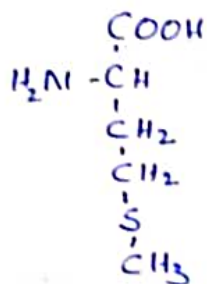


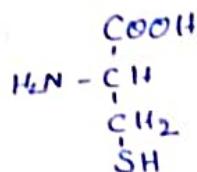
METABOLISM OF SULPHUR CONTAINING AMINO ACIDS

METHIONINE



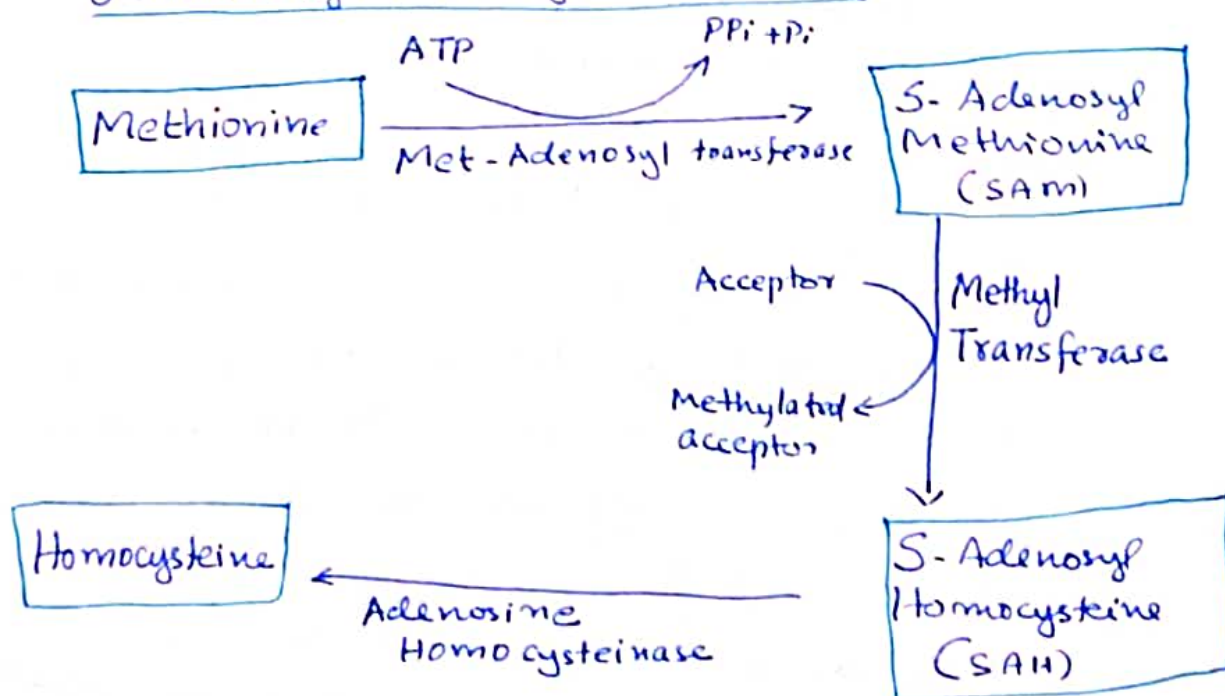
Essential
Gluco-genic
Active form - SAM
Methyl group donor

CYSTEINE



Non essential
Gluco-genic

Methionine is a methyl group (CH_3 -) donor in transmethylation reactions. Active form of Met is S-Adenosyl Methionine (SAM). After donating methyl group it becomes S-Adenosyl Homocysteine (SAH)

