UNIVERSITY OF BASRAH

AL-ZAHRAA MEDICAL COLLEGE

MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH

The module: Metabolism

Session 5, Lecture 1

Duration : 1 hr

Protein,amino acid & nitrogen metabolism

Module staff

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Marks Essentials of Medical Biochemistry.

Ganong's Review of Medical Physiology .

For more discussion, questions or cases need help please post to the session group

Learning outcomes (LO)

- Describe how amino acids are catabolized in the body. LO1
- Describe how ammonia is metabolized in the body. LO2
- Explain the clinical relevance of measuring creatinine in blood and urine. LO3
- Explain the clinical consequences of a defect in phenylalanine metabolism. LO4

LO1

- **Protein is an essential component of the diet since it supplies the body with amino acids, some of which cannot be synthesized in the body (the essential amino acids).**
- **Lack of adequate protein in the diet is a major cause of illness in developing countries**

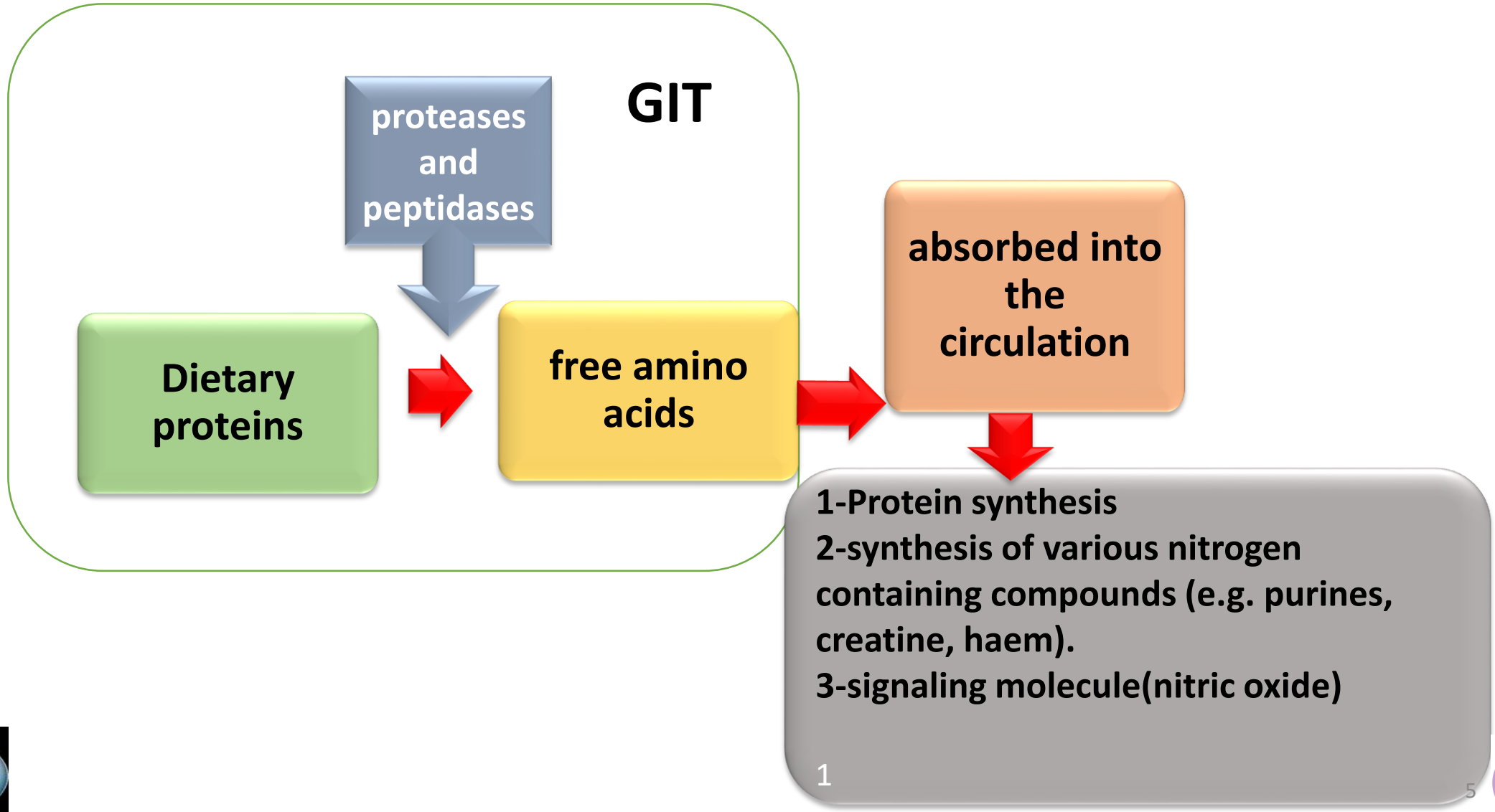
LO 1

- Amino acids are not stored by the body ,therefore, amino acid must be obtained :

- from the diet.
- synthesized de novo(essential amino acids).
- or produced from normal protein degradation.

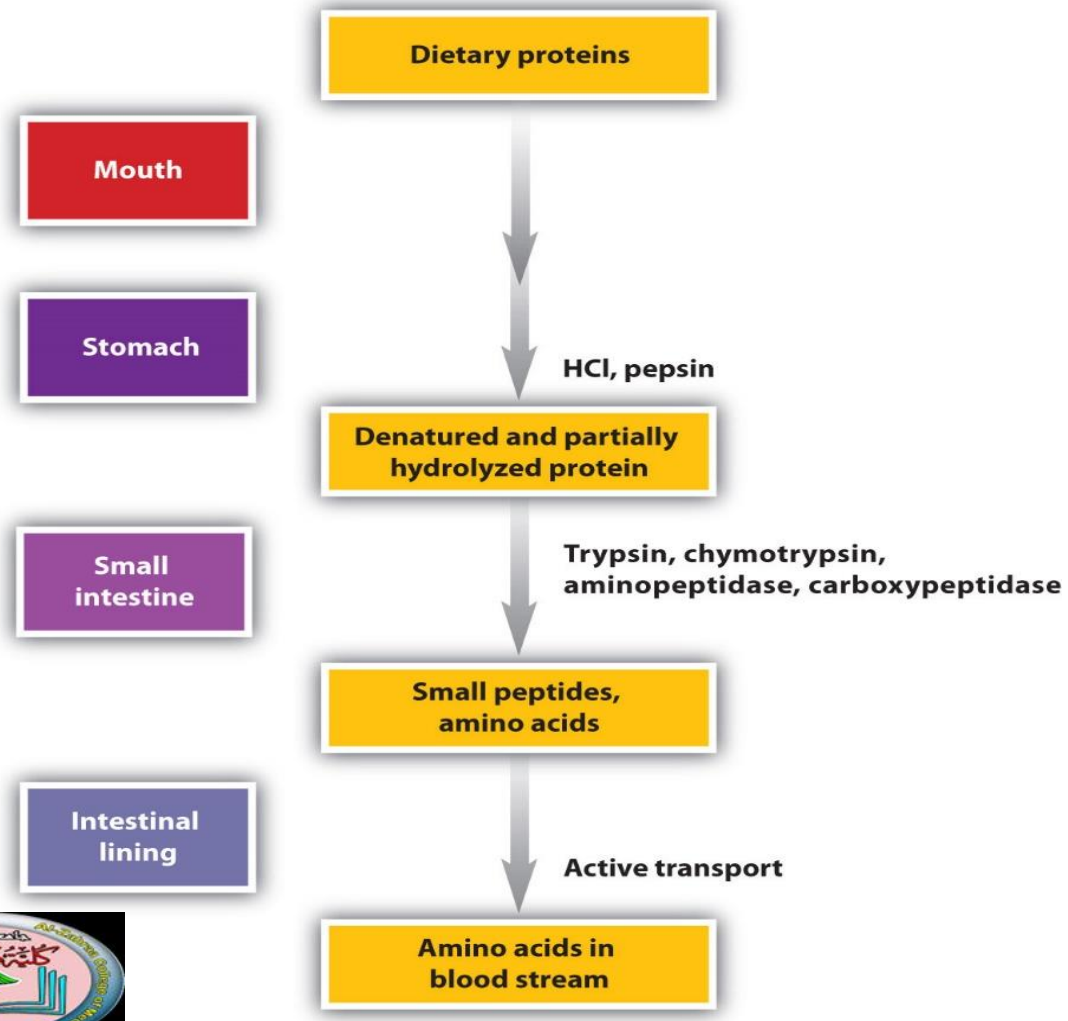
Any amino acids in excess of the biosynthetic needs of the cell are rapidly degraded.

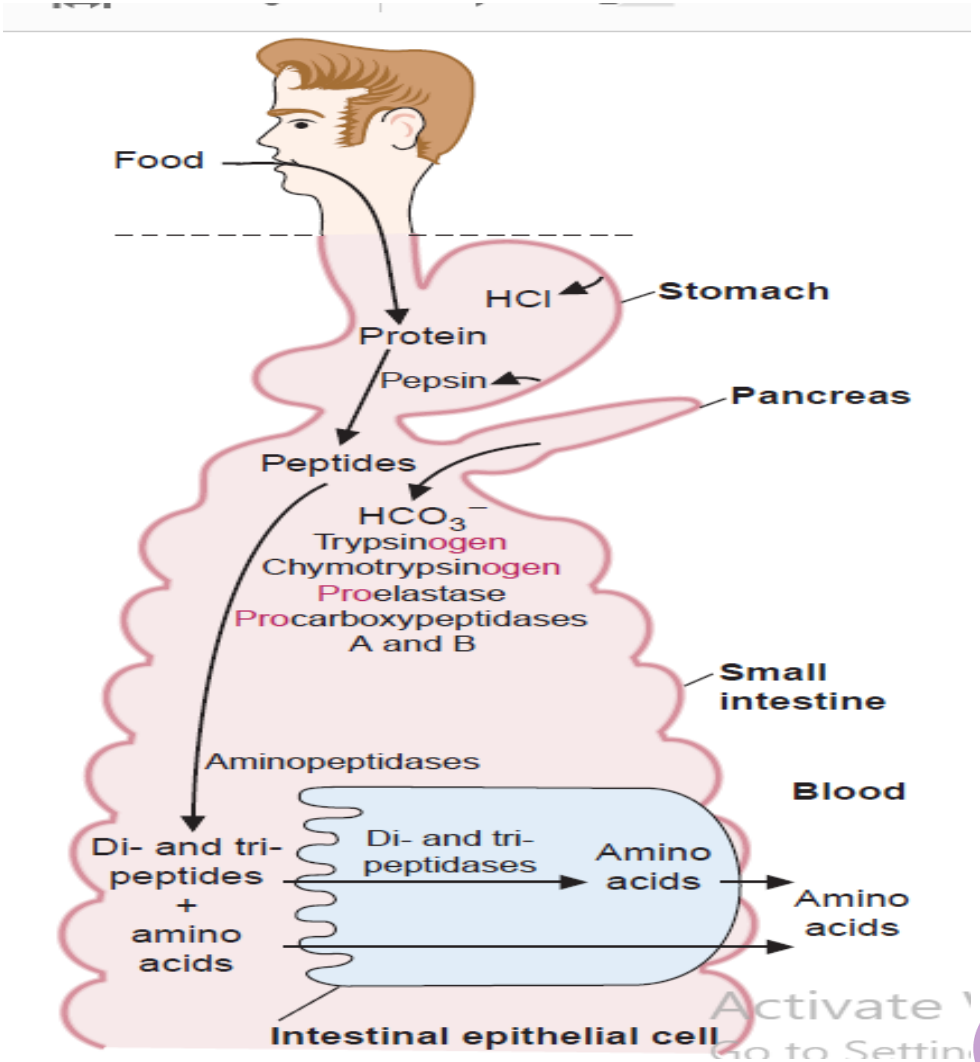
LO1 Stage 1 catabolism of dietary protein



