with α-ketoglutaric acid. The glutamic acid then gets oxidative deaminated to form α-ketoglutaric acid and ammonia.

The process of amino acid catabolism involving the combined action of an amino, transferase (transaminase) and glutamate dehydrogenase may be depicted in Fig. 16.1.

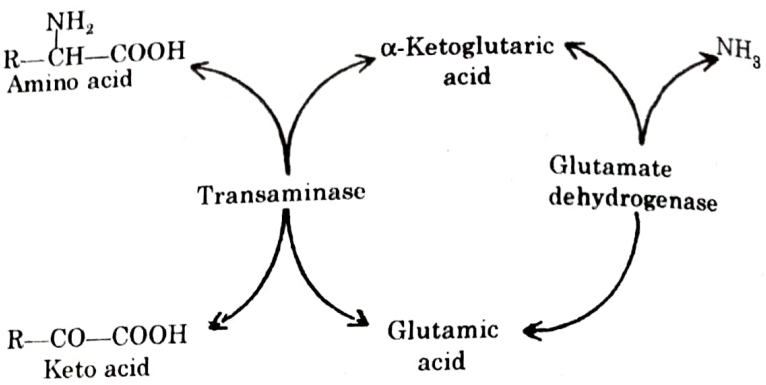
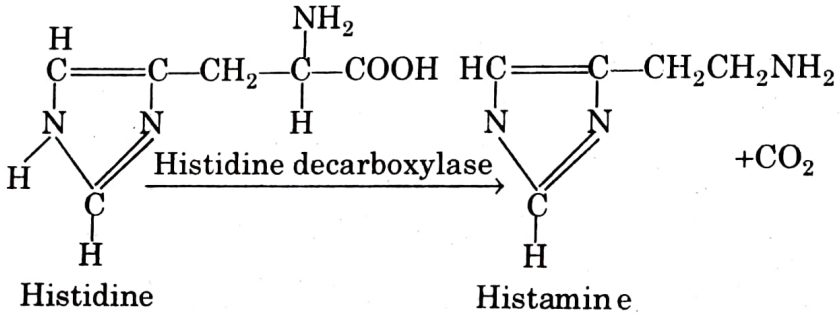


Fig. 16.1. Overall catabolism (transdeamination) of amino acids.

Decarboxylation of Amino Acids

Amino acid decarboxylases have been found to catalyse the removal of CO_2 from the carboxyl group of amino acids. All decarboxylases need pyridoxal phosphate as coenzyme. For example, histidine has been decarboxylated to histamine by histidine decarboxylase.



Also, 3, 4-dihydroxyphenylalanine has been decarboxylated to dopamine, tryptophan to tryptamine, tyrosine to tyramine, glutamate to amino butyrate, and so on. Such amines are called biogenic amines. Many of these amines possess strong pharmacological effects while others are important as precursors of hormones or as coenzymes.

The various amino acids and their corresponding biogenic amines with their significance are given is Table 16.1.

Table 16.1
BIOGENIC AMINES

Amino acid	*Decarboxylation product*	*Significance*
1	*2*	*3*
Serine	Ethanolamine	Phosphatides
Threonine	Propanolamine	Vitamin B_{12}
Cysteine	β-Mercaptoethyl amine	Coenzyme A
Aspartic acid	β-Alanine	Coenzyme A, Pantothenic acid
Glutamic acid	γ-Aminobutyric acid	Brain (ganglia inhibitor)
Histidine	Histamine	Vasodilator and hence decreases blood pressure

1	2	3
Tyrosine	Tyramine	Uterus contracting, increases blood pressure
3, 4-Dihydroxy-phenylalanine	Dopamine (→ epinephrine)	Tissue hormone (→ hormone)
Tryptophan	Tryptamine	Hormone
6 Hydroxy-tryptophan	Serotonin (→ Melatonin)	Tissue hormone (hormone)

Except the decarboxylation of glutamic acid in brain tissue, other decarboxylation reactions have been found to be irreversible.

Disposal of the Nitrogen

Ammonia is constantly produced in the tissues. It is a toxic substance and should be removed rapidly from the circulation (*detoxication*) by the liver which converts it (ammonia) into glutamate, glutamine or urea. The various paths for the fixation of ammonia obtained from amino acids are as follows :

(i) Synthetic pathways.

(ii) Gutamate pathway.

(iii) Formation of urea.

