Done By :

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- Glucose and fatty acid →can be stored in the body
- Amino acid → it should be excreted

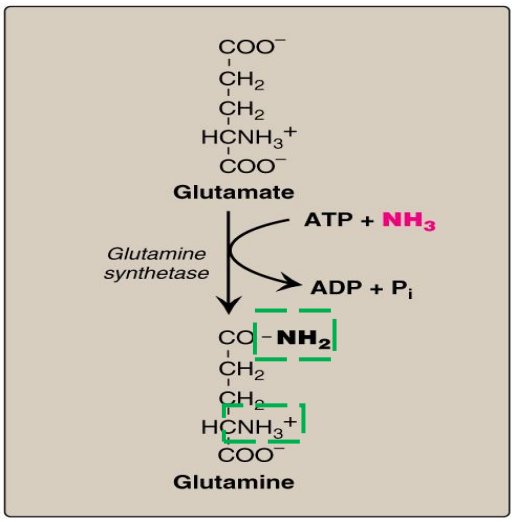
Degradation of Amino Acid :

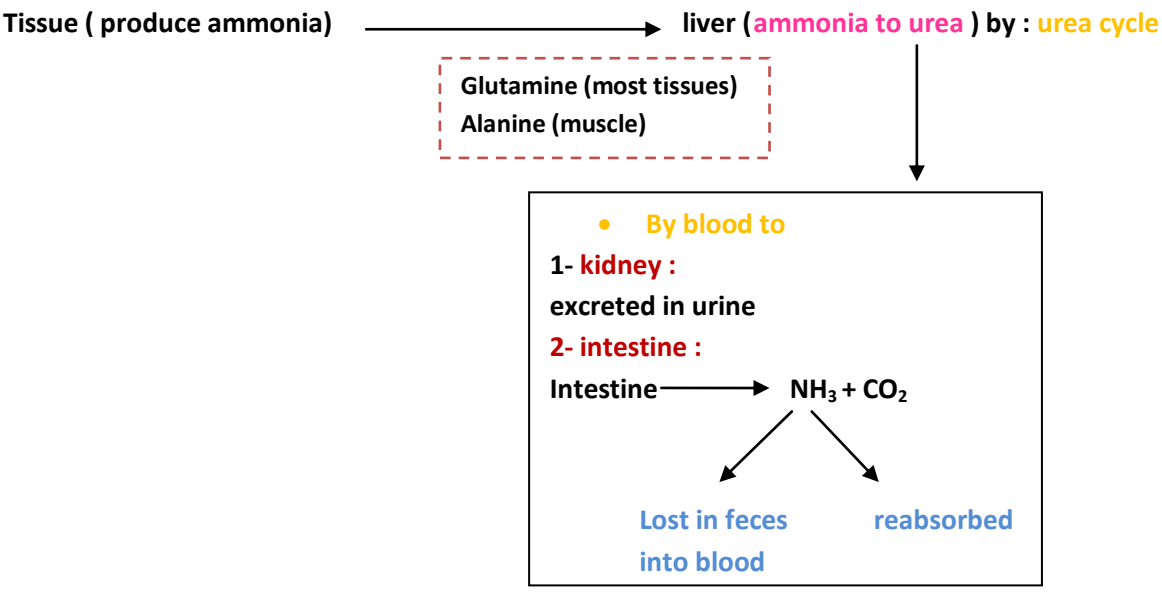
Removal of α-amino group → Ammonia (NH_3)

Remaining carbon skeleton → Energy metabolism

- Ammonia is produced by all tissues and the main disposal is via formation of urea in liver
- Blood level of NH_3 must be kept very low, otherwise, hyperammonemia and CNS toxicity will occur (NH_3 is toxic to CNS)
- To solve this problem, NH_3 is transported from peripheral tissues to liver via formation of:
  - ✓ Glutamine (most tissues)
  - ✓ Alanine (muscle)