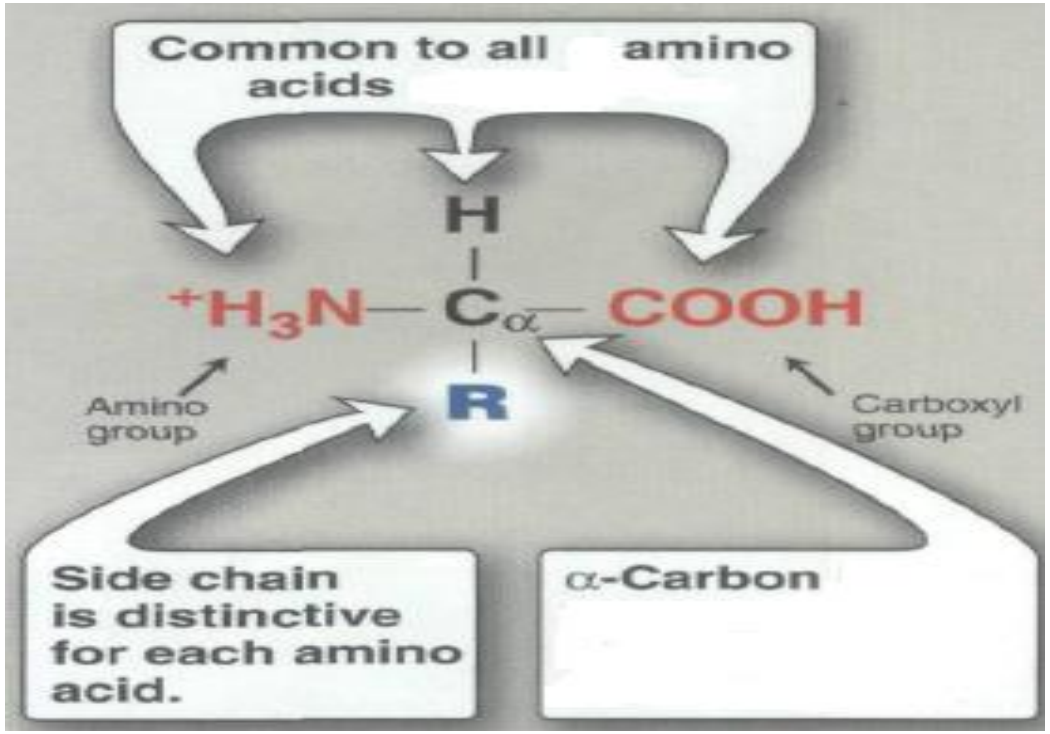
LO1

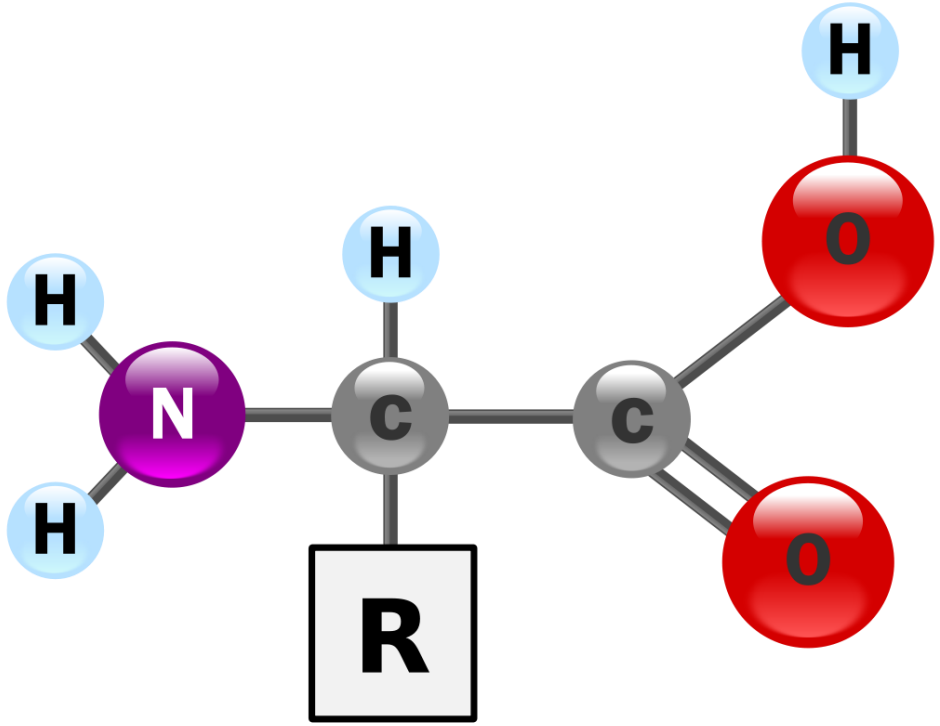
Stage 1 catabolism of protein



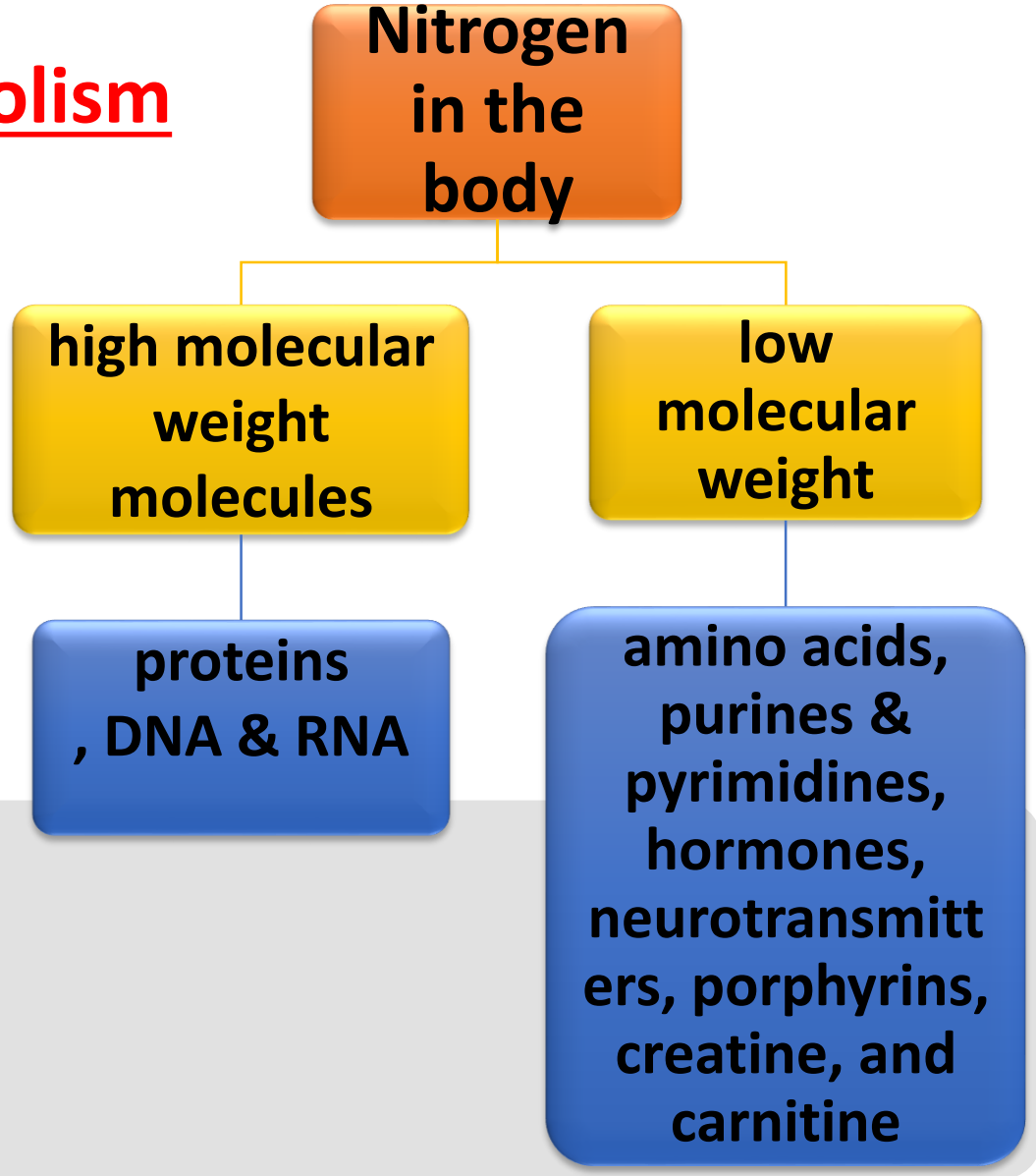


LO1


Common to all amino acids
H
+H3N— Cα— COOH
R
Amino group
Carboxyl group
Side chain is distinctive for each amino acid.
α-Carbon


H
O
H
H
N
C
C
O
H
R

LO1 Nitrogen metabolism



The total amount of nitrogen in the body (70kg male) is 2.0 kg (3% of the body weight)

LO1

Protein turnover

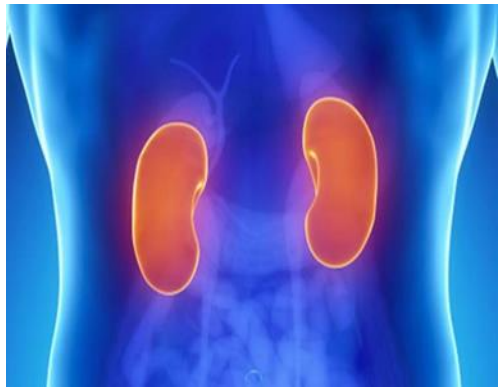
All body proteins undergo continuous breakdown & re-synthesis i.e. the turnover

The rate of turnover depend on protein and varies during growth (fast) and ageing (slows).

