Essential amino acids :

Lysine, Leucine, Isoleucine, Valine, Methionine, Phenylalanine, Threonine, Tryptophan

Nonessential amino acids:

serine, tyrosine, Alanine, glycine, aspartate , glutamate, aspargineproline , glutamine, cysteine ,

(Histidine & arginine are semi essential. They are essential only for infants growth, but not for old children or adults where in adults histidine requirement is obtained by intestinal flora & arginine by urea cycle)

Glucogenic	***Ketogenic***	***Glucogenic&Ketogenic***
Ala, Ser, Gly, Cys, Arg, His, Pro, Glu, Gln, Val, Met, Asp, Asn.	Leu , Lys	Phe,Tyr,Trp,Ile,Thr

Nitrogen Balance (NB)

Nitrogen balance is a **comparison between**

Nitrogen intake (in the form of dietary protein)

and

Nitrogen loss (as **undigested protein** in feces , **NPN** as urea, ammonia, creatinine & uric acid in urine, sweat & saliva & **losses** by hair, nail, skin**)**.

- NB is important **in** defining
  1. overall protein metabolism of an individual
  2. nutritional nitrogen requirement.

Three states are known for NB:

a)**Normal adult:** will be in nitrogen equilibrium,

Losses = Intake

b)**Positive Nitrogen balance:**

Nitrogen intake more than losses **(High formation of tissue proteins) occurs in growing children, pregnancy, lactation and convulascence.**

C)**Negative Nitrogen balance:**

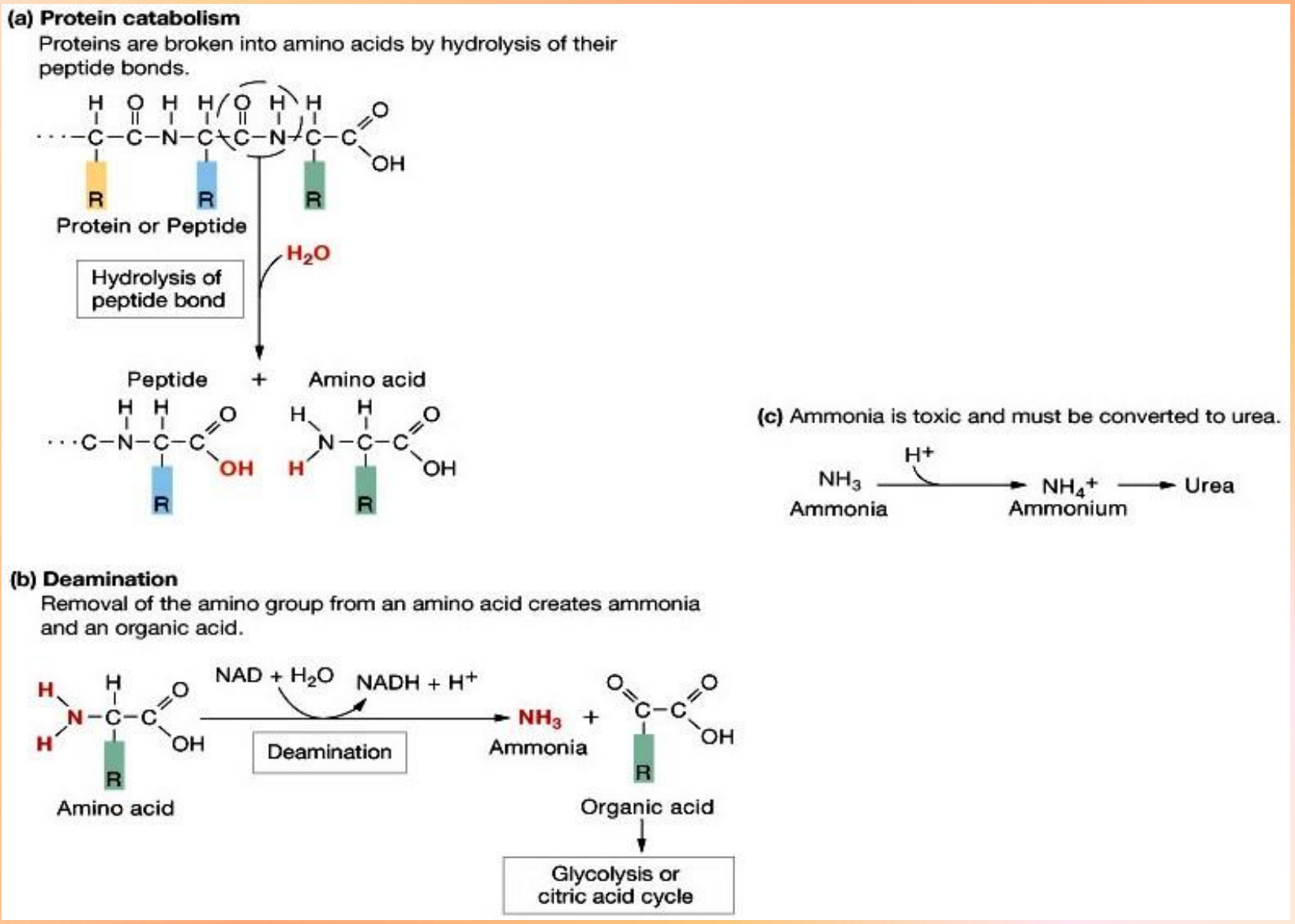
Nitrogen losses more than intake

occurs in:- (Low intake of proteins**)** in **starvation, malnutrition, GIT diseases**

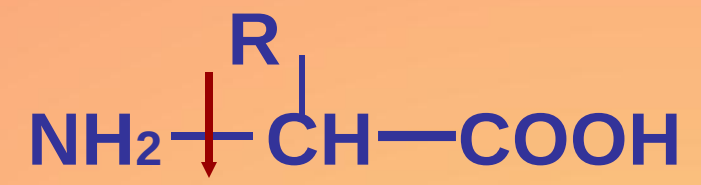
- (High loss of tissue proteins) in **wasting diseases like burns, hemorrhage& kidney diseases with albuminurea**

- (High breakdown of tissue proteins

Protein Catabolism

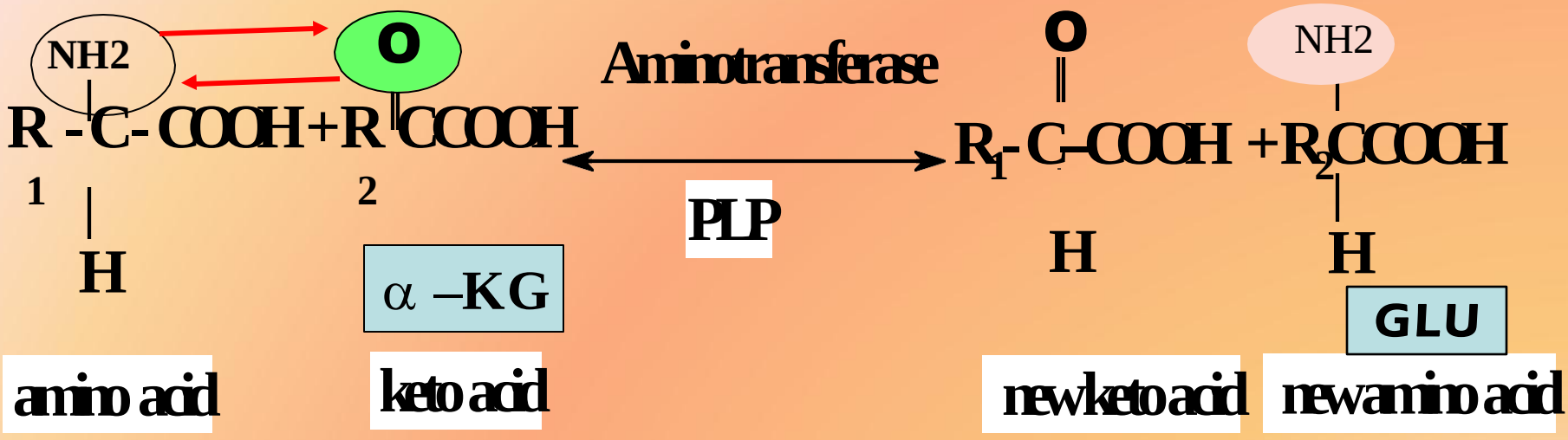


Metabolism OF AMINO ACIDS:



1. **Removal of amonia** by :
   - Deamination → **Oxidative deamination**
     1) glutamate dehydrogenase in mitochondria
     2) amino acid oxidase in peroxisomes
     Direct deamination (nonoxidative)
     1) dea. by dehydration ($-H_2O$)
     2) dea. by desulhydration ($-H_2S$)
   - Transamination (GPT & GOT)
   - and transdeamination.
2. **Fate of carbon-skeletons of amino acids**
3. **Metabolism of ammonia**

Transamination:



Aminotransferases are **active** both in cytoplasm and mitochondria e.g.:

1. Aspartate aminotransferase (AST), Glutamate oxaloacetate transaminase **(GOT)**

2. Alanine aminotransferase (ALT), Glutamate pyruvate transaminase, **(GPT)**

In all transamination reactions, **α-ketoglutarate** (**α –KG)** acts as amino group acceptor.