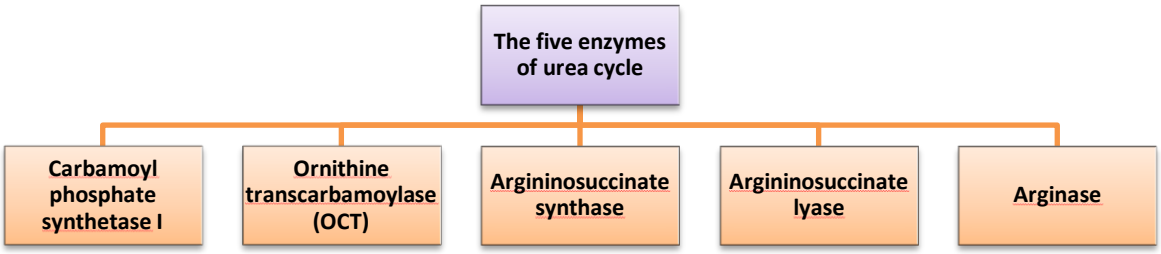
Glutamine itself is an amino acid so it will have to amine group when is going to take the ammonia group to





Urea cycle :

- Urea is the major form for disposal of NH_3
- Urea cycle occurs in the liver
- One nitrogen of urea is from NH_3 and the other nitrogen from aspartate
- Urea is transported in the blood to the kidneys for excretion in urine



Urea Cycle Regulation:

Rate-limiting enzyme:

- **Carbamoyl phosphate synthetase**

Activator of the enzyme:

- **N-Acetylglutamate**

Fate of Urea:

The action of intestinal urease to form NH_3 is clinically significant in renal failure:

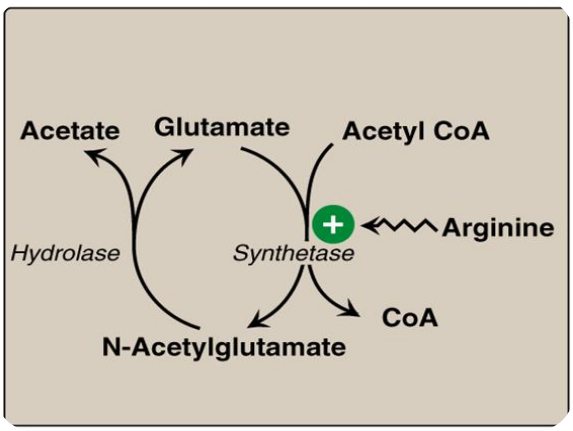
Renal failure → ↑ Blood urea → ↑ Urea to intestine → Urease → ↑ NH_3 blood level

(Acquired hyperammonemia)

Fate of Ammonia :

- **Urea formation by the liver**
- **Glutamine synthesis in brain**

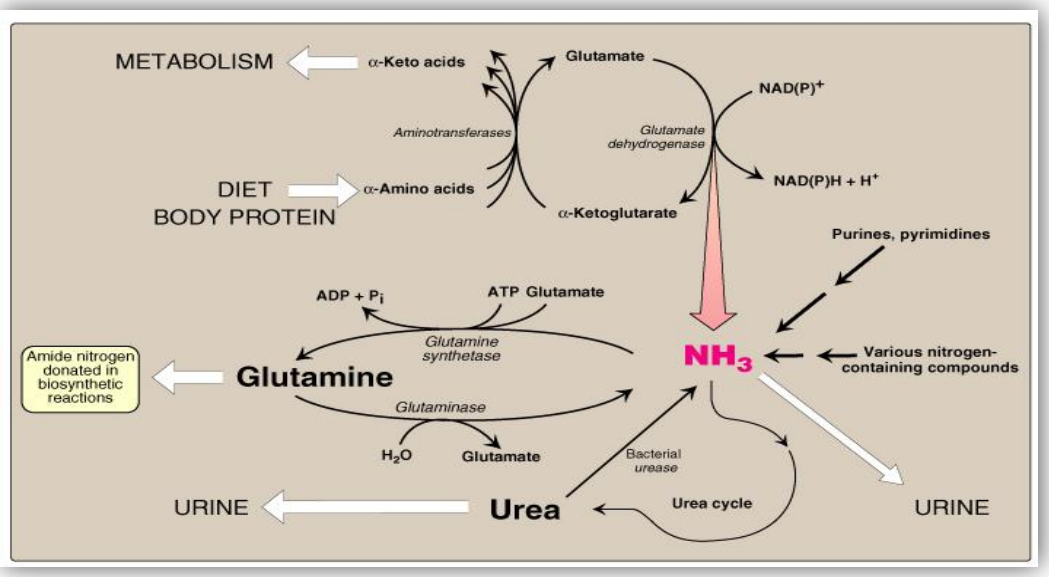
(**Major mechanism for removal of NH_3 in the brain**)