Normally the rate of protein breakdown **equals** the rate of re-synthesis

LO1 Nitrogen balance

- Most nitrogen enter the body as protein >90 % .
- Most nitrogen leaves the body in the urine as:
- Urea 85 %
- Creatinine 5 %
- Ammonia 3% and uric acid
- Some in sweat and faeces
- Some direct loss of protein (skin,hair,nail)



LO1

- **Positive N balance :**

Active growth

Pregnancy

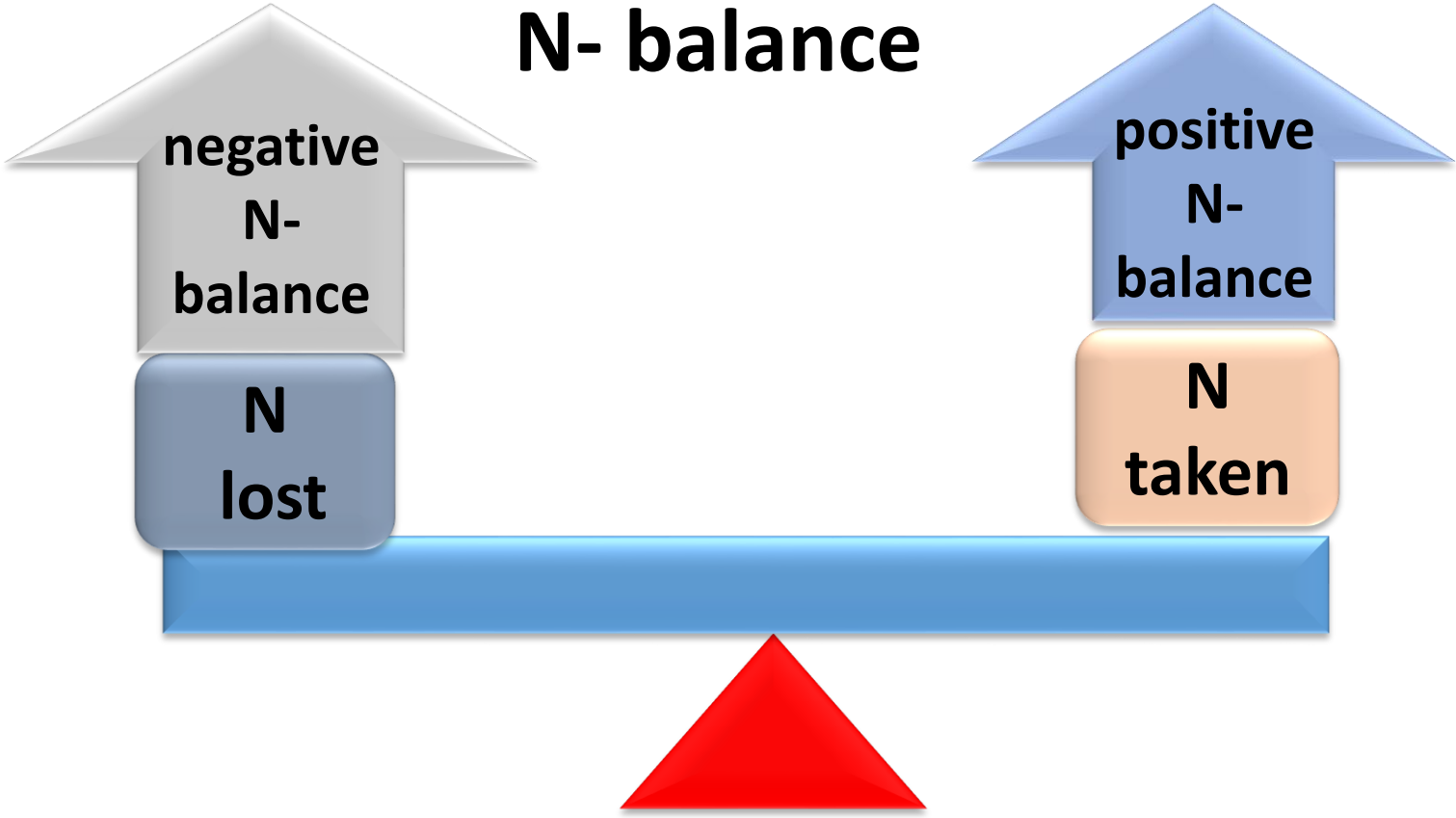
Tissue repair and convalescence

- **Negative N balance :**

Starvation

Malnutrition

Trauma.



LO 1 Stage 2 of metabolism

Free a.as are derived from dietary proteins or

from degradation of endogenous proteins

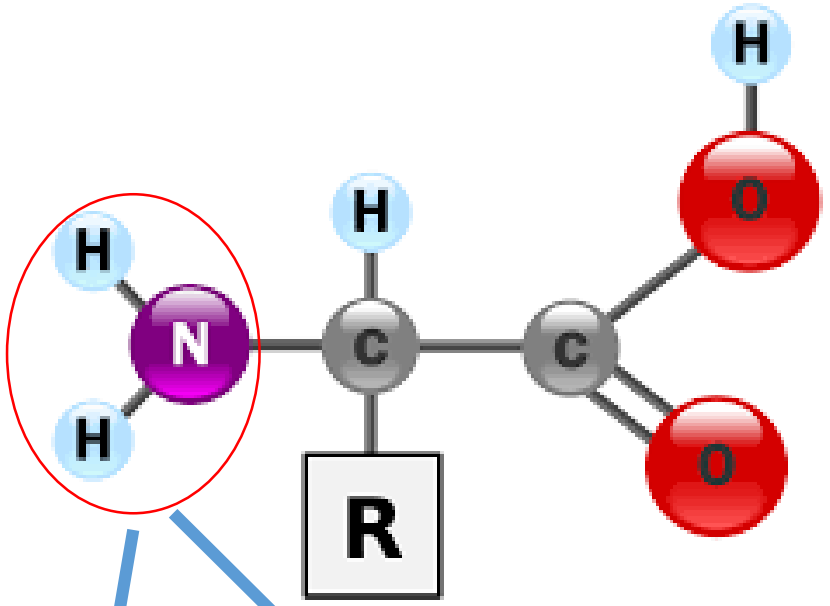
are metabolized in identical ways .

Their alpha amino nitrogen is first removed either by

Transamination or by oxidative and non oxidative deamination.

The resulting carbon skeleton is then degraded.

LO1 Stage 2 of metabolism



Aminotransferases

Alanine aminotransferase

Aspartate aminotransferase

amino acid oxidases

transamination

deamination

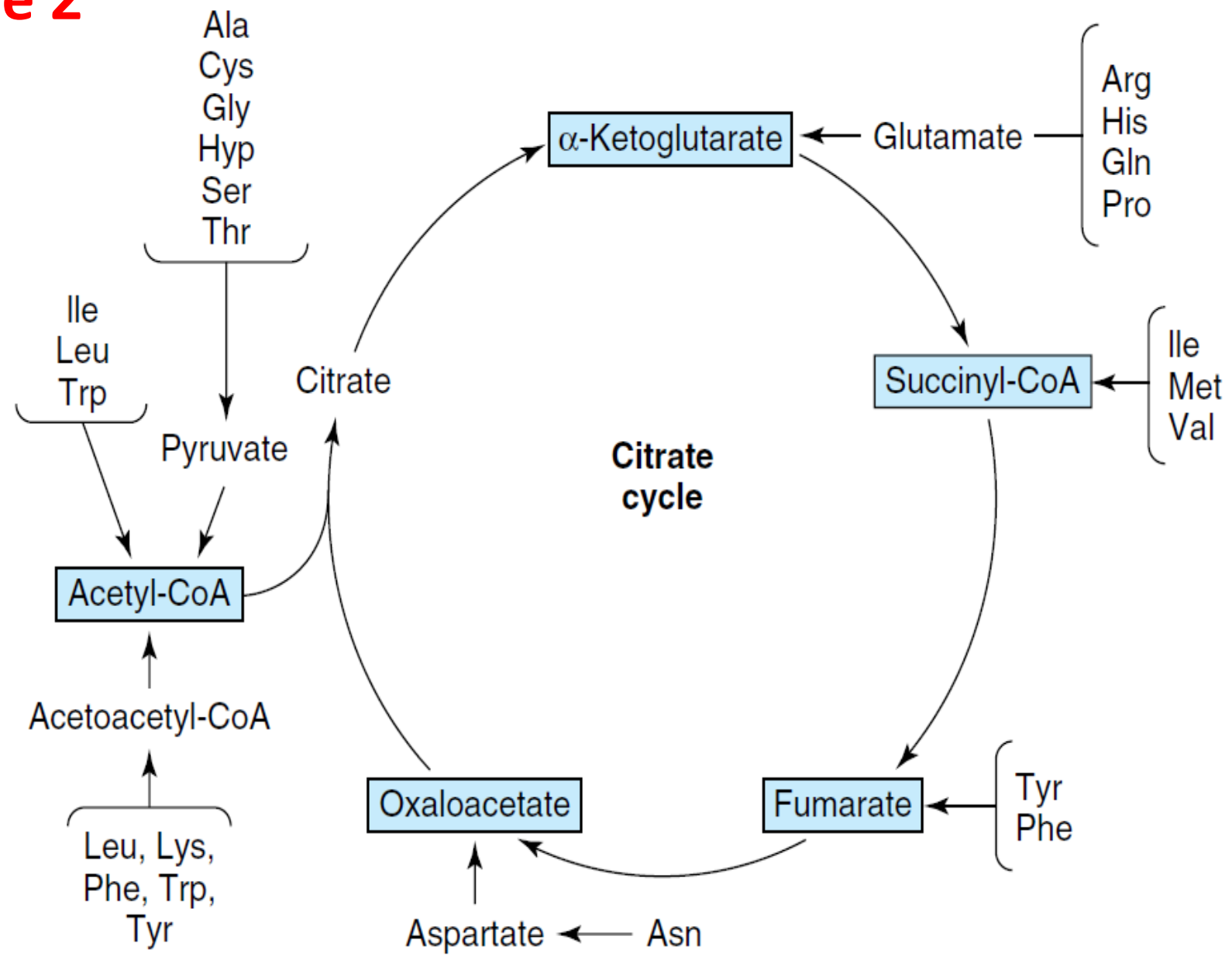
LO1 Stage 2 of metabolism

Catabolism of the carbon skeleton of amino acids

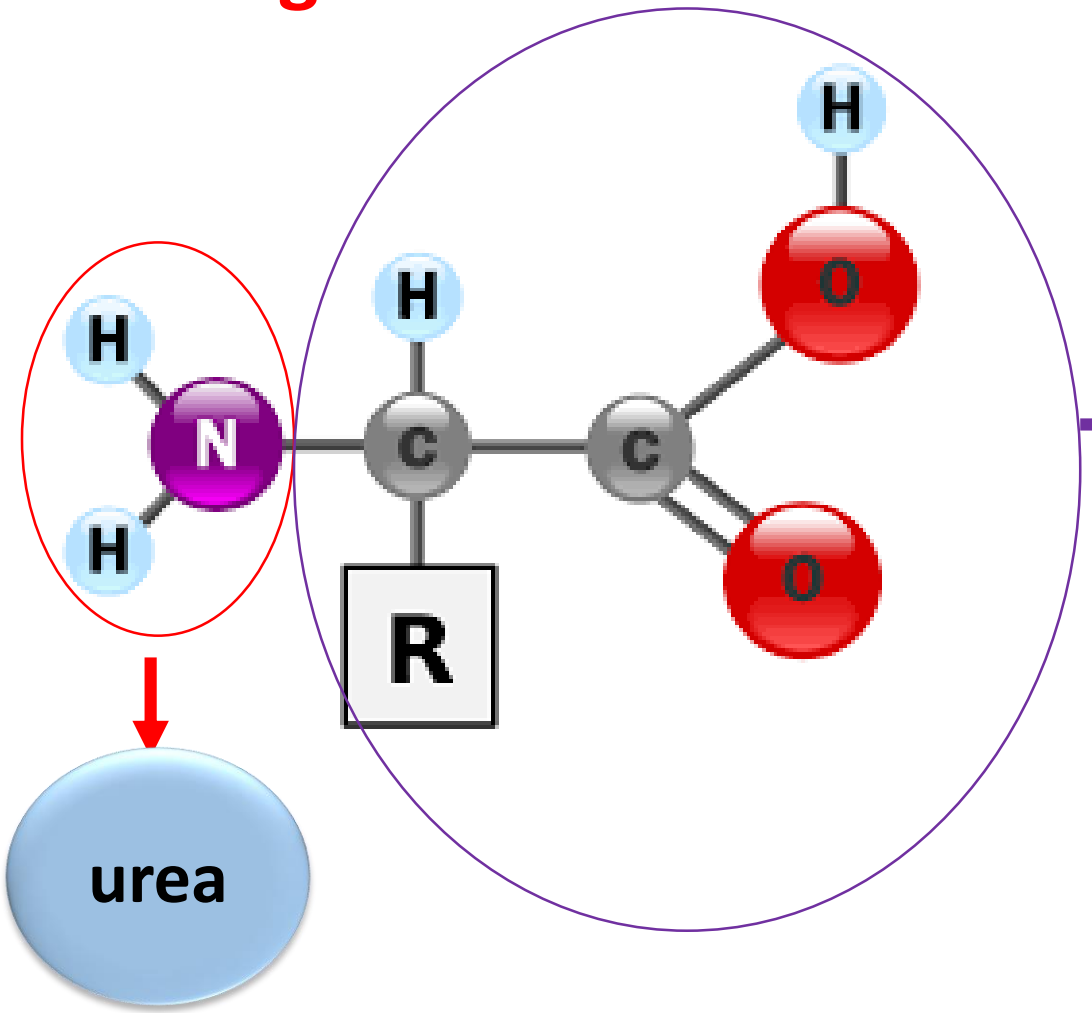
The hydrocarbon portion of a.as can be carried through a wide variety of pathways & utilized in the synthesis of numerous intermediates .