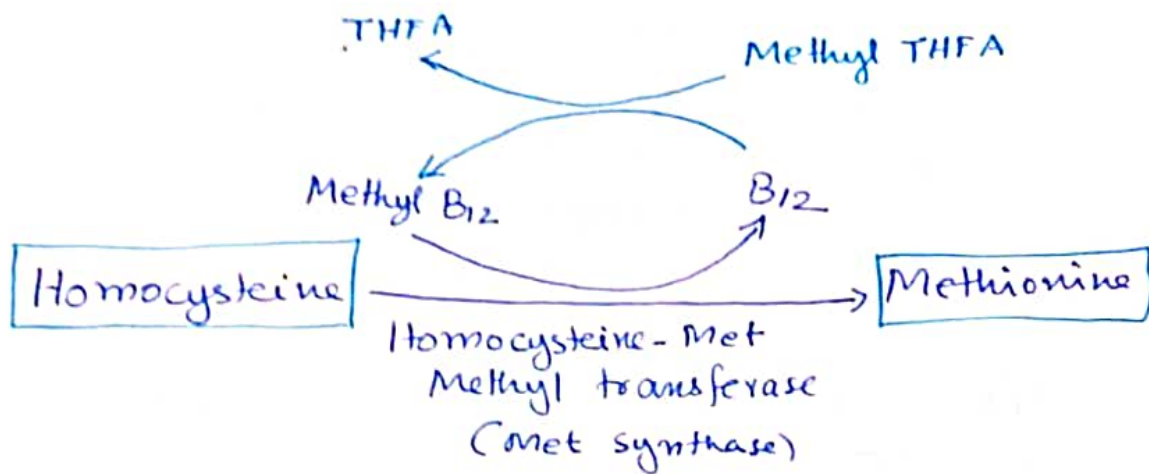


Homocysteine is toxic.
 → Thiolytes proteins
 → Activates Hageman's factor

Homocysteine is

serine metabolised in 2 ways

① Conversion of Homocysteine to Methionine



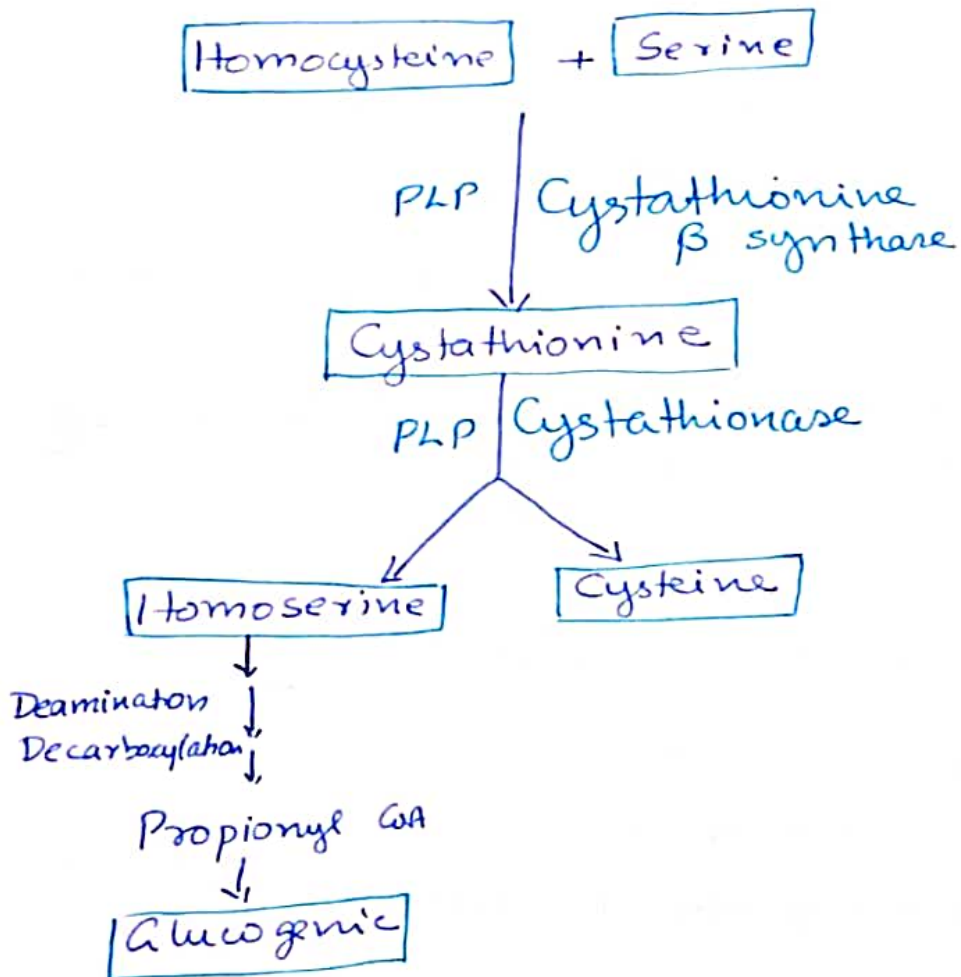
Significance

- ① Utilizes Homocysteine
- ② Deficiency of B₁₂ or Folic acid cause homocysteinemia and ~~homocysteinemia~~ homocystinuria

