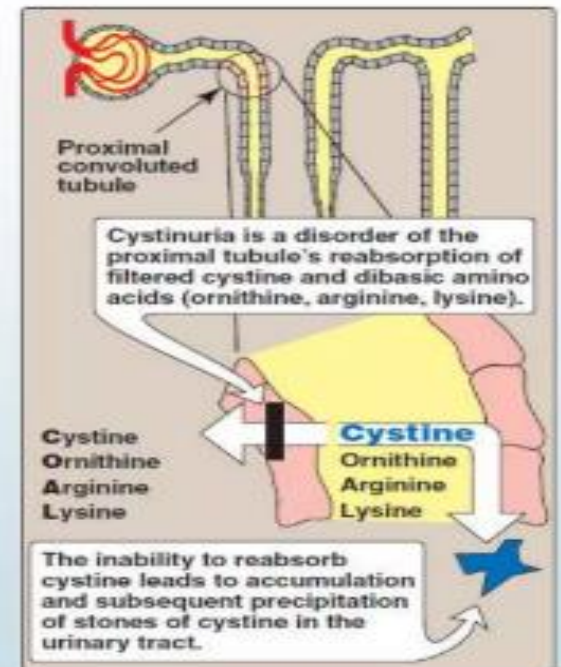


- Sodium - ● ●
- Potassium - ▲ ▲
- Amino Acids - ■ ■ ■ ■

Transport System	AAs Transported	Disorder Associated
<ul style="list-style-type: none"> • Small neutral amino acids 	<ul style="list-style-type: none"> • Alanine, Serine & Threonine 	<ul style="list-style-type: none"> • Hartnup disease
<ul style="list-style-type: none"> • Large neutral amino acids 	<ul style="list-style-type: none"> • Isoleucine, Leucine, Valine, Tyrosine, tryptophane, PA 	
<ul style="list-style-type: none"> • Basic amino acids 	<ul style="list-style-type: none"> • Arg, Lys, Ornithine & Cystine 	<ul style="list-style-type: none"> • Cystinuria
<ul style="list-style-type: none"> • Acidic amino acids 	<ul style="list-style-type: none"> • Glu acid & Asp acid 	
<ul style="list-style-type: none"> • imino acid and Glycine 	<ul style="list-style-type: none"> • Proline, OH-proline & Glycine 	<ul style="list-style-type: none"> • Glycinuria

Cystinuria- Common transporter for cystine, ornithine, arginine and lysine(COAL) is present in gut and renal tubules. Deficiency of transporter results in loss of these amino acids in the feces and urine.

Hart- Nup Disease- There is deficiency of transporter for tryptophan and neutral amino acid. no absorption of tryptophan takes place, tryptophan deficiency produce neurological and skin manifestation (pellagra-like rashes).



Absorption of intact proteins & polypeptides

- Short period, immediately after birth, the small intestine of infants can absorb intact proteins and polypeptide by endocytosis or pinocytosis
- Intact proteins and polypeptides are not absorbed by the adult intestine
- Macromolecular absorption in certain individuals appears to be responsible for antibody formation that often causes food allergy