Most, but not all amino acids undergo transamination reaction with few exceptions **(lysine, threonine and imino acids)**

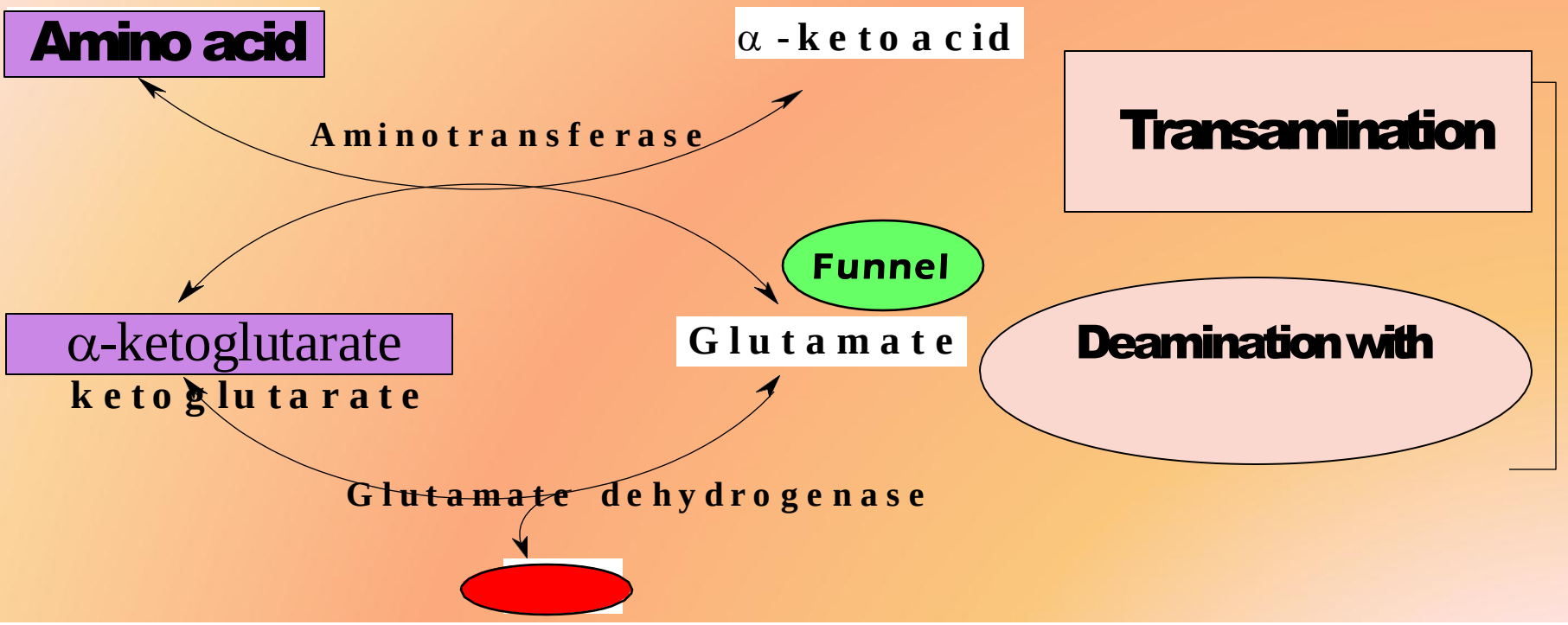
Metabolic Significance of Transamination Reactions

- It is an **exchange of amino nitrogen** between the molecules without a net loss

This metabolically important because:

1) There is **no mechanism for storage** of a protein or amino acids.
2) In case of low energy (caloric shortage), the organism depends on **oxidation of the ketoacids** derived from transamination of amino acids.
3) It is important for formation of the **non-essential amino acids**

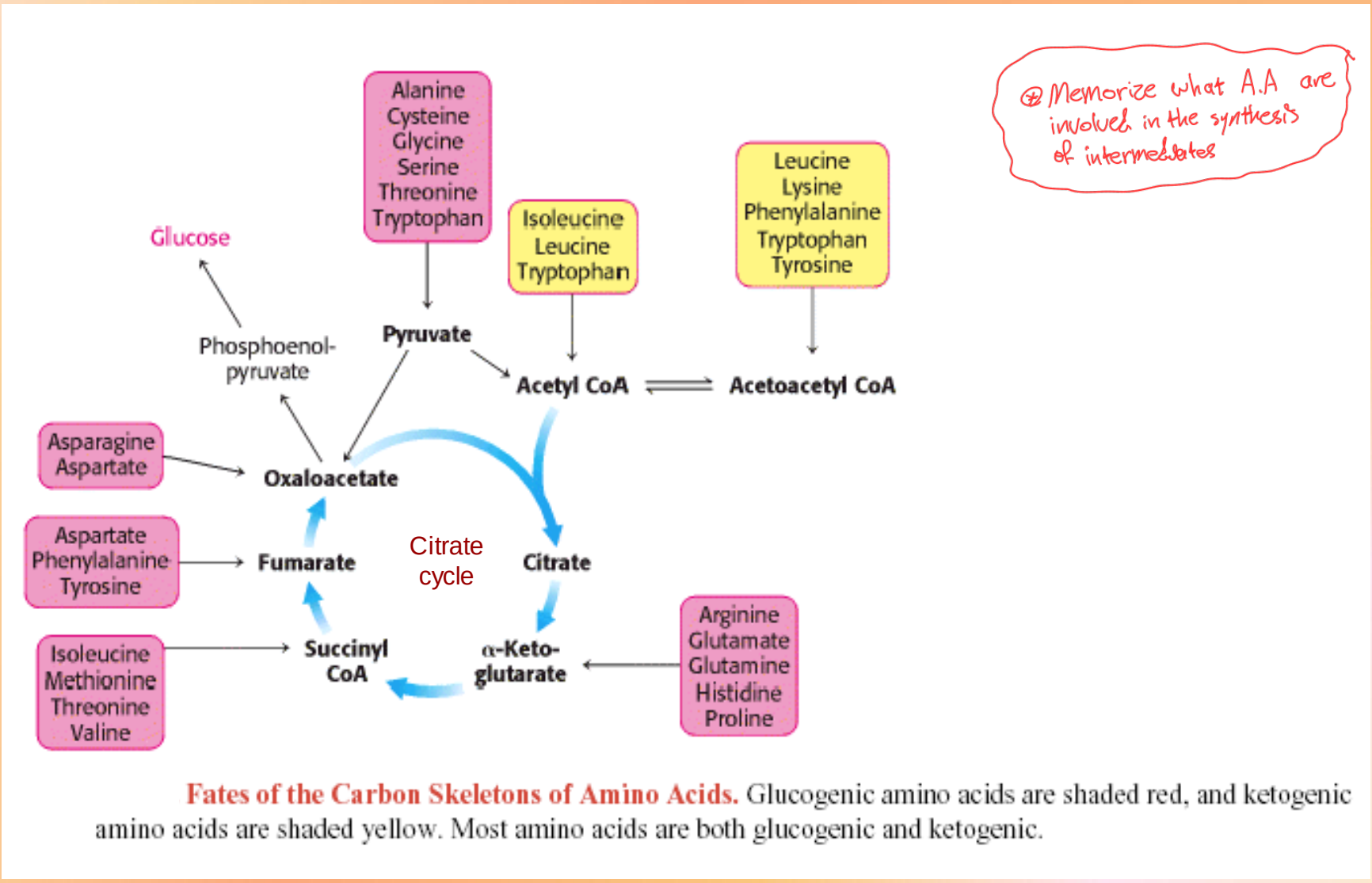
Transdeamination:



So… the most **important** and **rapid** way to deamination of amino acids **is first** transamination with α-ketoglutarate **followed** by deamination of glutamate.

Therefore **glutamate through transdeamination serves to a funnel ammonia from all amino acids.**

The common metabolic intermediates that arised from the degradations of amino acids are: acetyl CoA, pyruvate, one of the krebs cycle intermediates (α-ketoglutarate, succinyl CoA, fumarate& oxaloacetate)



Fates of the Carbon Skeletons of Amino Acids. Glucogenic amino acids are shaded red, and ketogenic amino acids are shaded yellow. Most amino acids are both glucogenic and ketogenic.