All a.as are ultimately convertible to either acetyl CoA , pyruvate , or intermediates of citric acid cycle .

LO1 Stage 2


Ala
Cys
Gly
Hyp
Ser
Thr
Ile
Leu
Trp
Pyruvate
Citrate
α-Ketoglutarate
Glutamate
Arg
His
Gln
Pro
Succinyl-CoA
Ile
Met
Val
Citrate cycle
Acetyl-CoA
Acetoacetyl-CoA
Leu, Lys,
Phe, Trp,
Tyr
Oxaloacetate
Fumarate
Tyr
Phe
Aspartate
Asn

LO1 Stage 2 catabolism of amino acids



pyruvate, oxaloacetate, fumarate, ketoglutarate, succinate, acetyl-coA.

LO1 Stage 2 of a.as. catabolism

metabolic intermediates ex. pyruvate, oxaloacetate, alpha ketoglutarate, succinate & fumarate → glucose.

These a.as called glucogenic a.as.

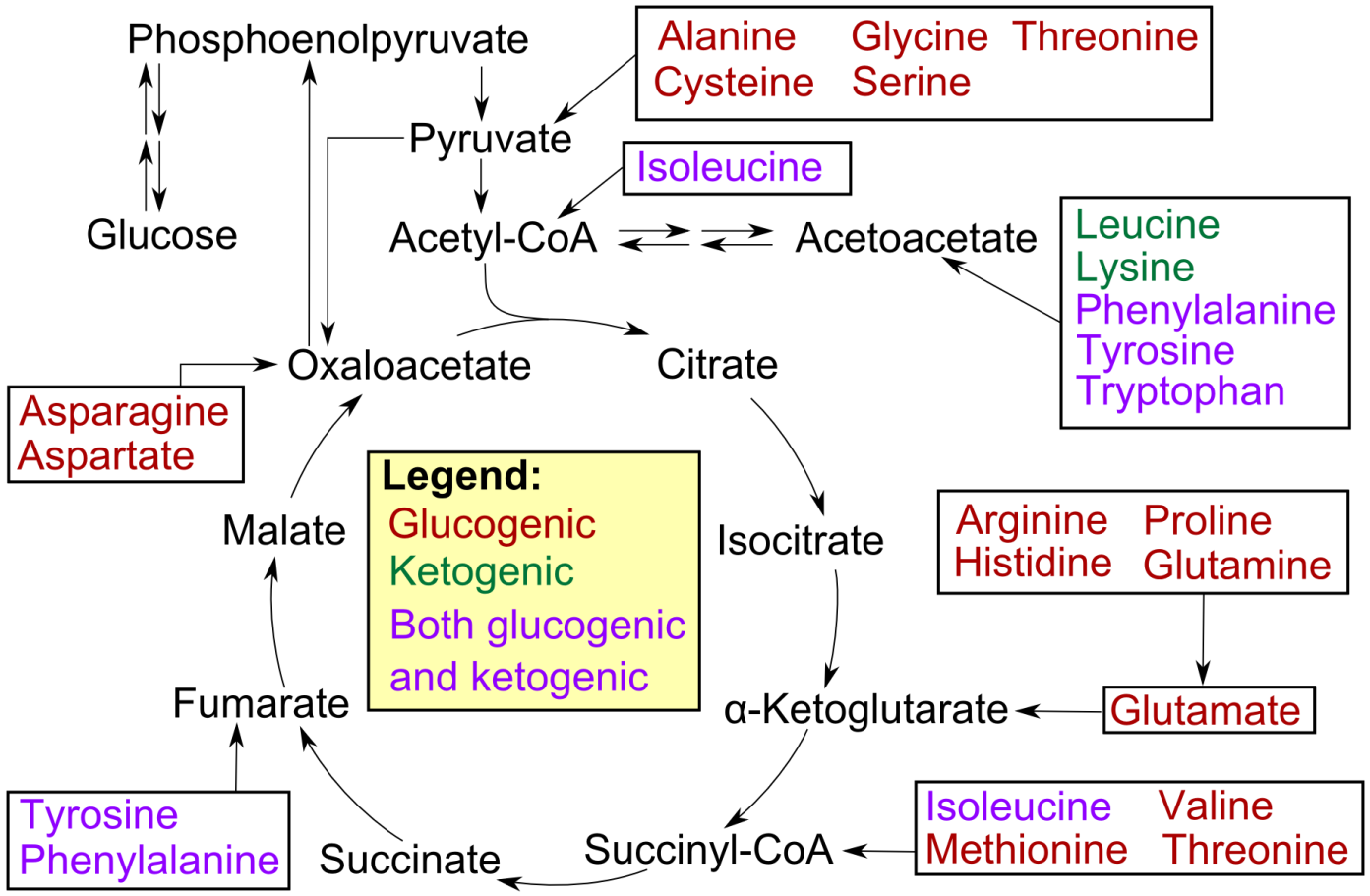
Other intermediates ex.acetoacetate or acetyle Co-A →

Ketone bodies.

These a.as. Called ketogenic a.as.

Some a.as. Are both glucogenic and ketogenic

LO1 Stage 2 of a.as. catabolism



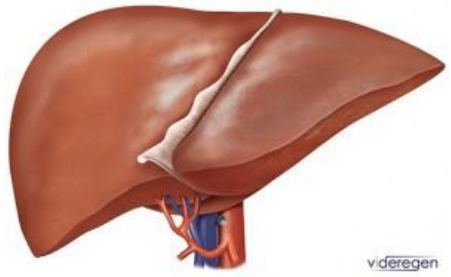
LO1

Glucogenic	Ketogenic	Glucogenic and Ketogenic
Alanine Arginine Asparagine Aspartate Cysteine Glutamate Glutamine Histidine Glycine Methionine Proline Serine Threonine Valine	Leucine Lysine	Isoleucine Phenylalanine Tryptophan Tyrosine

LO1

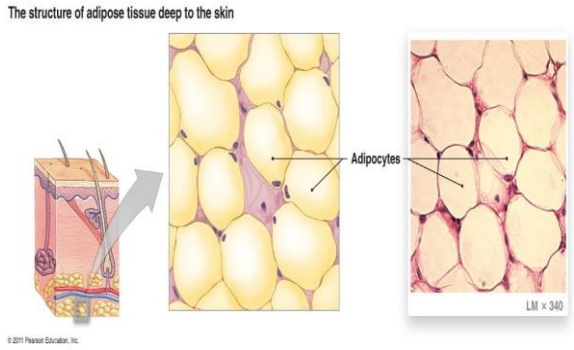
Cortisol H.
(Proteolysis)

Insulin, growth H.
(Protein synthesis)



Amino acid

Amino acid



LO1

Synthesis of N-compounds

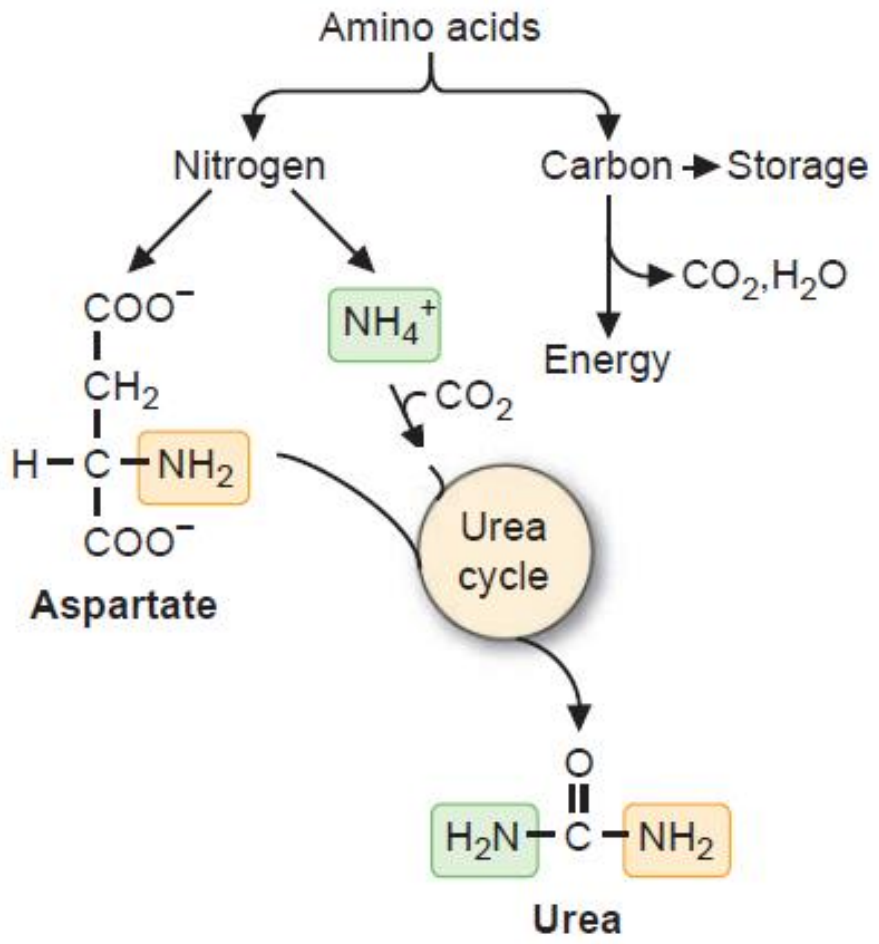
- Tryptophan → 5-hydroxytryptamine(5-HT) a neurotransmitter.
- Histidine → histamine a local mediator.
- Tyrosine → melanine,thyroid hormone & catecholamines.
- Glycine → purine,glutathione,porphyrins & creatine.

LO2 Ammonia metabolism

- **Most (98.5%) of the ammonia in the body is in the form of the ammonium ion .**
- **Hyperammonaemia**

CNS toxicity

??