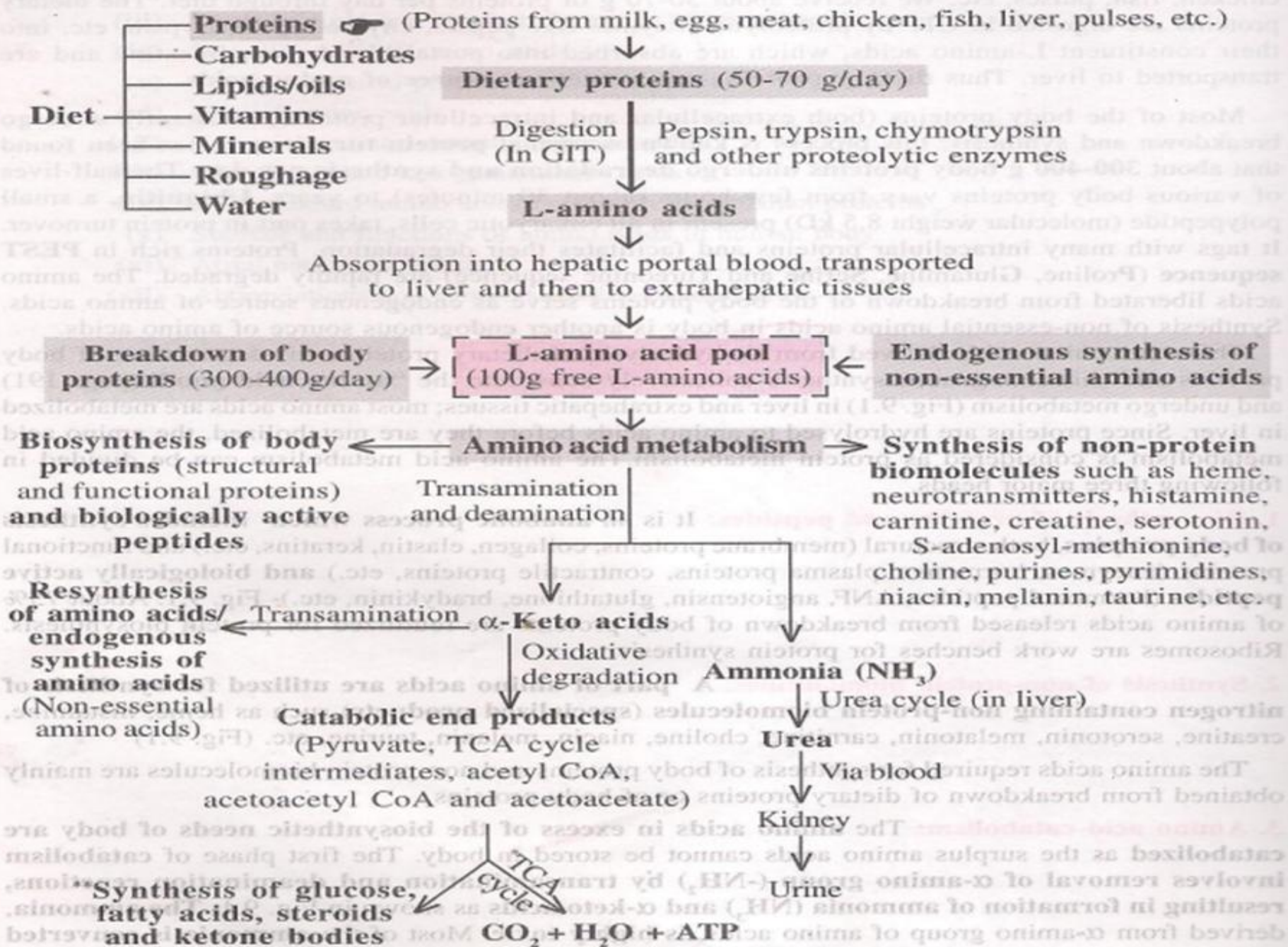


Fig. 9.1: Exogenous and endogenous sources of amino acids and their metabolic fates.

Biomedical significance of protein catabolism

- Most of body energy with intermediates compounds
- Maintain the nitrogen balance
- Diagnostic markers for liver disorders

Amino acids catabolism

- (1) Transamination reaction
- (2) Deamination reaction.