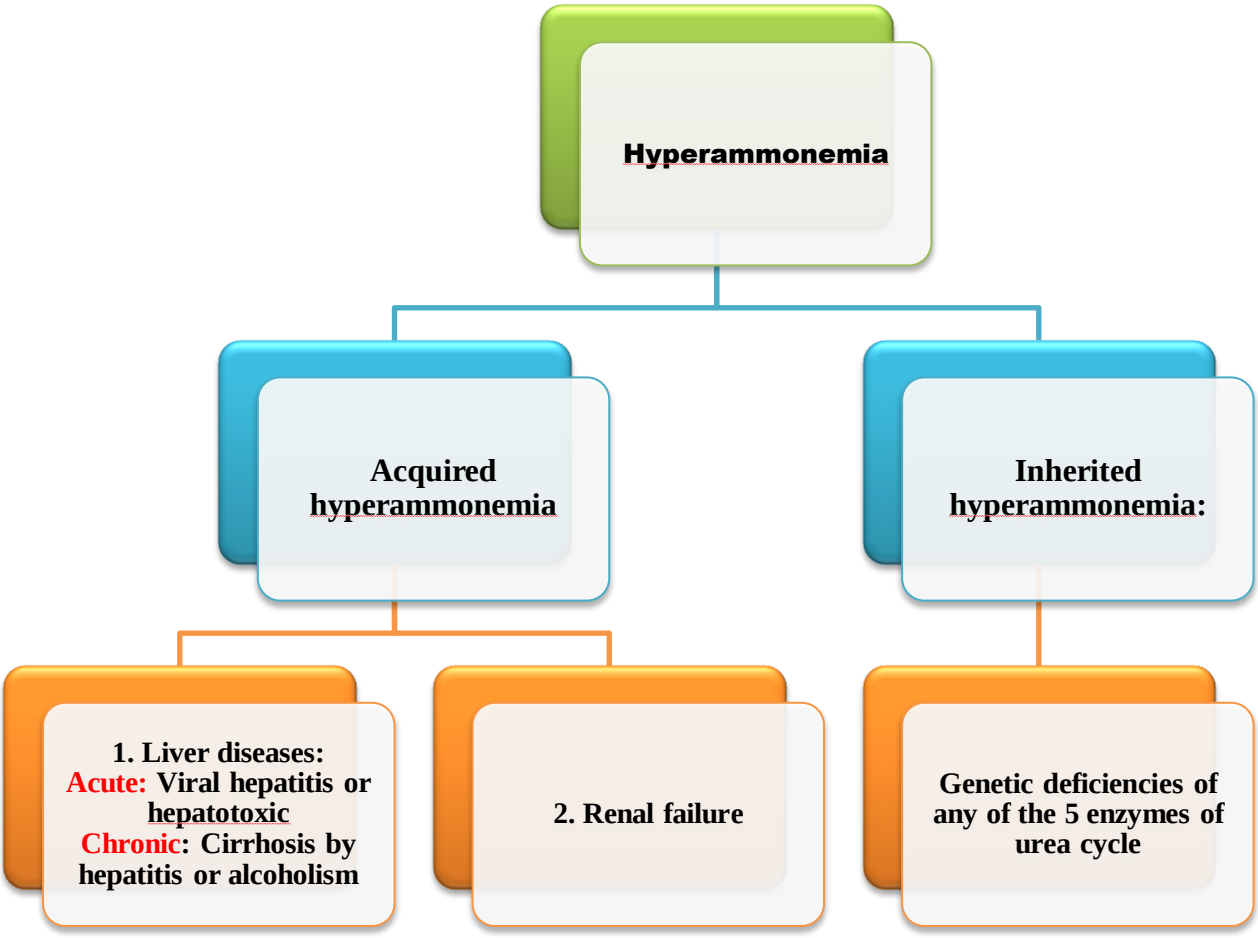


Sources of Ammonia:

- Amino acids
- Glutamine
  - (by renal glutaminase, NH_3 excreted in urine as NH_4)
- Bacterial urease in intestine
- Amines e.g., catecholamines
- Purines & pyrimidines

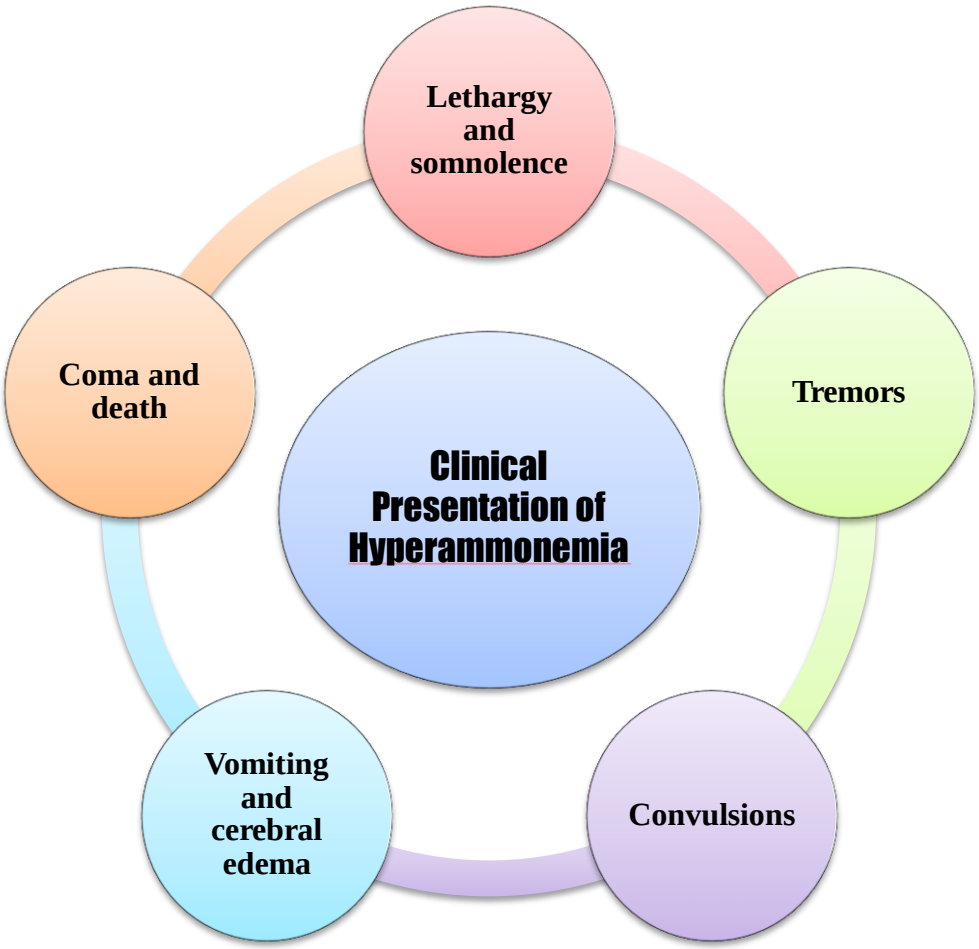
This image shows the source and the fate of ammonia





Inherited Hyperammonemia:

- **Ornithine transcarbamoylase deficency:**
  - X-linked recessive
  - Most common of congenital hyperammonemia
  - Marked decrease of citrulline and arginine
- **Others: Autosomal recessive**


Clinical Presentation of Hyperammonemia
Lethargy and somnolence
Tremors
Convulsions
Vomiting and cerebral edema
Coma and death