Sources of ammonia

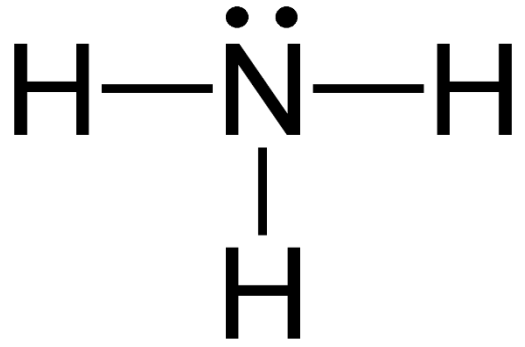
LO2

1- Oxidative deamination by both enzymes :

a- glutamate dehydrogenase.

Glutamate +NAD+ +H2O ⟷ α ketoglutarate+NH4+NADH+H

b-Action of amino acid oxidase.



2-Non oxidative deamination.

LO2

3- Hydrolysis of ketoglutaramic & ketosuccinamic acid ,belong to class of organic compounds known as short chain keto acid.

4- Hydrolysis of glutamine to glutamate by glutaminase.

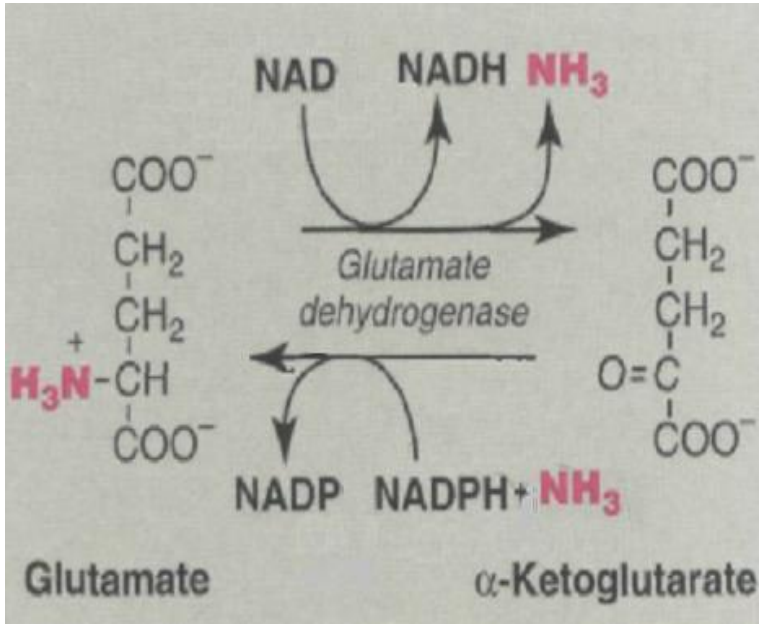
5-Hydrolysis of asparagine to aspartate by asparginase.

LO2

There are three mechanisms for the disposal of potentially toxic NH3 :

1- Interaction with alpha ketoglutarate to form glutamate (glutamate dehydrogenase).

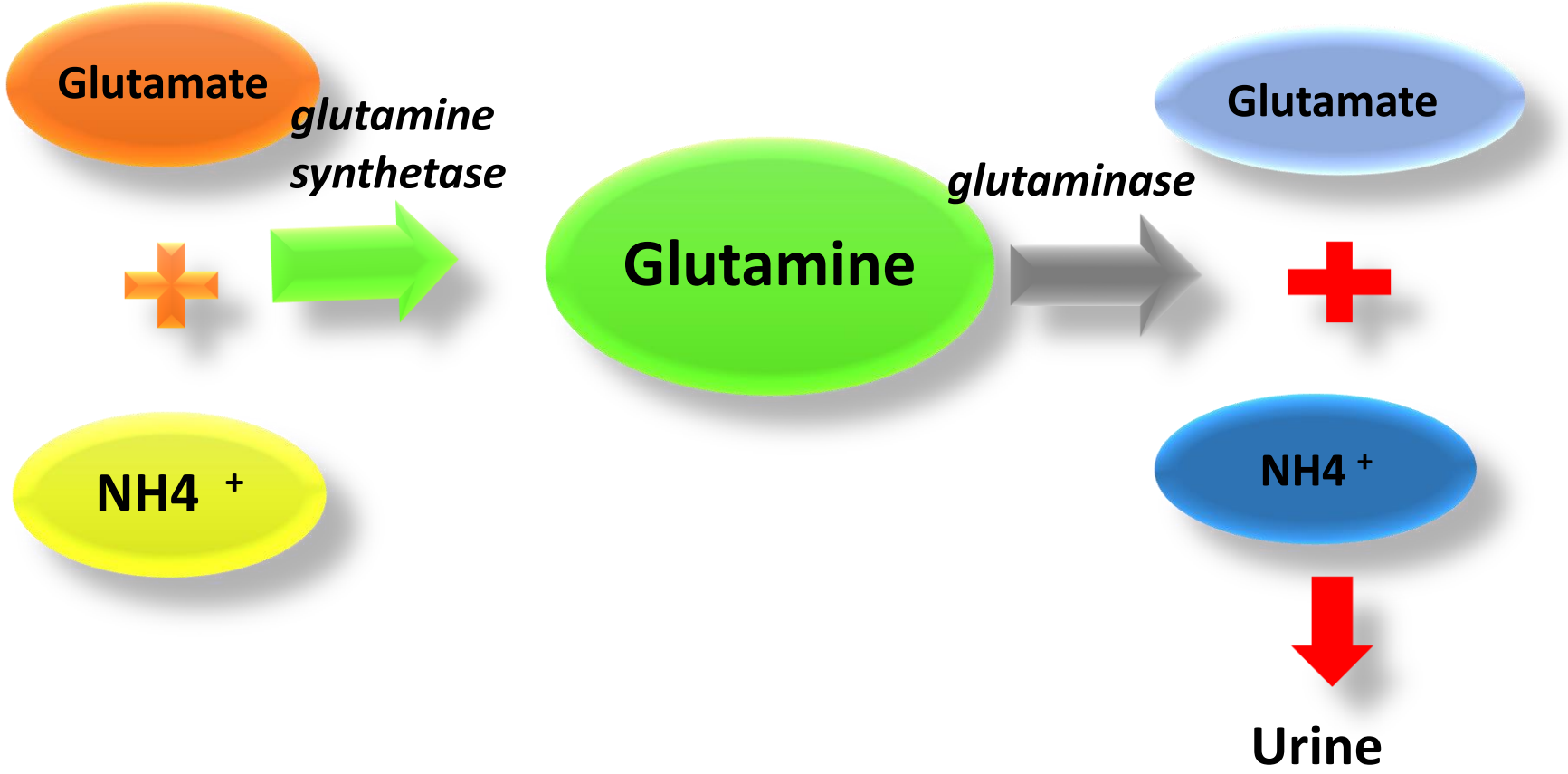
2- Synthesis of glutamine from glutamate.



LO2

Glutamine synthesis

liver and kidney



LO2

3- Synthesis of carbamoyl phosphate (in the liver)

$$CO_2 + NH_3 + 2ATP \xrightarrow[\text{synthetase}]{\text{car. Phosphate}} \text{carbamoyl phosphate} + 2ADP + Pi$$

*Ammonia also can be directly excreted from the body in the urine.

LO2

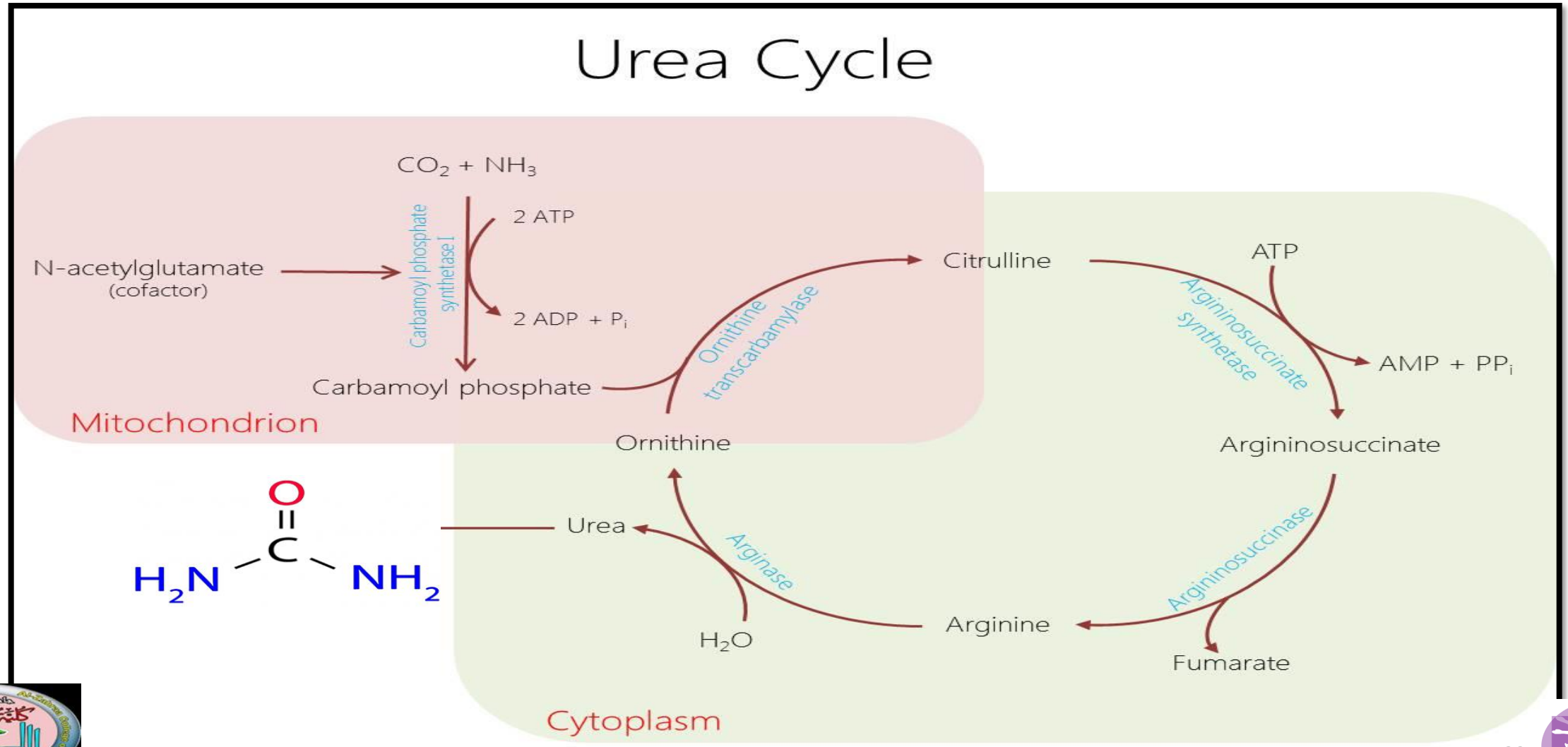
Urea synthesis

Urea is very soluble in water and can therefore be excreted in the urine.

It is nontoxic, metabolically inert and has a high nitrogen-content (47%) and is therefore a very effective way of disposing of unwanted nitrogen.