Transamination reaction

All amino acid except lysine, threonine and proline

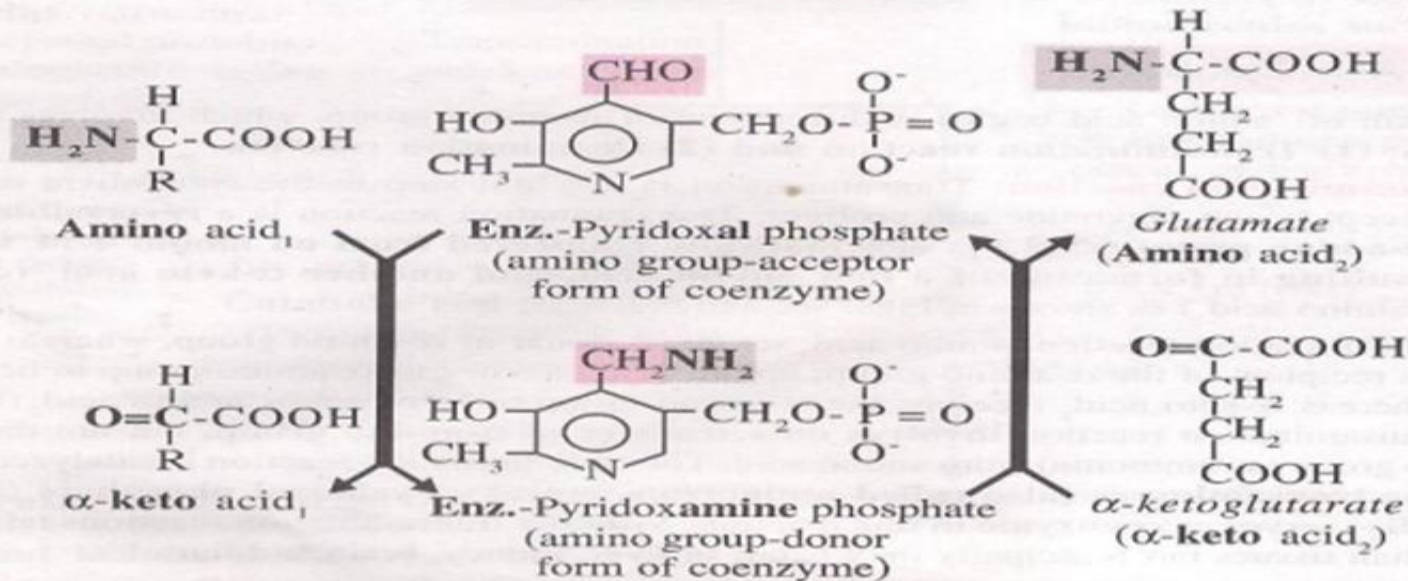
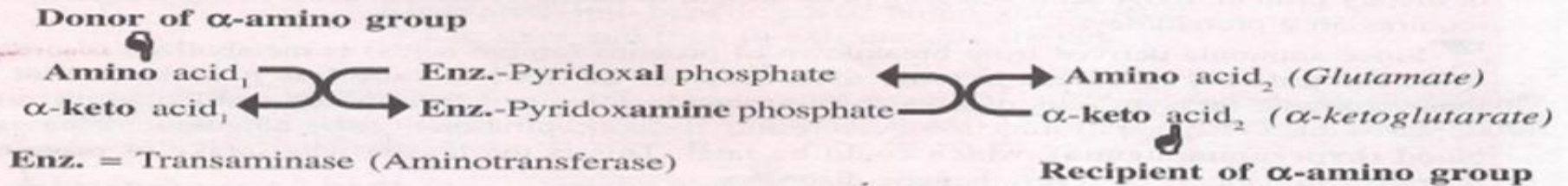


Fig. 9.3: Mechanism of transamination reaction.

Biomedical significance of

Aminotransferase

alanine aminotransferase (also
known as GPT)

aspartate aminotransferase (also
known as GOT)

Deamination Reaction

Deamination reactions are of two types:

- (a) Oxidative deamination
- (b) Non-oxidative deamination.

Oxidative deamination

-Oxidative deamination by L-glutamate dehydrogenase (GDH)

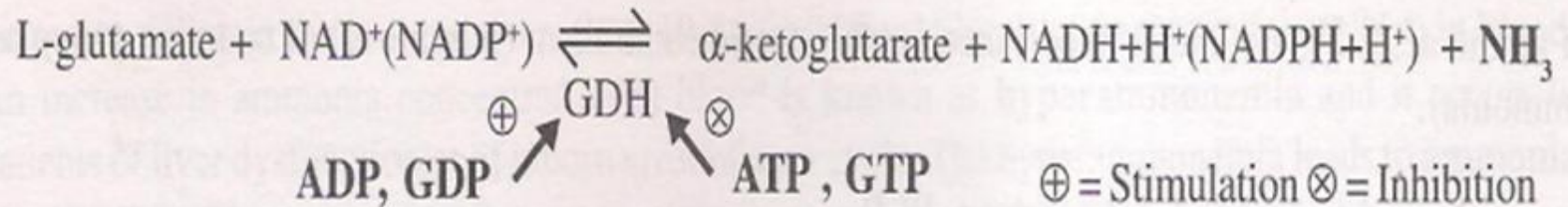


Fig. 9.6: Oxidative deamination of L-glutamate by L-glutamate dehydrogenase (GDH).