③ Folate trap (Methyl folate trap) :

During 1C group transfer by THFA, Methyl THFA can transfer Methyl group only to Methyl B₁₂. In B₁₂ deficiency all the folic acid will be trapped as methyl THFA. This ~~case~~ causes Folic acid deficiency in a patient with B₁₂ deficiency. This is called Folate trap.

② Formation of cysteine from homocysteine



Functions of cysteine

① **Glucogenic:** Cysteine is transaminated to β mercapto pyruvate

↓
Pyruvate
↓
Glucose

② **Formation of Coenzyme A.**

- ③ Formation of glutathione
- ④ Formation of Taurine: Taurine is a conjugating agent formed from cysteine. It is used for conjugation of bile acids.
- ⑤ 2 Cysteine in a polypeptide chain can combine to form Cystine.
 (2 Cysteine) This produces a (S-S) disulphide bond.

HOMOCYSTINURIAS

↑ levels of Homocysteine in blood (Homocysteinemia) can lead to excretion of Homocysteine in urine (Homocystinuria)

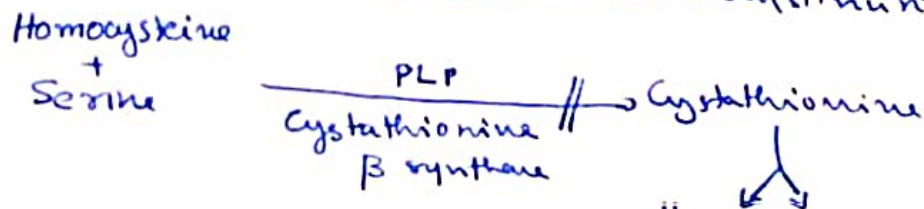
Homocystinuria can be

< Congenital
 < Acquired

Congenital Homocystinuria

Causes

- ① Deficiency of Cystathionine β synthase
 (Classical homocystinuria)



② Deficiency of Met Methylene THFA reductase (43)
[Enzyme that provides methyl THFA]

Biochemical defects

- Homocysteine inactivates proteins.
- It ^{it} interfere with collagen cross linking
- Leads to weak connective tissue

Clinical features

- Mental retardation
- Skeletal deformities like flat foot
- Charlie Chaplin gait
- Subluxation of lens, visual impairment

Acquired homocystinuria

Causes

① Deficiency of vit B₁₂, Folic acid, B₆

[vit B₁₂ and folic acid are required
for Homocysteine - Met methyl
transferase]

[vit B₆ (PLP) is required for
cystathionine β synthase]

② Use of antivitamin

③ Hypothyroidism

④ In renal failure, homocysteinemia
is seen (Homocysteine not excreted)

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Biochemical defects

Homocysteine thiolates LDL. This causes aggregation of LDL and more chance of IHD.

Homocysteine activates Hageman's factor. This can cause intravascular clotting.

Clinical features

Increased ~~in~~ chance of ~~Myo~~ IHD, Myocardial infarction and CVA.

Diagnosis

- ① Blood homocysteine $\uparrow$
(Normal 5-15 $\mu\text{mol/L}$)
- ② Urine - Cyanide Nitroprusside test (+)

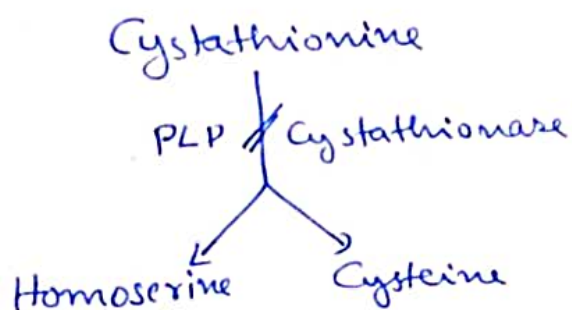
Treatment

Congenital: Dietary restriction of methionine

Acquired: $\rightarrow$ Treat the cause
 $\rightarrow$ Give Vit B₁₂, Folic acid, B₆

Cystathionuria

- Due to cystathionase deficiency
- Also due to B₆ deficiency



C/F : mental retardation, endocrine disorders

Cystinuria

Defect in renal tubular reabsorption of Cystine.