Urea is synthesized in the liver by the urea cycle (a series of 5 enzymes) and transported via the blood to the kidneys for excretion in urine

LO2
Urea cycle



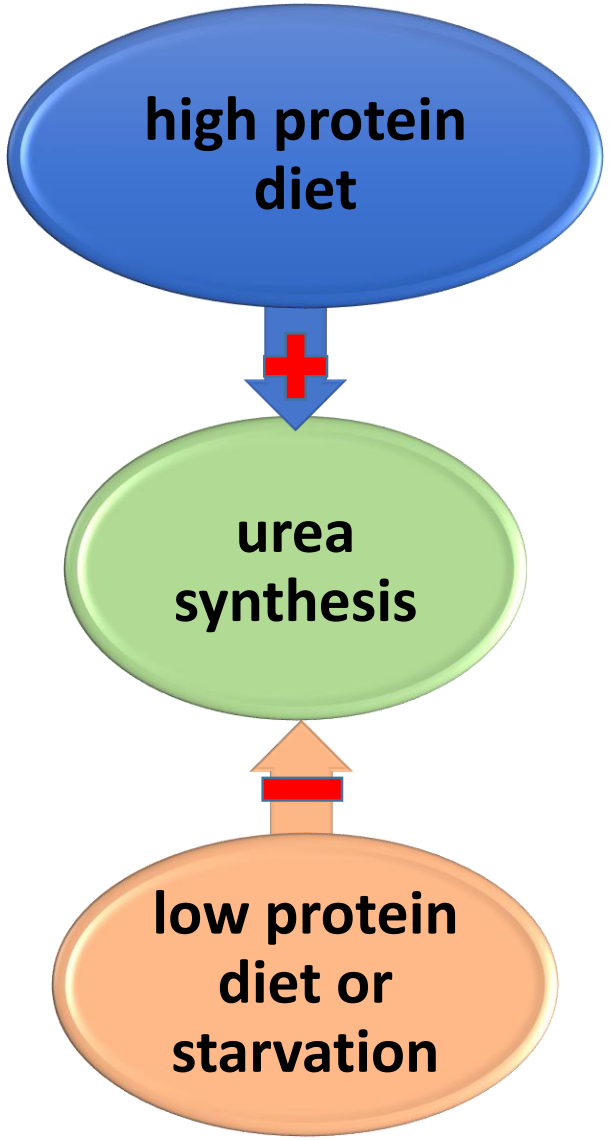
LO2

The overall reactions of the cycle are:

$HCO_3^- + NH_4^+ + aspartate + 3ATP \rightarrow CO(NH_2)_2 + fumarate + 2ADP + AMP + 4Pi$

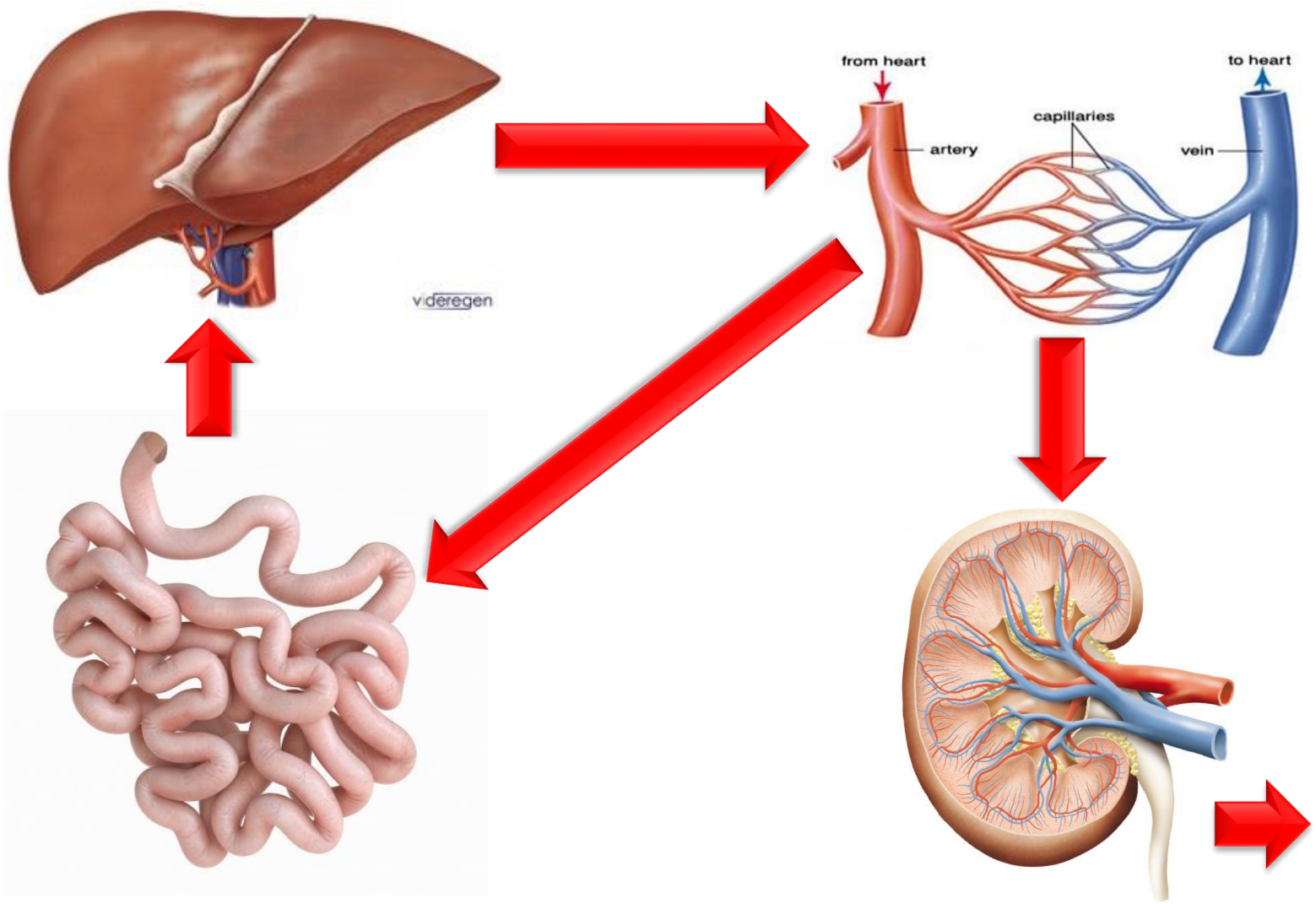
LO2 Regulation of urea synthesis

Explain why ,the treatment of starving individuals involve the gradual re-introduction of protein???



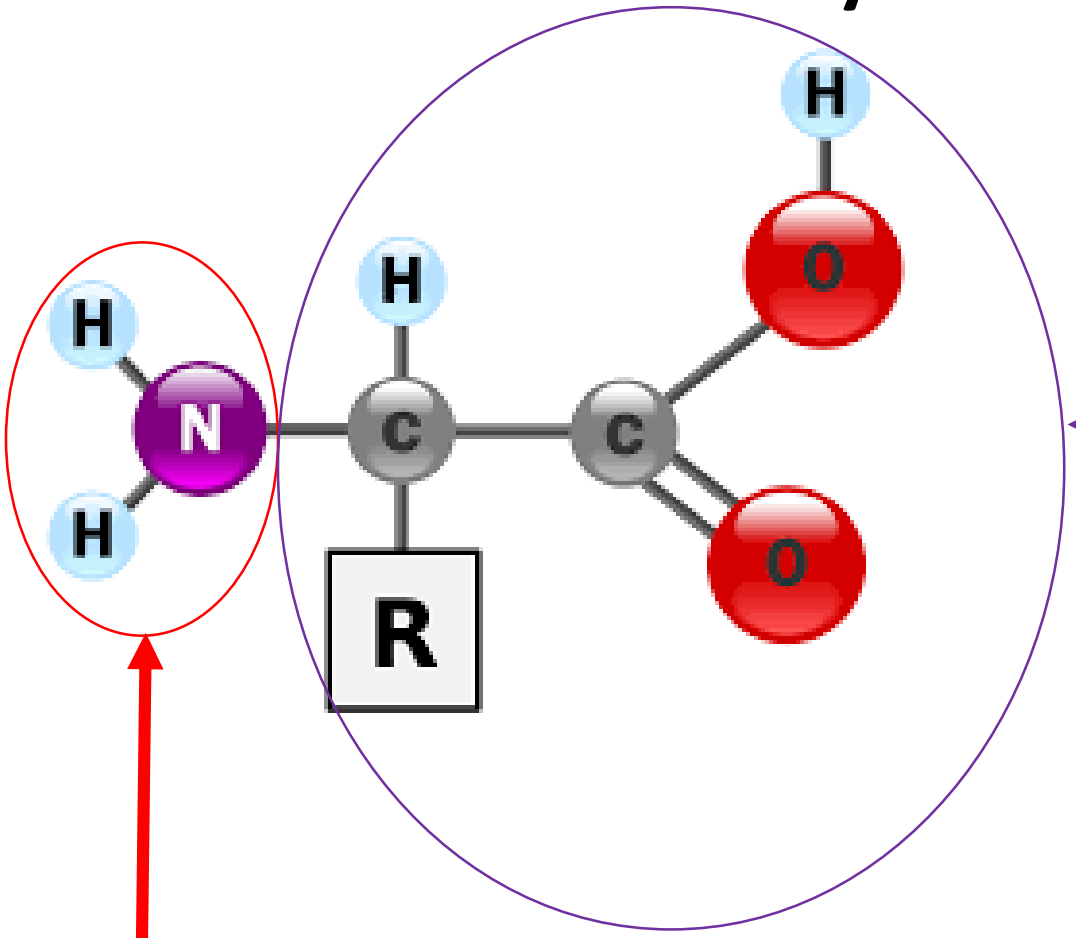
LO1

Metabolic fate of urea



LO2

Amino acid synthesis



glycolysis , pentose phosphate pathway, Krebs cycle

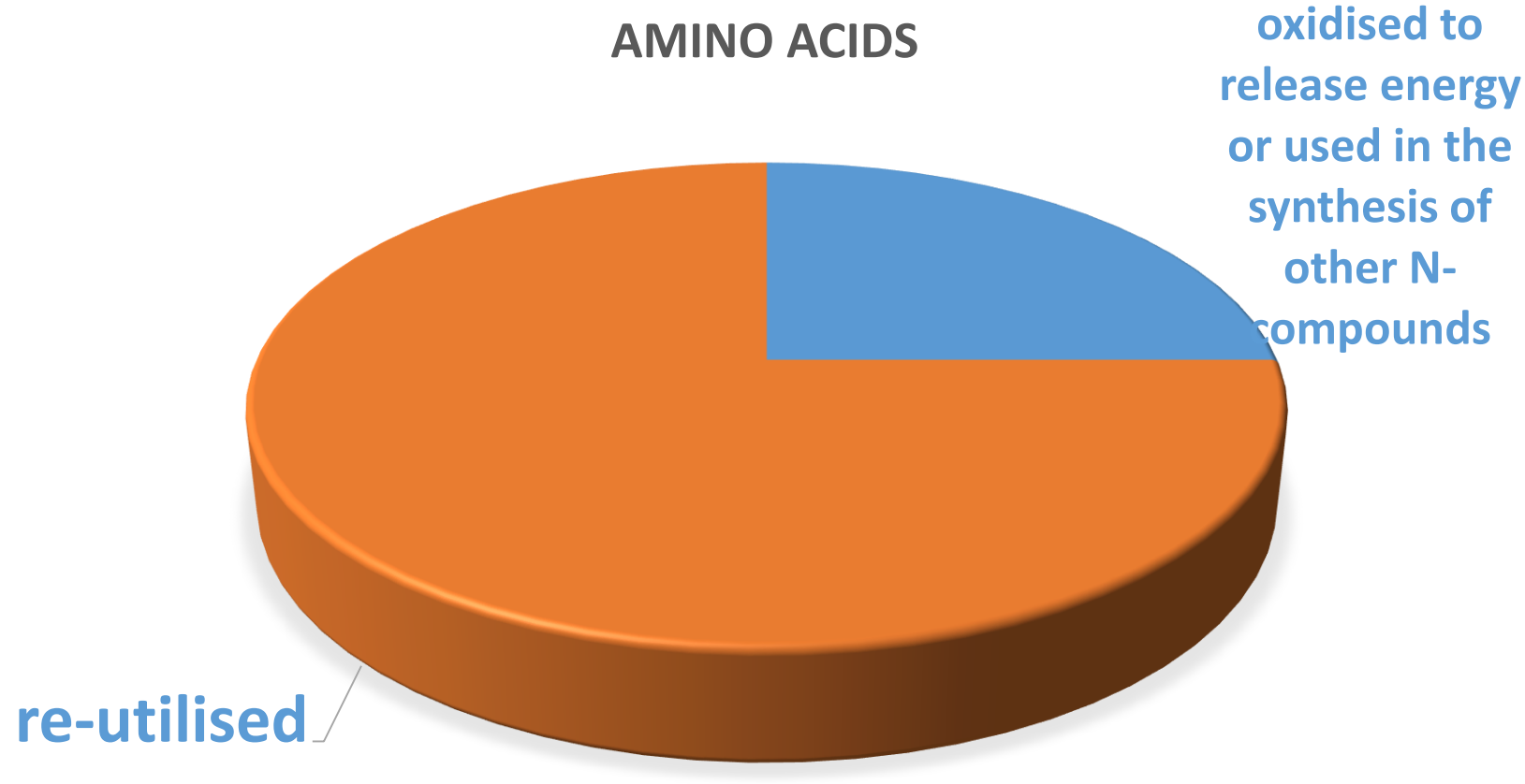
other amino acids by the process of transamination or from ammonia