-Oxidative deamination by L-amino acid oxidase

-Oxidative deamination by D-amino acid oxidase

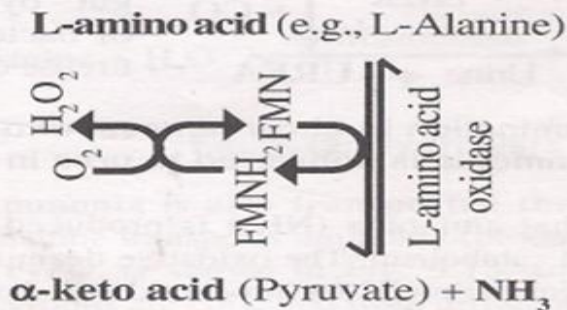
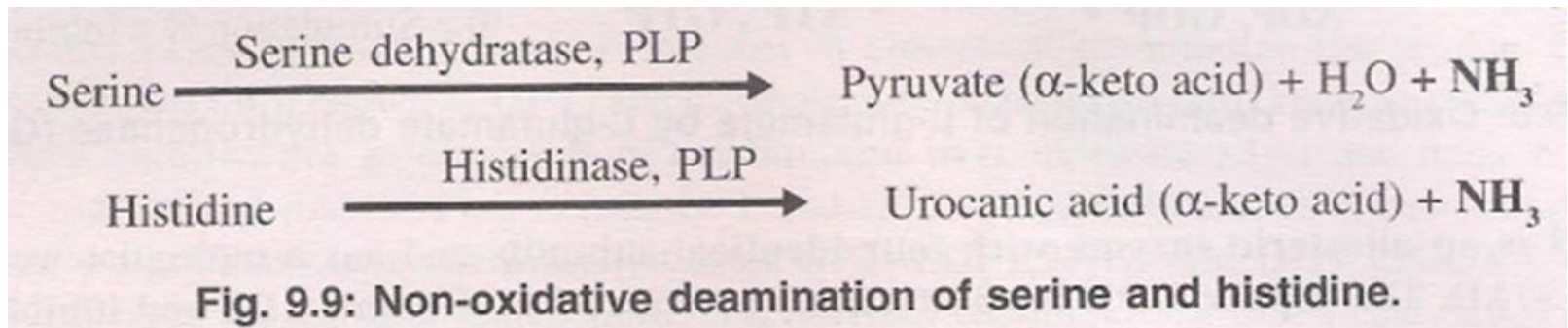


Fig. 9.7: Oxidative deamination of L-amino acid by L-amino acid oxidase.



Fig. 9.8: Oxidative deamination of D-amino acid by D-amino acid oxidase.