METABOLISM OF AMMONIA

Ammonia is formed in body from:

a) From amino acids: 1.Transdeamination in liver

2. amino acid oxidases and amino acid deaminases in liver and kidney.

b) Deamination of physiological amines: by monoamine oxidase (histamine, adrenaline, dopamine and serotonine)

C) Deamination of purine nucleotides: especially adenine nucleotides

d) Pyrimidine catabolism.

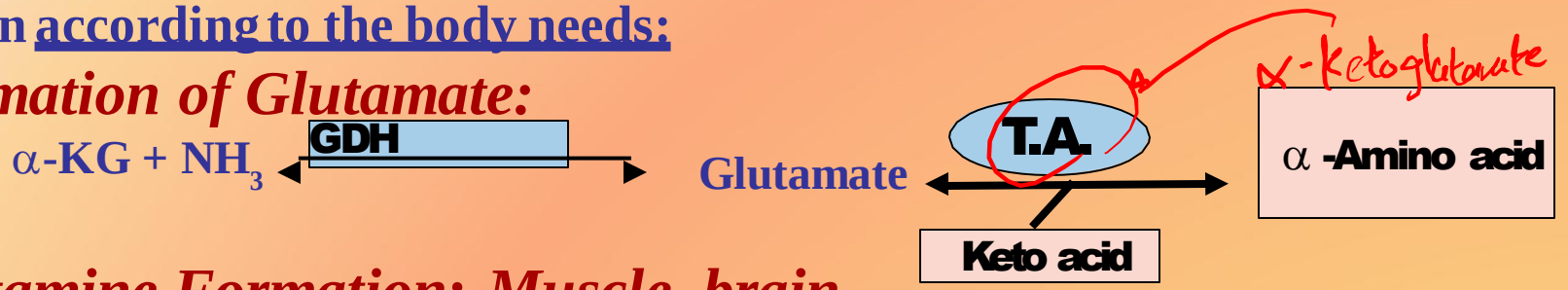
e) From bacterial action in the intestine **on dietary protein& on urea in the gut.**

NH_3 is also produced by glutaminase on glutamine .

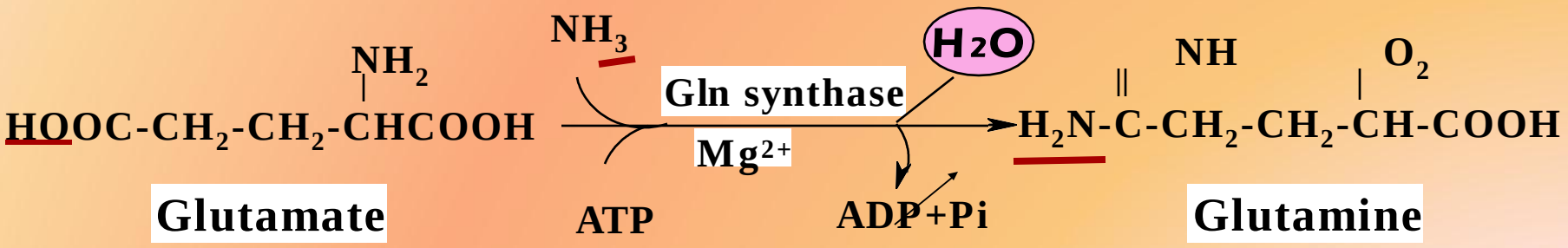
Metabolic Disposal of Ammonia

Ammonia is toxic to CNS, it is fixed into nontoxic metabolite for reuse or excretion according to the body needs:

a) Formation of Glutamate:



b) Glutamine Formation: Muscle, brain



Glutamine is storehouse of ammonia & transporter form of ammonia.

In brain, glutamine is the major mechanism for removal of ammonia while **in liver** is urea formation.

..**Circulating glutamine** is removed by kidney, liver and intestine where it is deamidated by glutaminase .

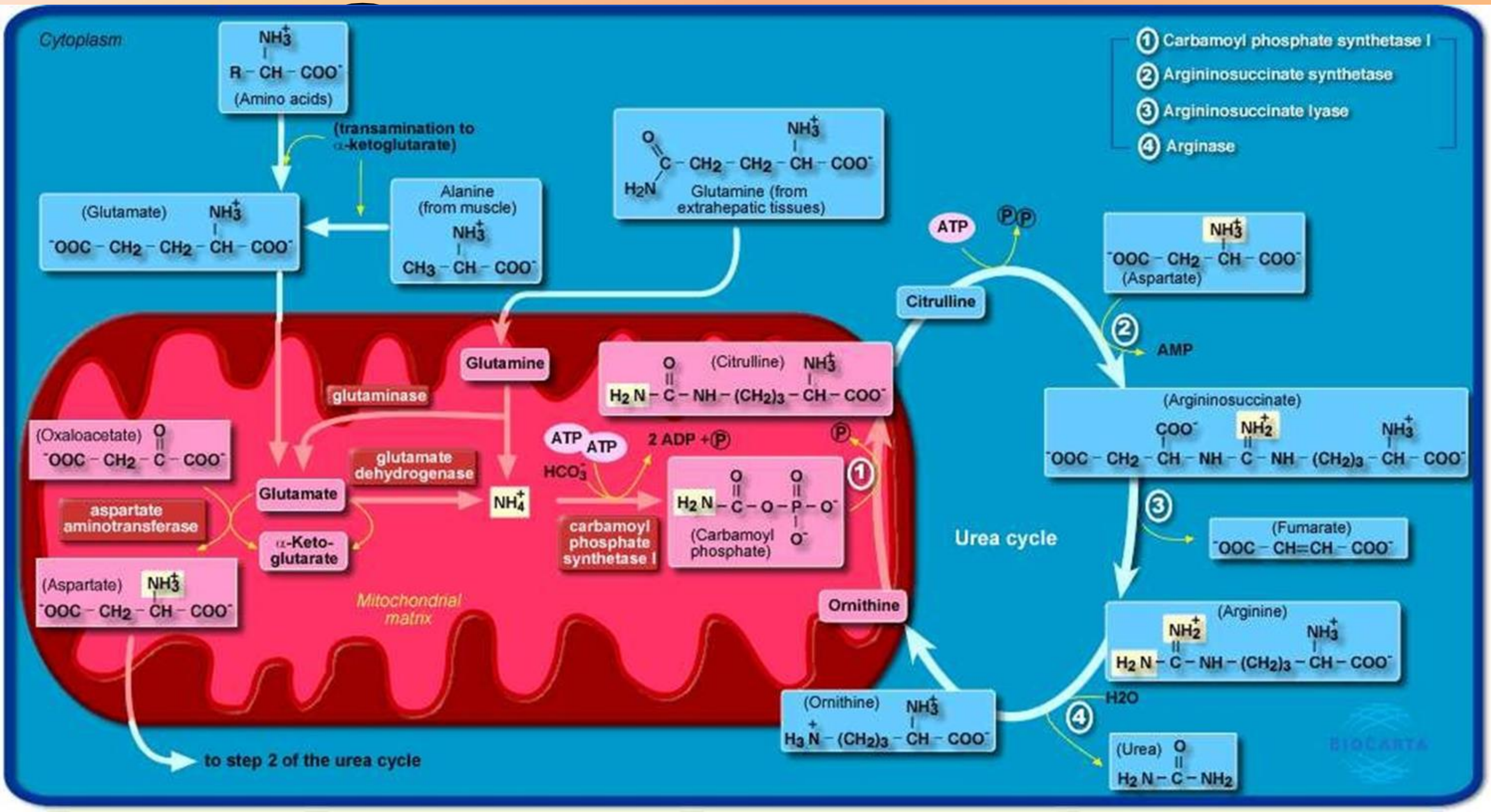
c) Urea formation

c) Urea Formation

- Urea is the **principal end-product** of protein metabolism in humans.
- It is important route for **detoxication** of NH_3.
- It is **operated** in liver, **released** into blood and **cleared** by kidney.
- Urea is **highly soluble**, **nontoxic** and has a **high nitrogen content** (46%), **so** …it represents about **80-90% of the nitrogen** excreted in urine per day **in man**
- **Biosynthesis of urea in man is an energy- requiring process.**
- **It takes place partially in mitochondria and partially in cytoplasm.**

The Urea Cycle

مهم جداً بكامل تفاصيله!