LO1

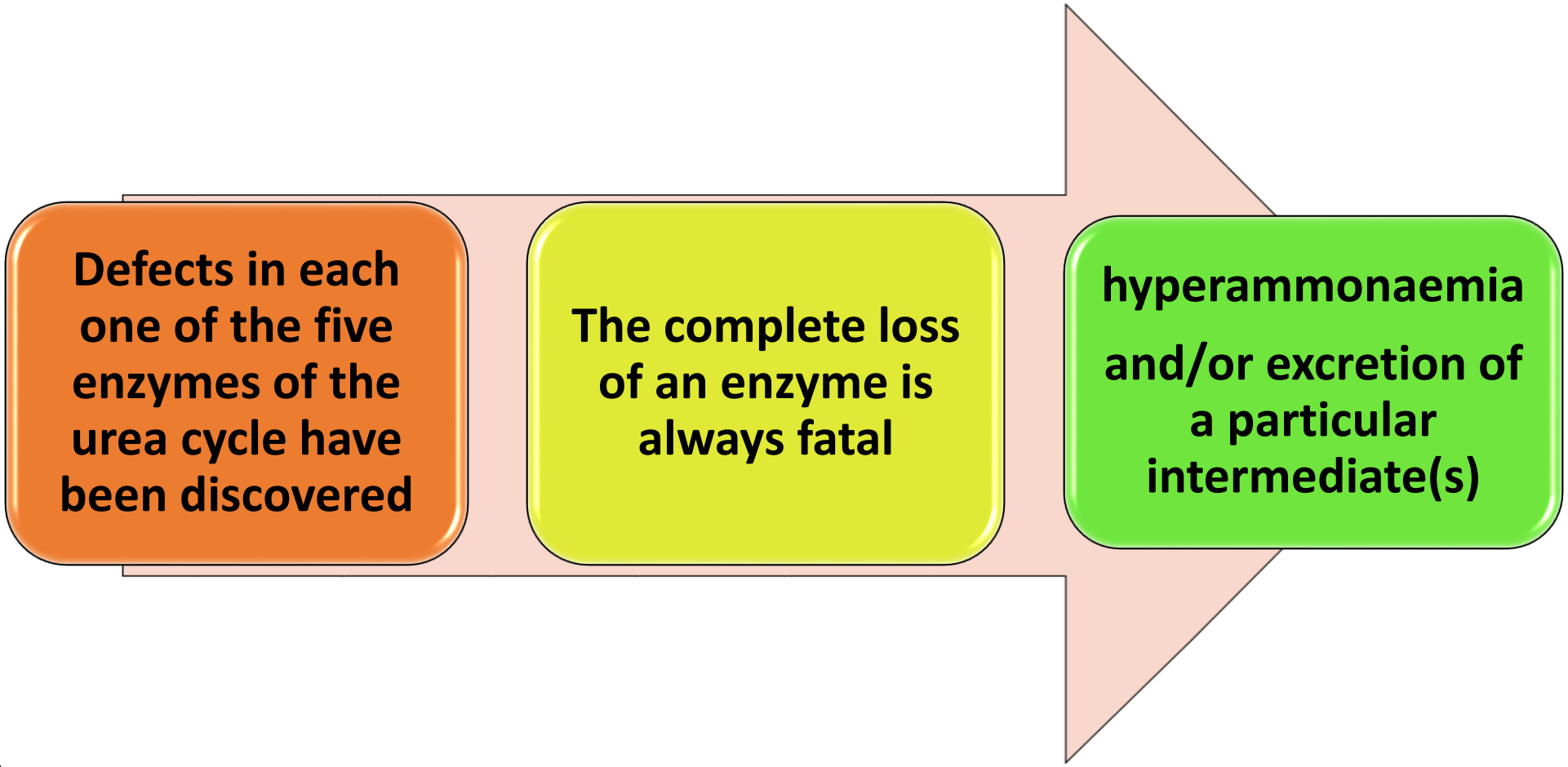
Essential	Conditionally Non-Essential	Non-Essential
Histidine	Arginine	Alanine
Isoleucine	Cystine	Asparagine
Leucine	Glutamine	Aspartate
Lysine	Glycine	Glutamate
Methionine	Proline	Serine
Phenylalanine	Tyrosine	
Threonine		
Tryptophan		
Valine		

LO2

Amino acid reutilization



LO2 Inherited diseases of the urea cycle



LO2

clinical picture

vomiting, lethargy & irritability

mental retardation, seizures, coma and eventually death.

Treatment

low protein diets

keto acids diets

LO3
The clinical relevance of measuring creatinine in blood and urine

- since almost all creatinine is filtered from the blood by the kidneys and released into the urine, blood levels are usually a good indicator of how well the kidneys are working.
- The quantity produced depends on the size of the person and their muscle mass. For this reason, creatinine concentrations will be slightly higher in men than in women and children.

LO3

- Blood creatinine measurements, along with age, weight, and sex, are used to calculate the estimated glomerular filtration rate (eGFR), which is used as a screening test to look for evidence of early kidney damage.
- Blood and urine creatinine levels may be used to calculate a creatinine clearance. This test measures how effectively the kidneys are filtering small molecules like creatinine out of the blood.

LO3

- Urine albumin/creatinine ratio (ACR). This more accurately determines how much albumin is escaping from the kidneys into the urine.
- It is used to screen people with chronic conditions, such as diabetes and high blood pressure (hypertension) that put them at an increased risk of developing kidney disease.

LO4

Disorders of amino acids metabolism

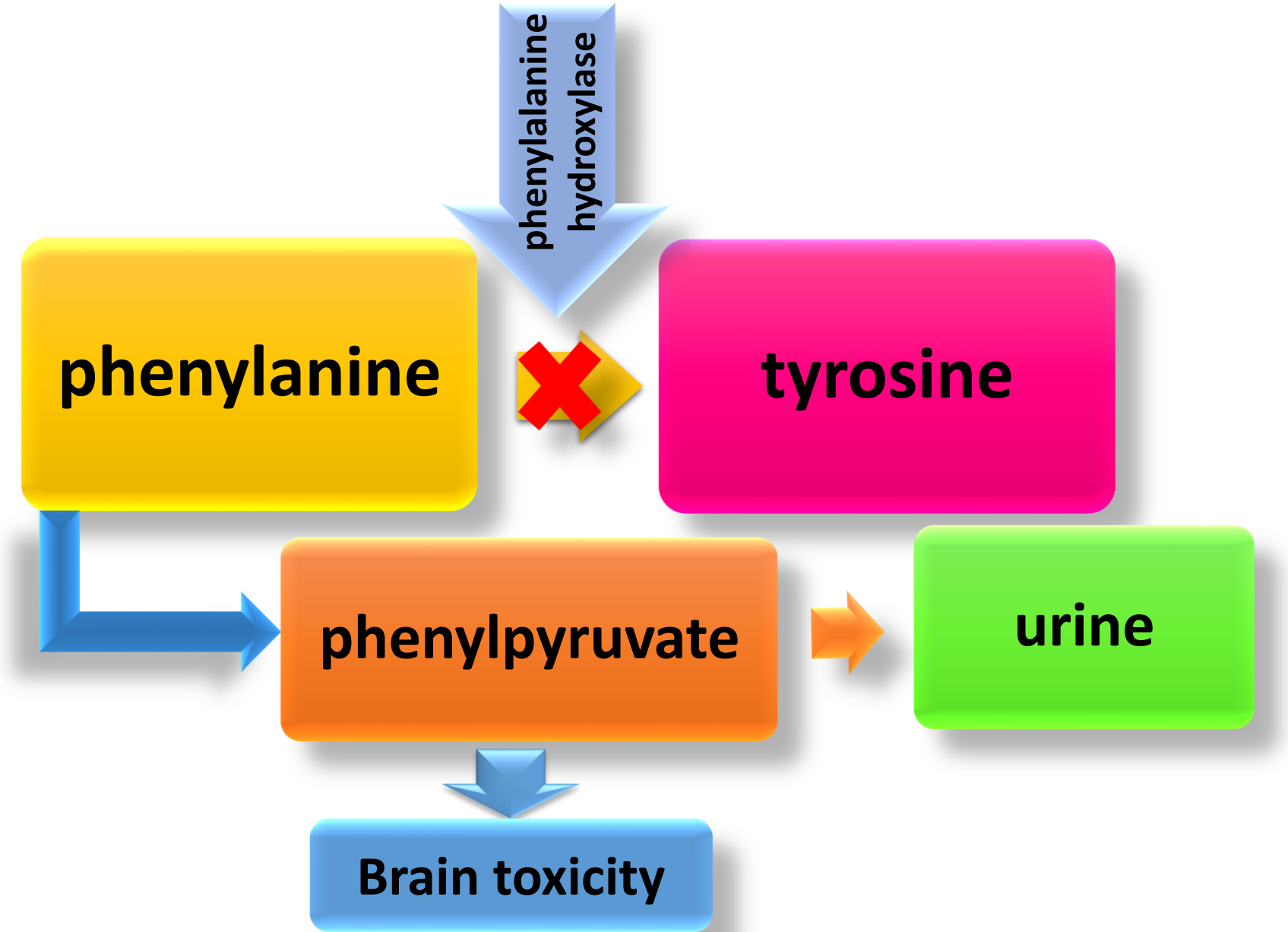
Phenylketonuria

Impaired ability to convert phenylalanine to tyrosine due to deficiency of phenylalanine hydroxylase .