Non-oxidative deamination

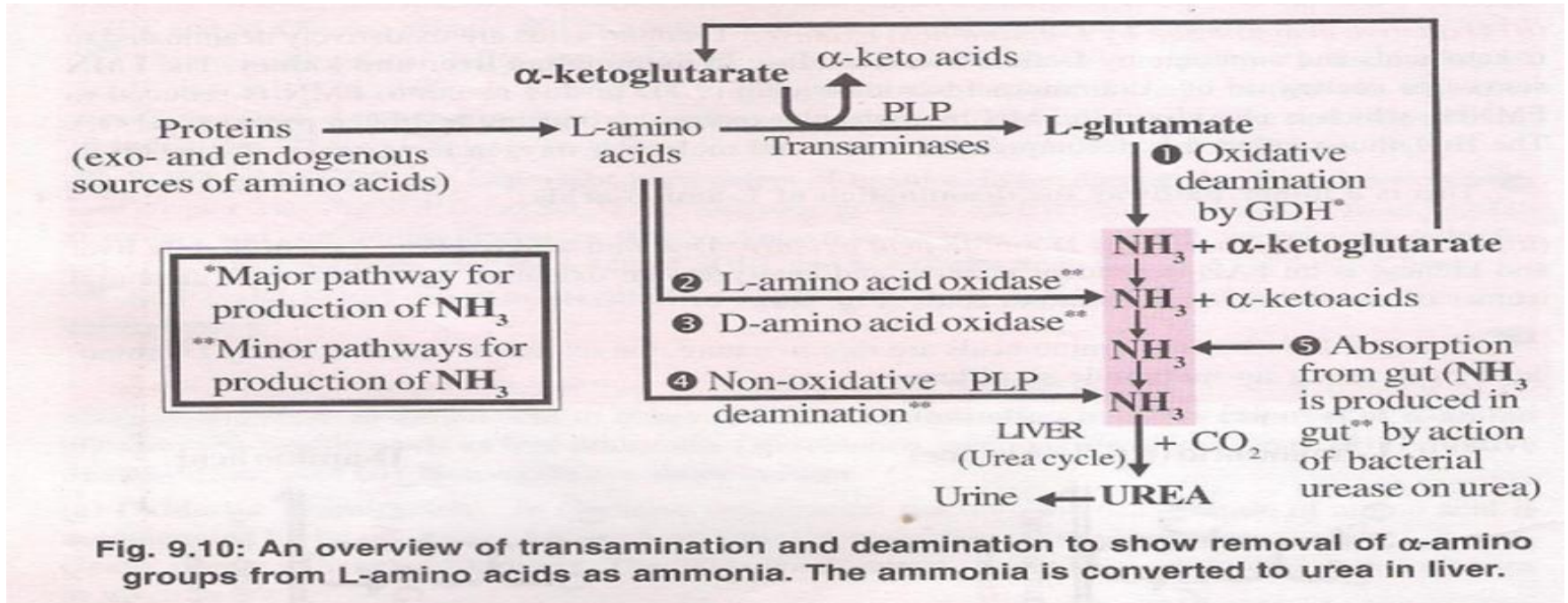


Metabolic fate of ammonia (NH₃)

The metabolic fate of NH₃ can be described in four heads:

- (i) Production of ammonia
- (ii) Transport of ammonia,
- (iii) Conversion of ammonia to urea
- (iv) Disposal of urea.

Production of ammonia (NH₃)



Transport of ammonia

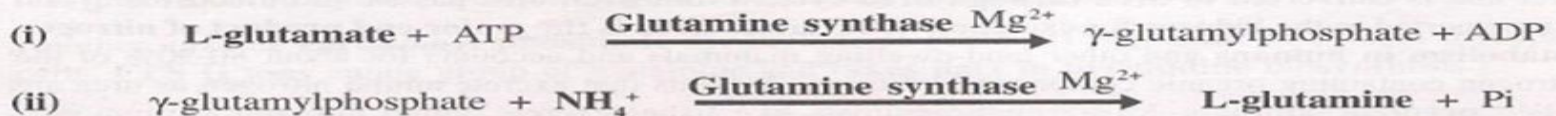


Fig. 9.11: Synthesis of L-glutamine from L-glutamate and ammonia by glutamine synthase.

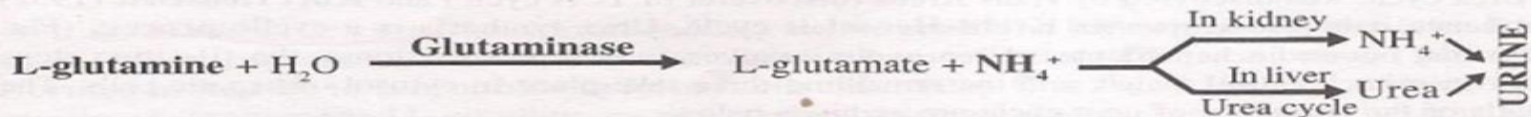


Fig. 9.12: Hydrolysis of L-glutamine by glutaminase.