The common transporter for

Cystine
Ornithine
Lysine
Arginine

is defective.

These 4 amino acids appear in urine

It can cause renal stones

Cystinosis

Due to ~~intra~~ cellular transport defect of cysteine

Liver, spleen, Bone marrow etc affected

Metabolism of Sulphur

Organic Sulphur = Sulphur seen in proteins, sulfatides, Mucopolysaccharides etc

Inorganic Sulphur = Derived from S containing amino acids

Excretion of S in urine is as

- Inorganic sulphates
- Organic / Etheral sulphates
- Neutral Sulphur

Active Sulfur = PAPS
(Phospho Adenosine Phospho sulfate)

MSUD (Maple Syrup Urine Disease)

Defect in metabolism of branched chain amino acids

Branched chain α keto acid decarboxylase
(First enzyme in branched chain ketoacid dehydrogenase multi-enzyme complex). This is a TPP dependent enzyme

Branched chain ketoacids excreted through urine

Clinical features

Burnt sugar smell of urine
Severe mental retardation
Severe acidosis, convulsions, coma
Death within first year

Tests

Rothera's test (+)

DNPH (Dinitrophenylhydrazine test) +ve

Treatment ① Restrict branched chain a.a.
② Thiamine in some cases

Tryptophan

Functions of Tryptophan

- ① Both glucogenic & ketogenic
- ② Formation of niacin
- ③ Formation of serotonin
- ④ Formation of melatonin

Formation of Niacin

Trp can be converted to niacin (NAD^+)

60 mg Trp = 1 mg niacin

Formation of niacin from Trp requires 2 important enzymes

① Kynureninase (Requires PLP as coenzyme)

② QPRTase:

(Quinolinate Phosphoribosyl transferase)