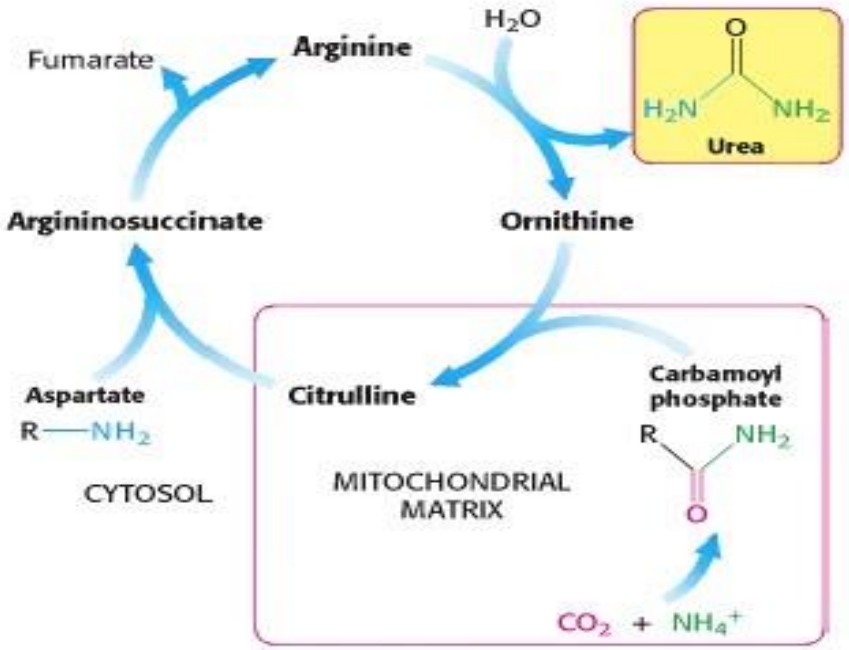


Figure 23.16. The Urea Cycle.

Figure 23.17. Metabolic Integration of Nitrogen Metabolism. The urea cycle, the citric acid cycle, and the transamination of oxaloacetate are linked by fumarate and aspartate.

Metabolic Significant Aspects of Urea Cycle

A) *Energy Cost:* . Three ATP molecules and four high-energy phosphate bonds are utilized in the reactions..

B) *urea cycle is related to TCA cycle:*

1. CO_2
2. ***Aspartate arises via transamination of oxaloacetate with glutamate***. Thus, depletion of oxaloacetate will decrease urea formation
3. **Fumarate** enters TCA cycle

C) *Sources of Nitrogen in* urea :**free NH3** and **aspartate**.

N.B. **glutamate** is the **immediate source** of both NH_3 (via oxidative deamination by Glu. Dehyd.) and **aspartate** nitrogen (through transamination of oxaloacetate by AST).

Importance of Urea Cycle

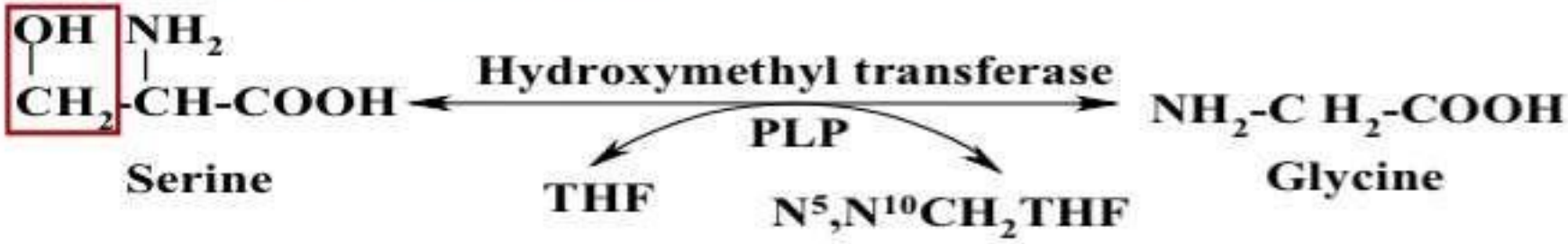
1. **Formation of arginine (in organisms synthesizing arginine) & formation of urea (in ureotelic organisms, man) due to presence of arginase.**
2. **Liver** shows much **higher** activity of arginase than brain or kidney for formation of urea while **in brain or kidney** is the synthesis of arginine.
3. Synthesis of **non-protein amino acids** (ornithine and citrulline) in body.

METABOLISM OF INDIVIDUAL AMINO ACIDS

1. Metabolism of Glycine: nonessential, glucogenic.

Biosynthesis of glycine:

1



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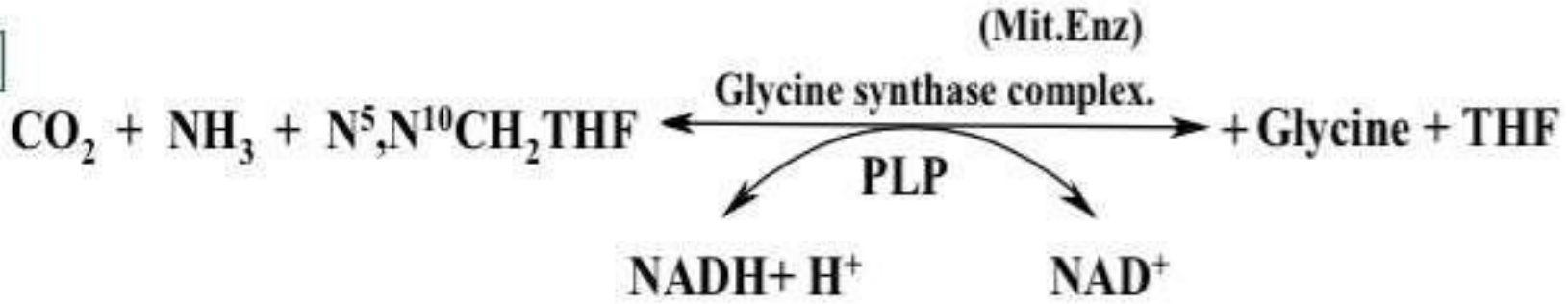


Special Functions of Glycine:

a-Protein, Hormones & enzymes.

b- Heme c- Purines (C_4,C_5,N_7) d- Creatine

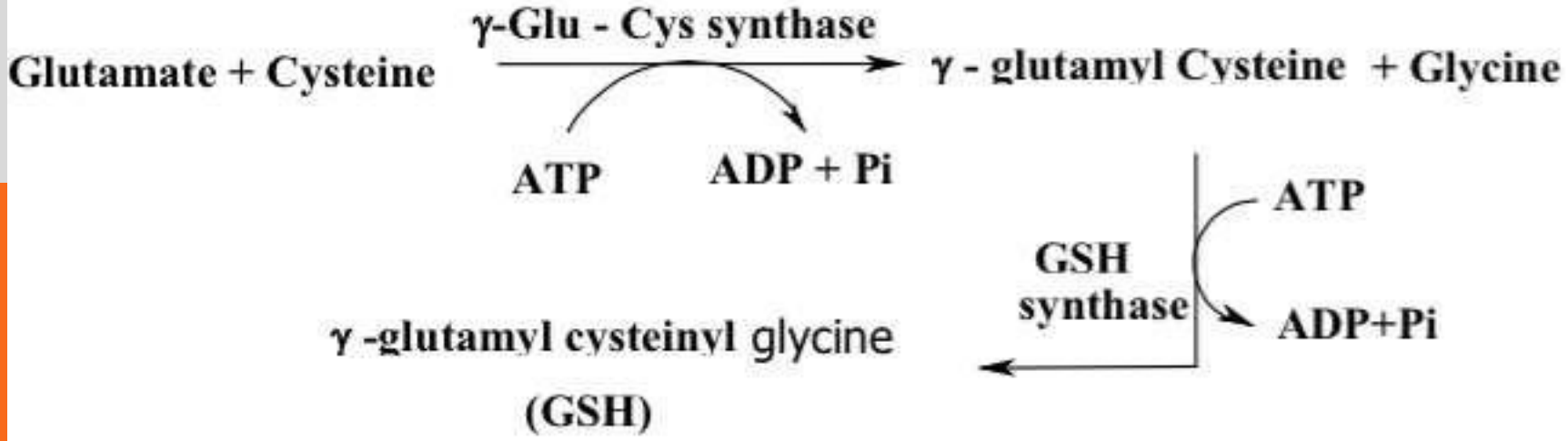
e- Glutathione

f- Conjugating reactions:

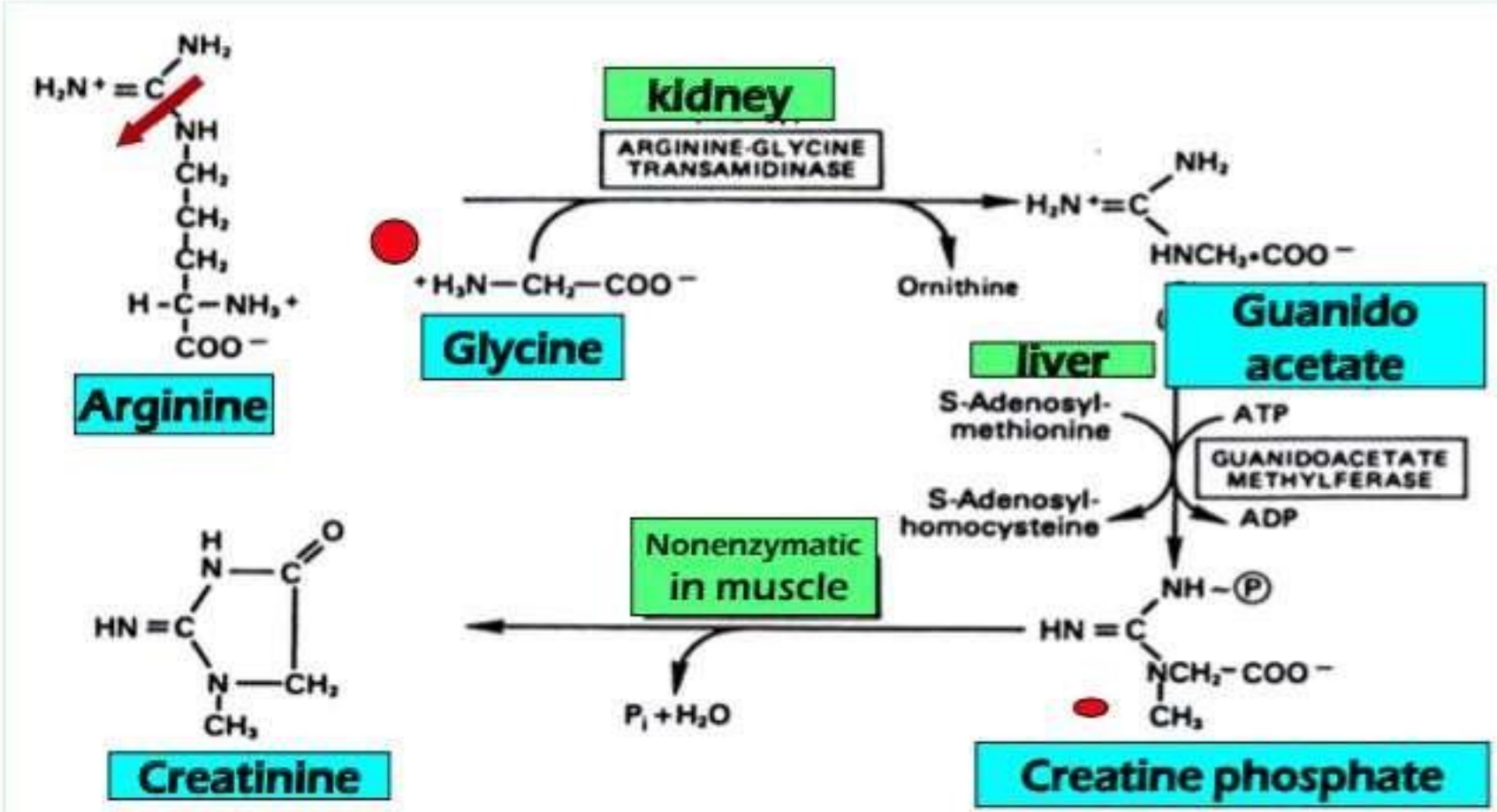
- Glycine + Cholic acid → glycocholate.
- Glycine + Benzoic acid → Hippuric acid

1.Formation of Glutathione (GSH)

Dest.FR & Peroxides

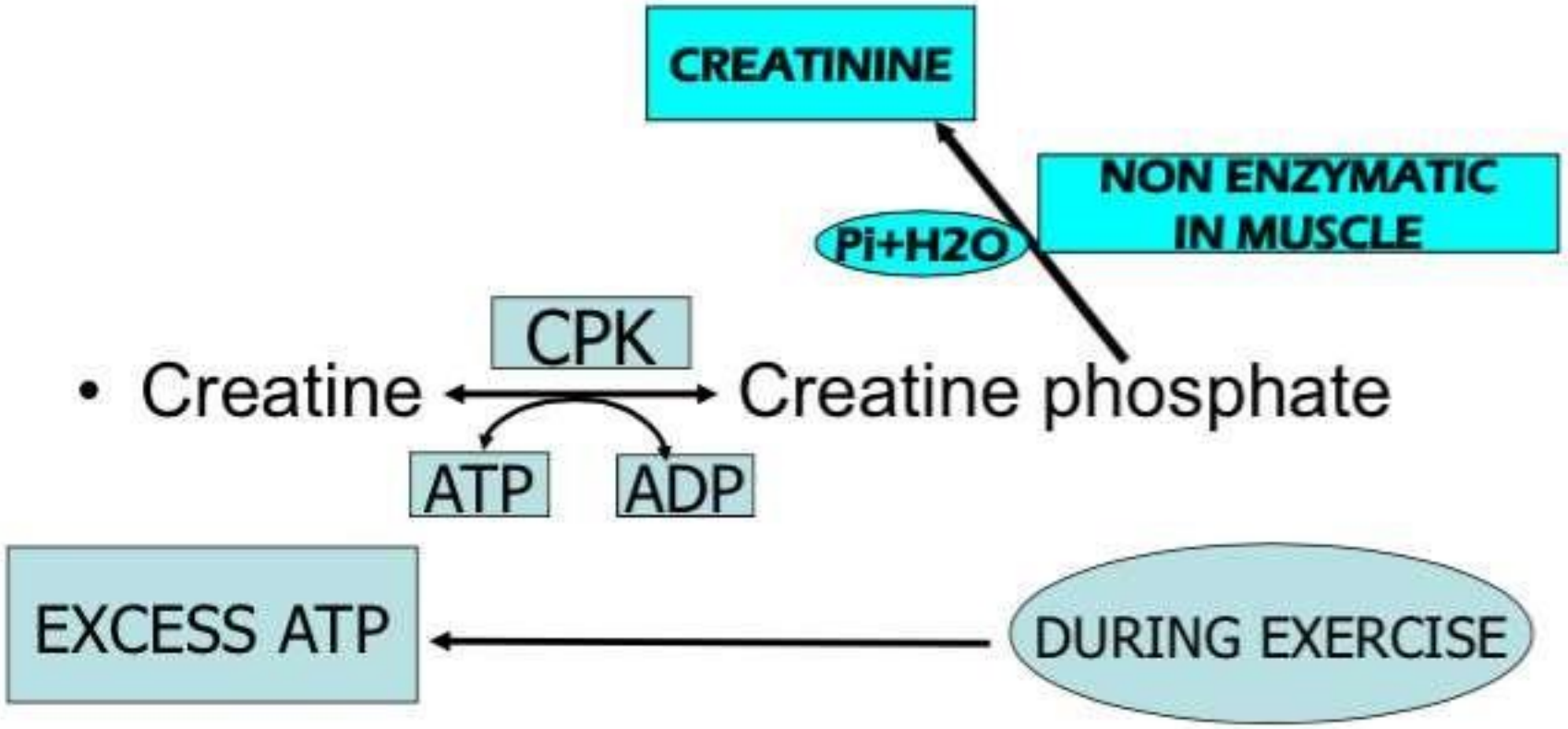


2. Formation of creatine (Methyl guanidoacetate)



* Creatinine is the metabolic end-product of the Muscle and then is excerted into the urine.
- it's a marker for kidney function

* Male's creatinine is slightly higher than Female because of the bigger muscle mass.



- Cr-P is the storage form of high energy phosphate in muscle
- Creatinine is excreted in urine & increases on kidney failure due to its filteration is decreased.
  Its level is constant per 24 hrs
  & is proportional to muscle mass in human.