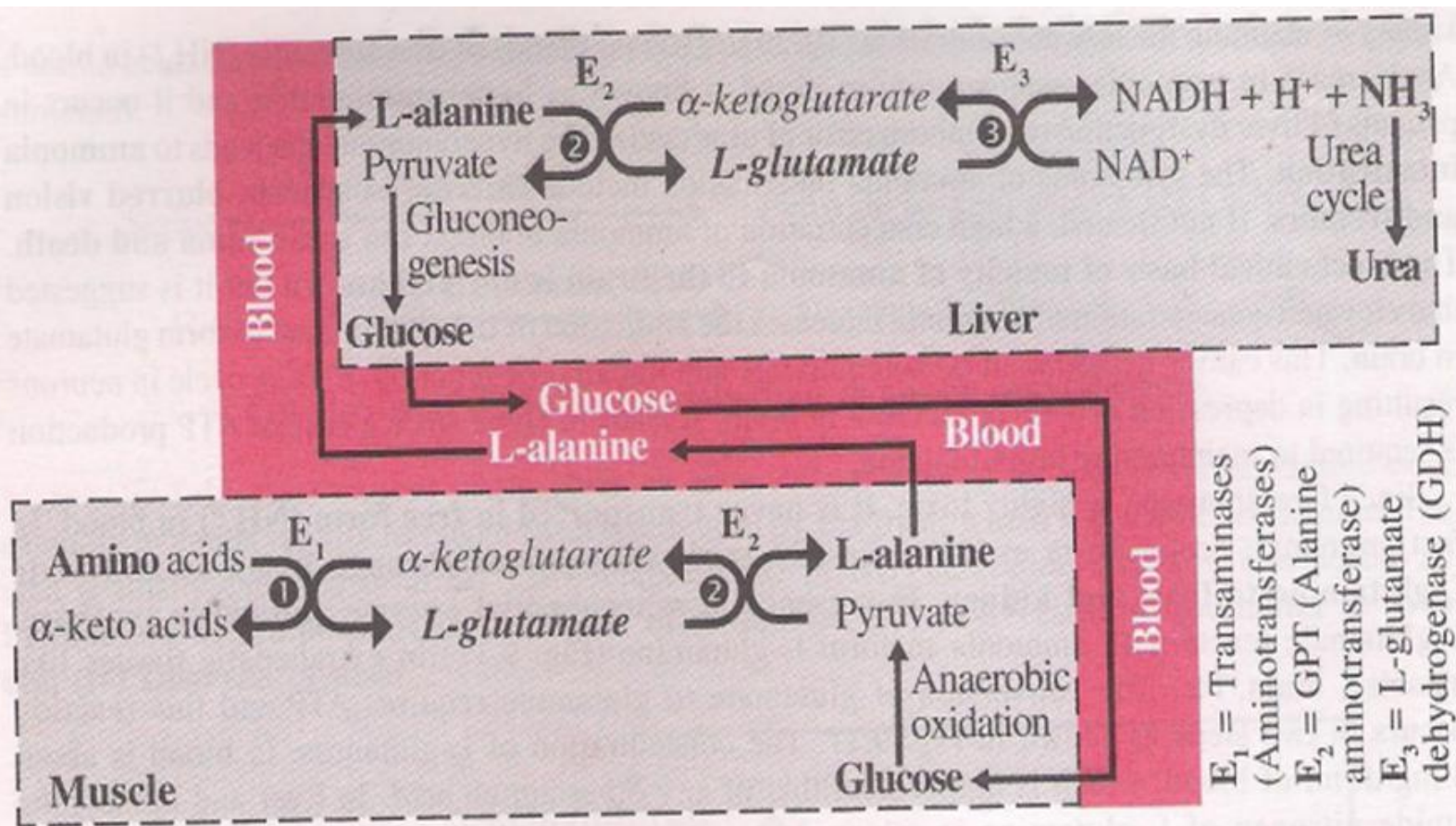


Fig. 9.13: Glucose-alanine cycle.