Rate limiting enzyme

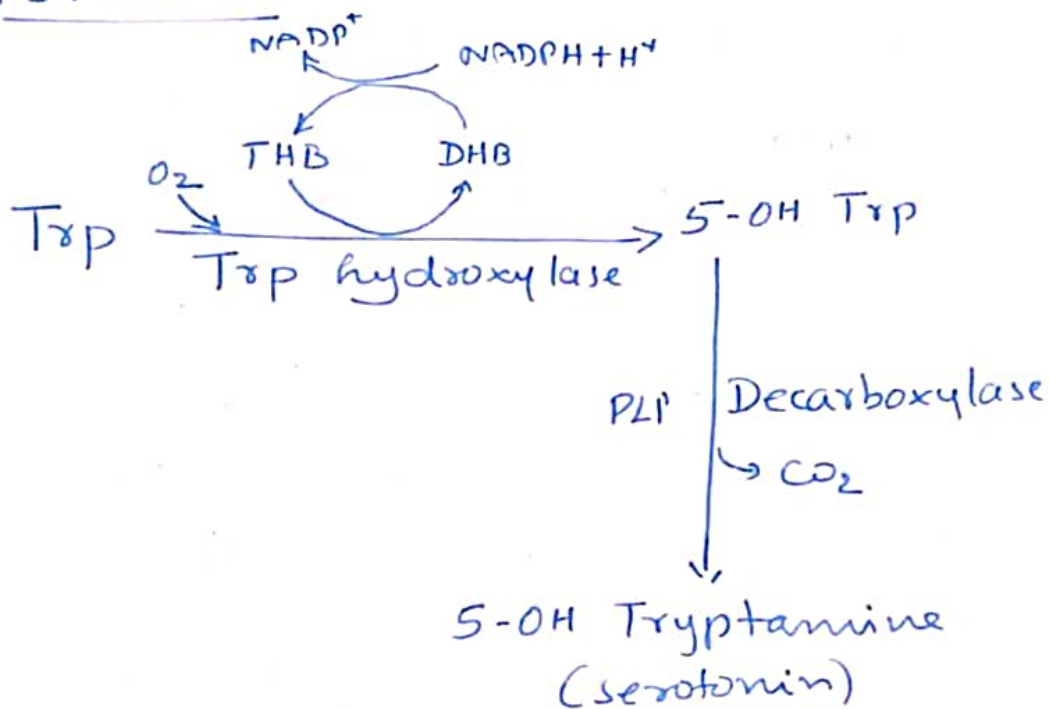
Inhibited by Leucine

Any condition which causes Trp deficiency can lead to Pellagra

Serotonin

Serotonin is 5-hydroxy tryptamine

Formation

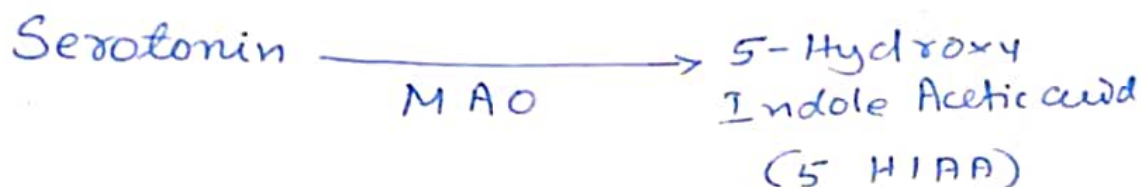


Functions of serotonin

- ① Neurotransmitter
- ② Antidepressant in brain
- ③ Regulation of sleep, mood, appetite etc
- ④ Formation of melatonin

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Catabolism of Serotonin



Significance of 5 HIAA

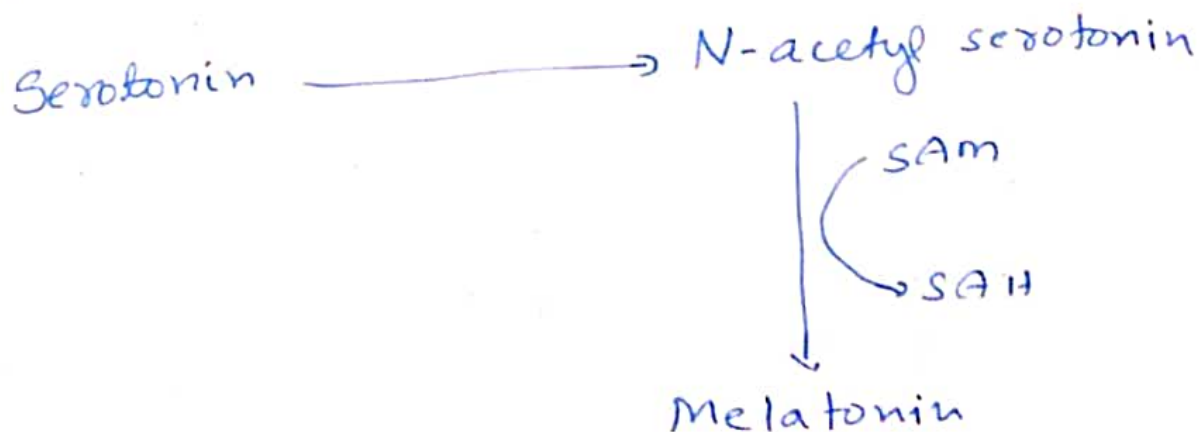
End product of serotonin catabolism

Normal urinary excretion 2-7 mg/day

5 HIAA excretion increased in
carcinoid tumors

Formation of melatonin

Melatonin is a neurotransmitter
produced by pineal gland.



Hartnup disease

Defect in intestinal absorption and renal tubular reabsorption of neutral amino acids ; especially Trp

Autosomal recessive inheritance

Trp level ↓↓ed ; Niacin level ↓

C/F

Pellagra like symptoms

Neuropsychiatric manifestations

Diagnosis - by Obermeyer test

Treatment : Supplement the deficient amino acids

GLUTAMIC ACID

Non essential ; Glucogenic

Formation

By transamination of α ketoglutarate

Utilization

- ① Glucogenic pathway
- ② Formation of GABA and glutamine
- ③ Formation of Glutathione
- ④ Transport of ammonia from tissues to ~~liver~~ ^{Liver}