3. Metabolism of Sulfur-Containing amino acids

(Methionine, cyteine & Cystine):

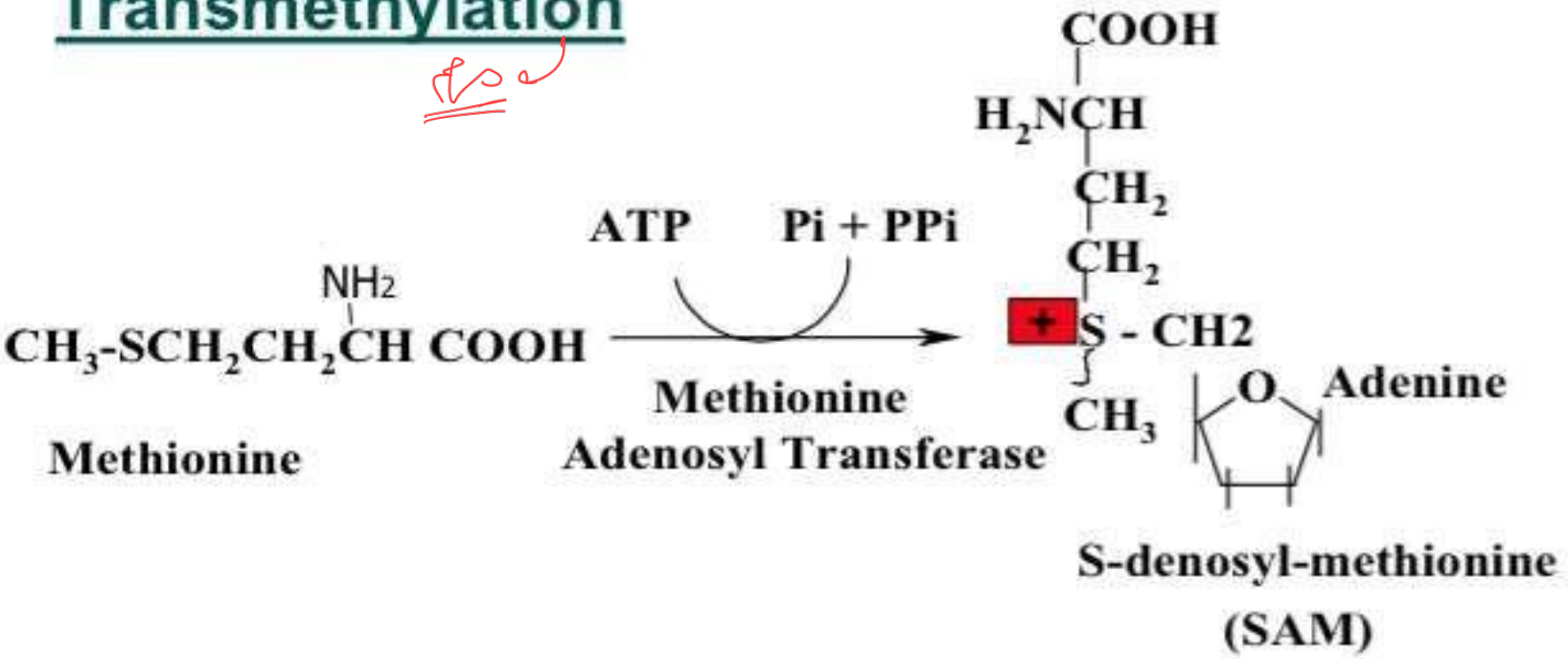
a) Metabolism of methionine: (essential)

Met. ⟶ Cysteine (diet.pr.)

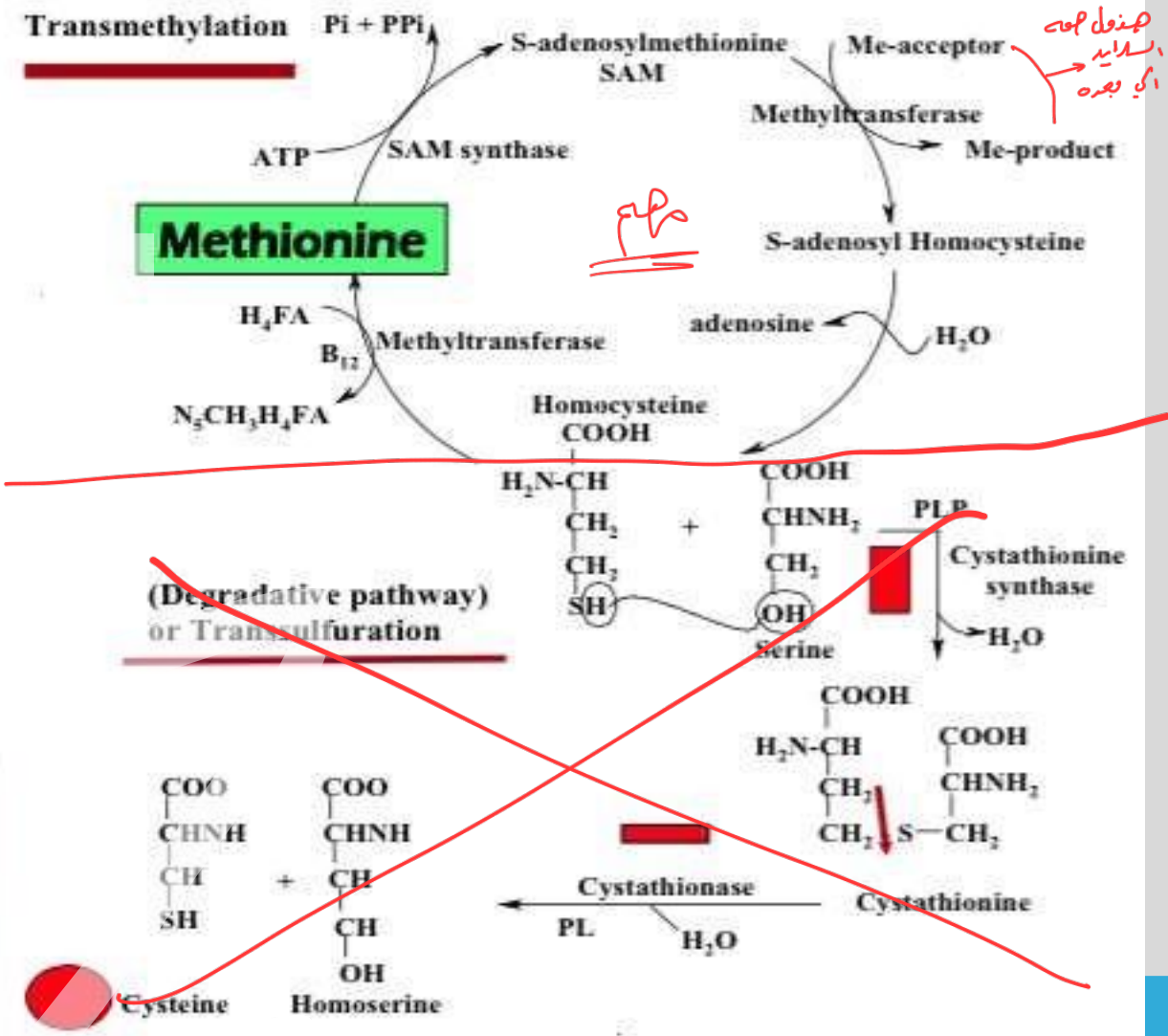
- **2 principal metabolic pathways:**

  Transmethylation and transsulfuration

- **Transmethylation**



Homocystinuria
Lack of Cystathionine synthase

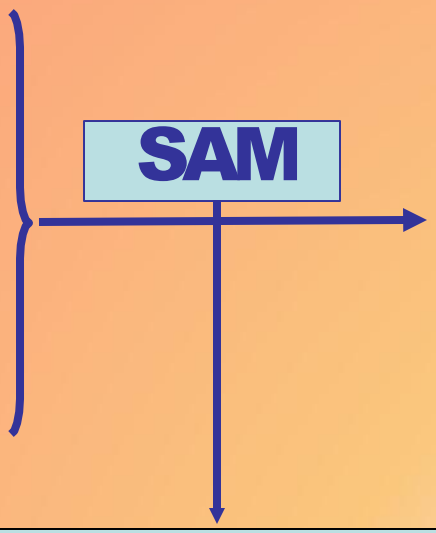


C-skeleton of cysteine From serine & S from methionine

In transmethylation there are:

Methyl acceptors

1 Guanidoacetic acid
2 Norepinephrine
3 Ethanolamine
4 Uracil



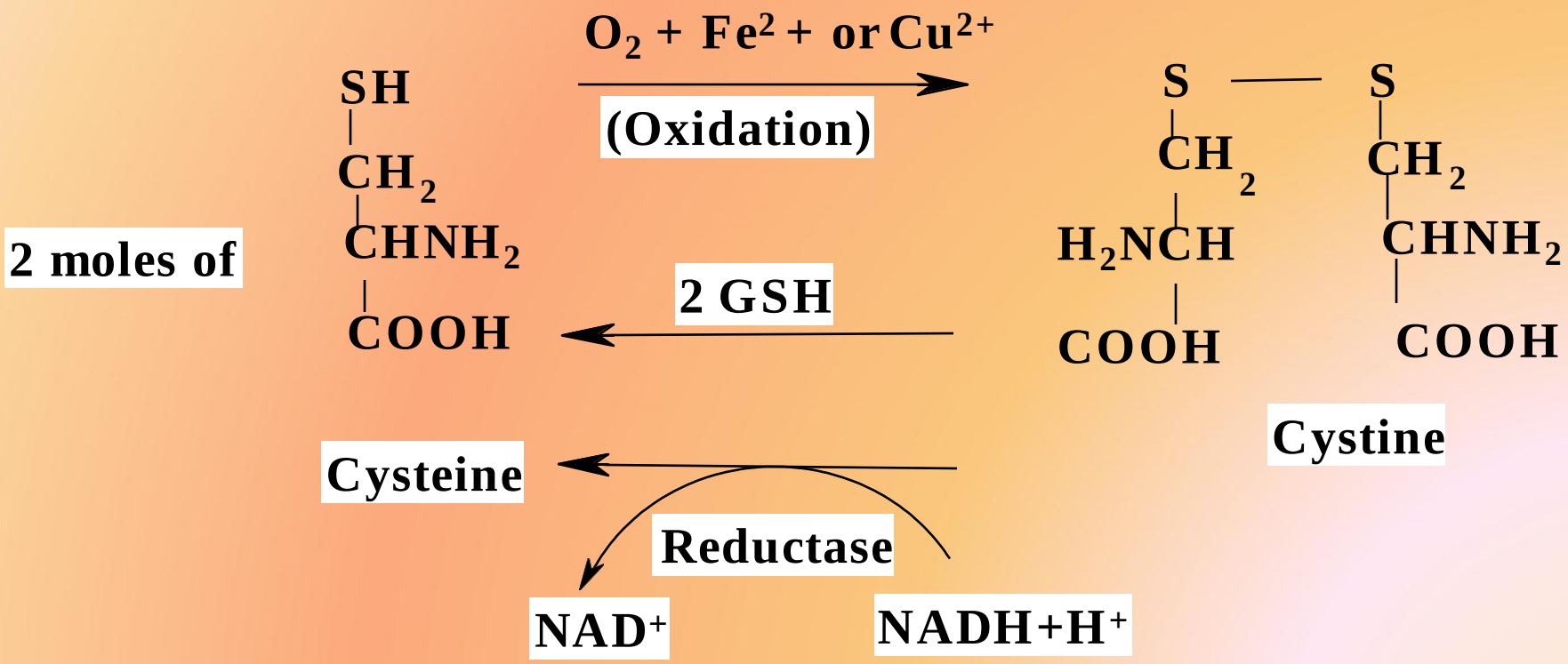
Methyl Compounds

Creatine
Epinephrine
Choline
Thymine

SAH
(S-Adenosyl Homocysteine)

Metabolism of Cysteine& Cystine:

- They are interconvertable &They are not essential
- can be synthesized from Met & Ser



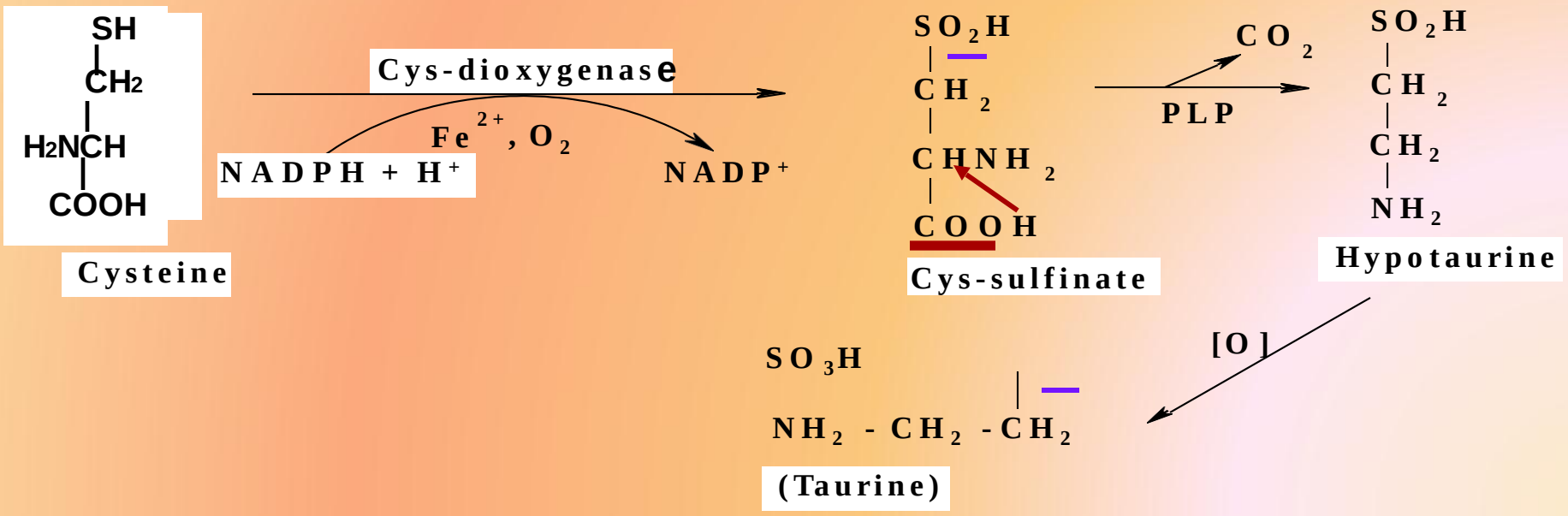
Biochemical functions of cysteine

1 PAPS Formation: (3'-phosphoadenosine,5'-phosphosulphate) active sulphate used in formation of sulfate esters of steroids, alcohol, phenol,some lipids, proteins and mucopolysaccharides

2 Sulfur of COASH, GSH, vasopressin, insulin

3 Detoxication reaction of bromo, chloro, iodobenzene, naphthalene and anthracene & of phenol, cresol, indol and skatol that is formed by the action of **intestinal bacteria** on **some amino a cids** in large intestine **with** formation of **ethereal sulfates which is water soluble and rapidly removed by the kidney**