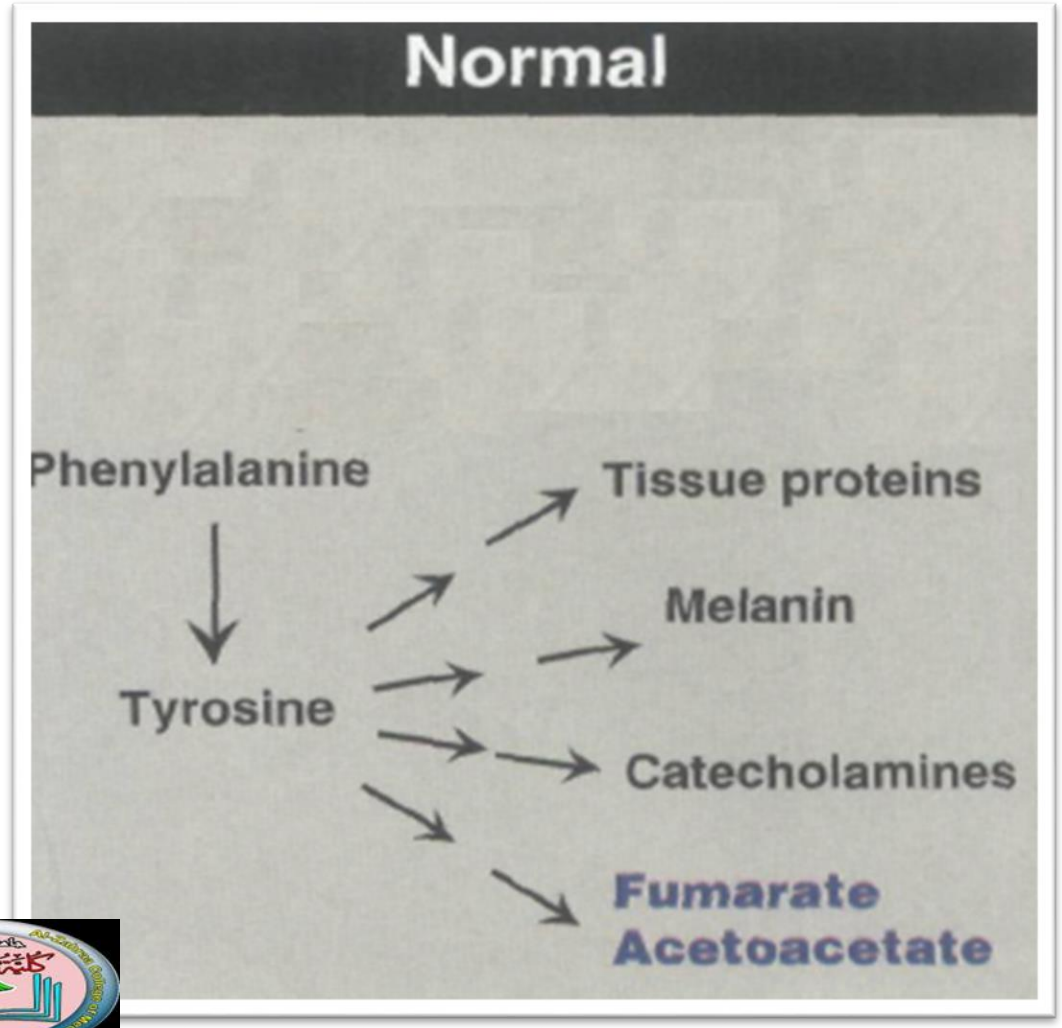
is the most common clinically encountered inborn error of amino acid Metabolism.

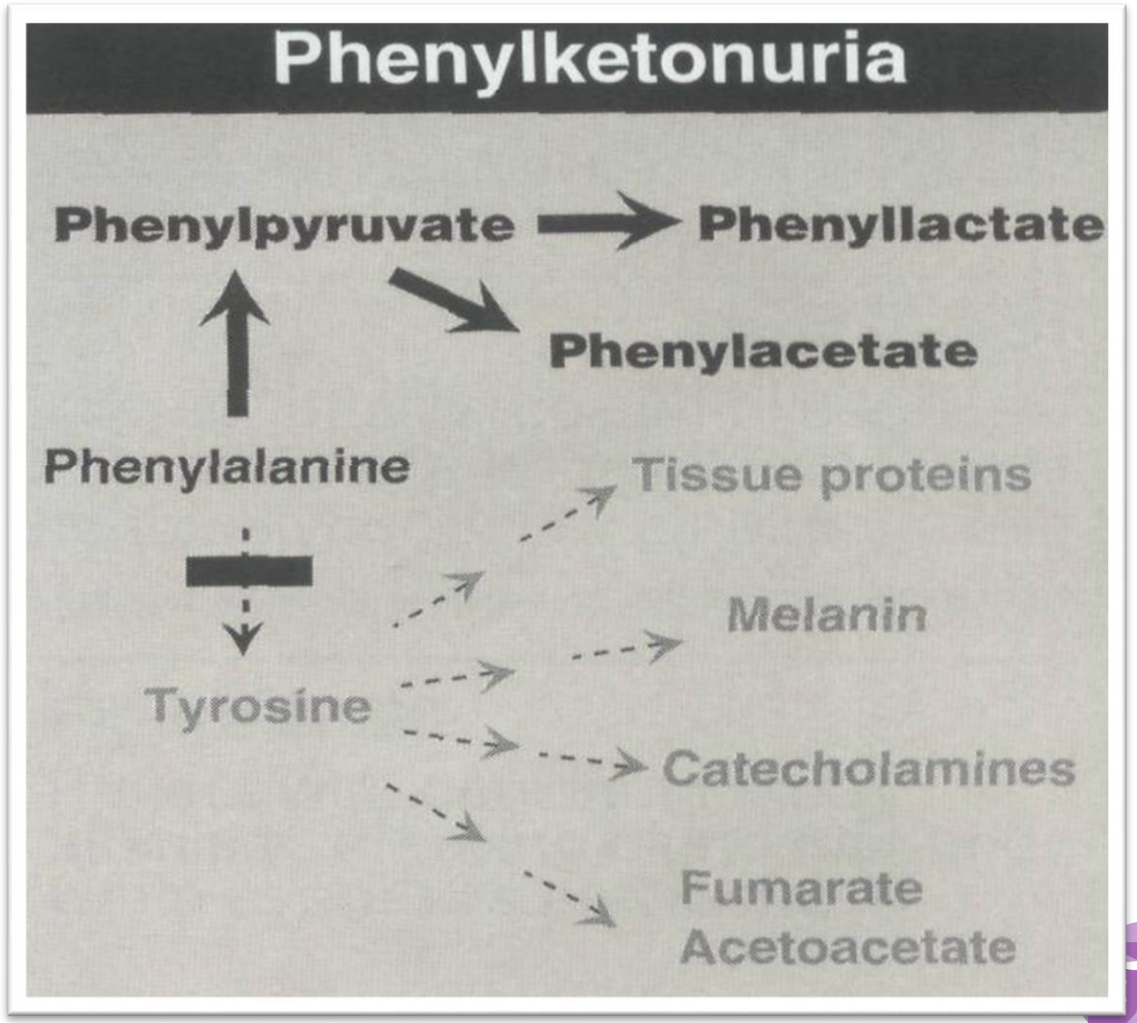
LO4

Phenylketonuria (PKU)



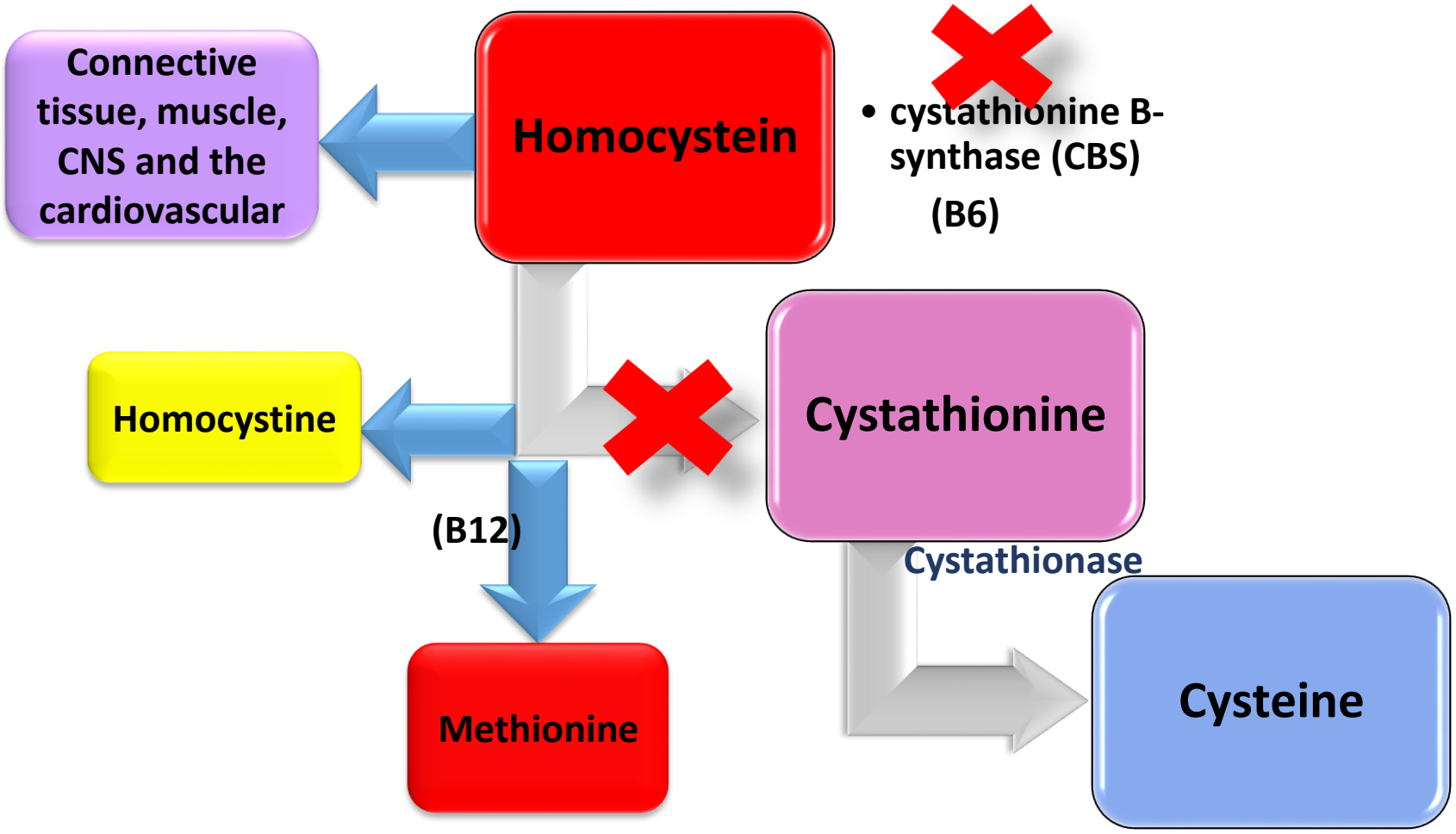
LO4


Normal
Phenylalanine
Tissue proteins
Melanin
Tyrosine
Catecholamines
Fumarate
Acetoacetate


Phenylketonuria
Phenylpyruvate
Phenyllactate
Phenylacetate
Phenylalanine
Tissue proteins
Melanin
Tyrosine
Catecholamines
Fumarate
Acetoacetate

LO4

Homocystinuria




Thank
You