4 Taurine Formation (with bile acids form taurocholate)

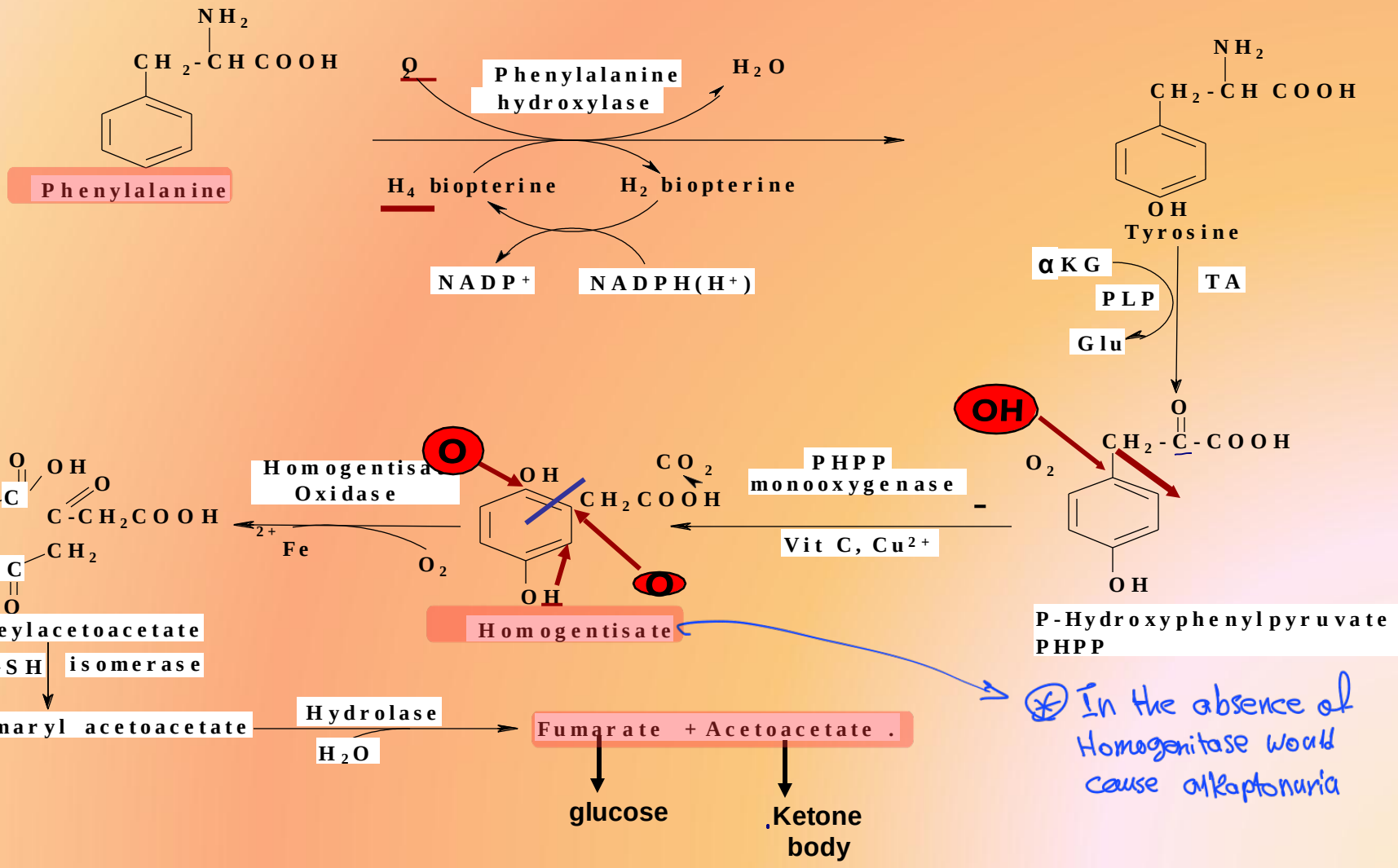


4. Aromatic amino acids

Pathway 1 مسار

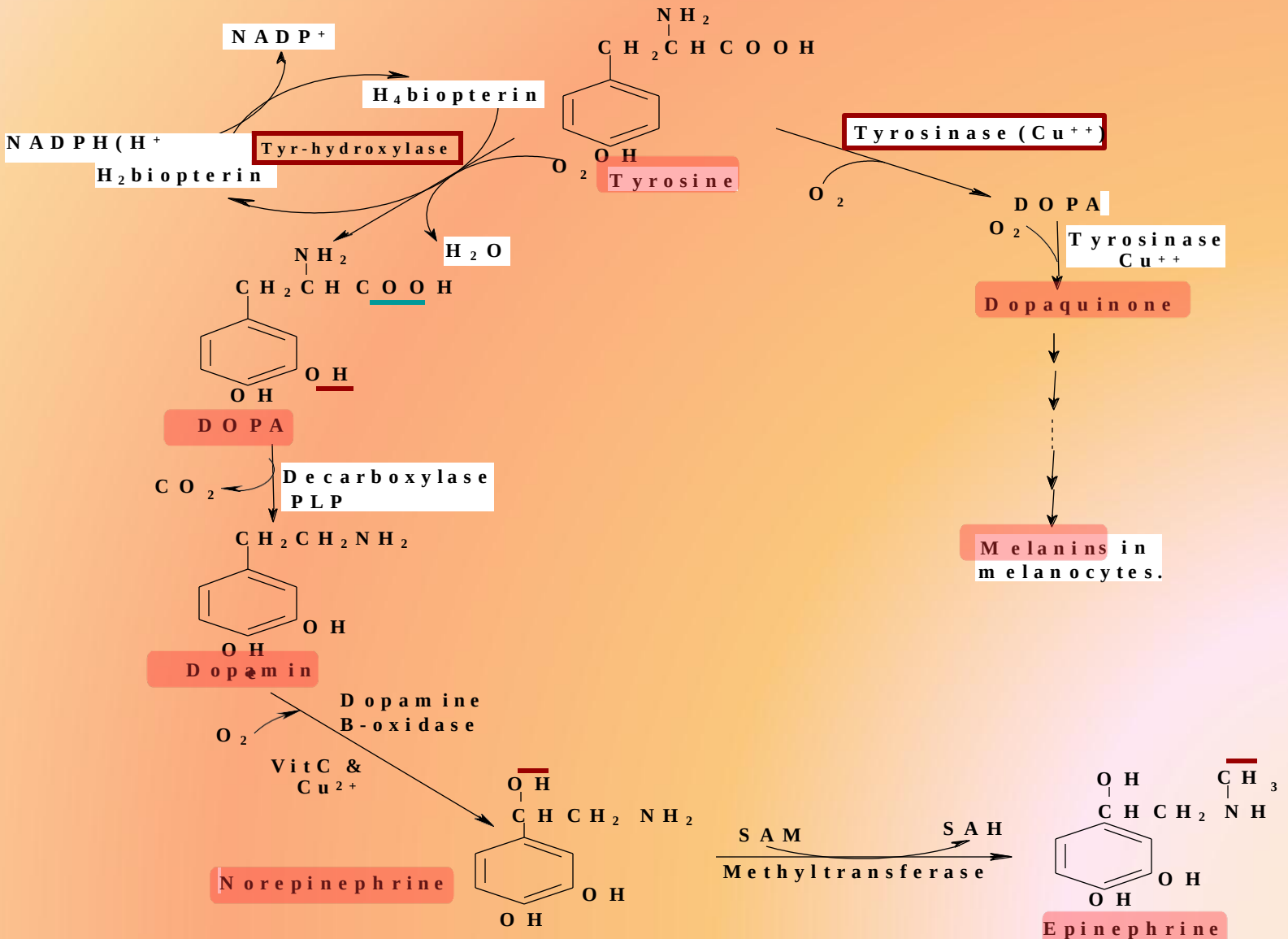
a) Metabolism of Phenylalanine

ketogenic)&(glucogenic



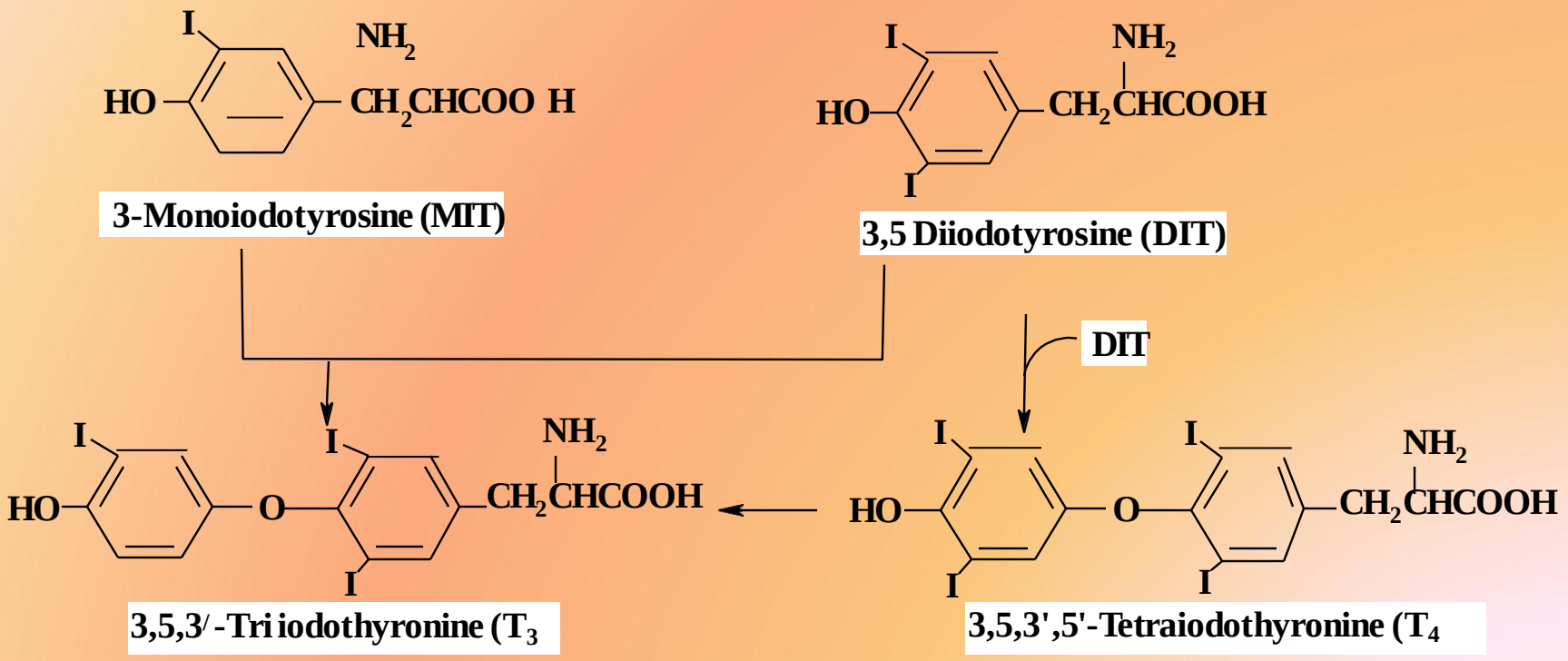
b) Tyrosine is a precursor of:

-1DOPA (3.4 dihydroxy phenylalanine)



-2Thyroid hormones:

Thyroxine Formation:



Amino acids as precursors of neurotransmitters

1. Serine Choline --- Acetyl choline.
2. Arginine ----------NO
3. Tryptophan----------Serotonin
4. Histidine----------Histamine
5. Phenyl alanine------dopa,dopamine, NE&E
6. Glutamic acid--------GABA

Absence of GABA may cause epilepsy.