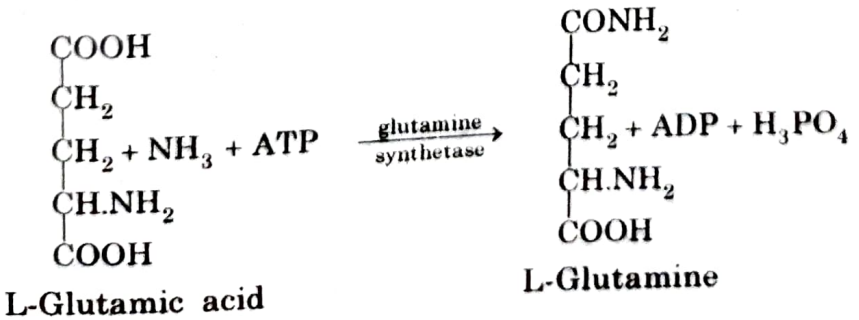
(iv) Direct excretion.

(v) Formation of creatine and creatinine.

We shall discuss these one by one.

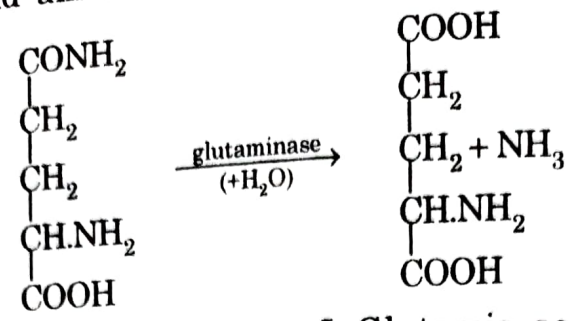
(i) *Synthetic pathways :* Ammonia may involve in the reductive amination of a-keto acids (derived from carbohydrates) to form new amino acids. This is termed as reversal of transdeamination reactions. Ammonia may also involve in the synthesis of purines, pyridines and porphyrins. In these syntheses, ammonia does not act in the free state but in the form of carrier such as glutataminate, aspartate, carbamoyl-phosphate and glycine.

(ii) *Glutamate pathways :* In extrarenal tissues ammonia is converted into glutamine in the presence of glutamine synthetase, an enzyme present primarily in the brain and liver.



L-Glutamic acid L-Glutamine

Glutamine is not a toxic substance and it travels from the various tissues through the blood to the kidneys where it gets hydrolysed by *glutaminase* to glutamic acid and ammonia.

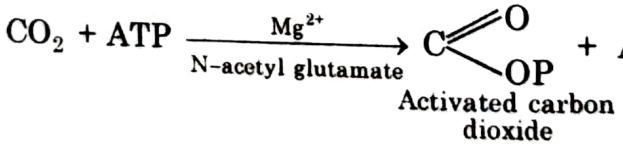


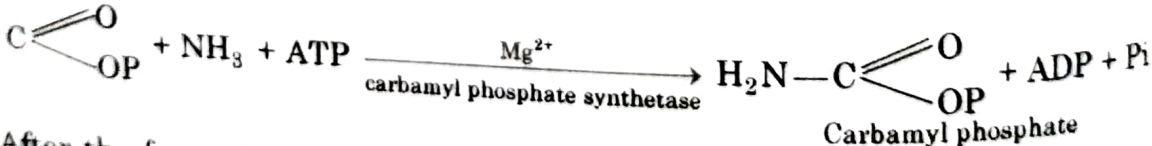
L-Glutamine L-Glutamic acid

The ammonia thus liberated accounts for about 60% of the urine ammonia.

(iii) *Direct excretion :* Usually deamination of amino acids takes place in extrarenal tissues in which the ammonia is immediately channelled into certain metabolic pathways which bind it. If the removal of amino group from the amino acid (deamination) takes place in kidney in the absence of immediate physiological requirements for synthetic purposes, the liberated ammonia gets excreted directly into the urine. The source of urinary ammonia accounts for about 40% of the total urinary ammonia (60% of urinary ammonia is obtained by the hydrolysis of glutamine in kidney).

(iv) *Formation of urea :* The conversion of ammonia to urea in the liver occurs by the ornithine cycle proposed by Krebs. This cycle starts with a carrier molecule called ornithine (amino acid). Before the actual ornithine cycle takes place, ammonia (derived by deamination of amino acids) and carbon dioxide (derived from Krebs cycle) combine in the presence of ATP to form carbamyl phosphate (amido phosphate). This reaction takes place in two steps :





After the formation of carbamyl phosphate the actual ornithine cycle starts in which the former compound undergoes reaction with the α-amino group of ornithine to form citrulline in the presence of *ornithine carbamyl transferase.*

Citrulline then undergoes condensation with the amino group of aspartate to form arginosuccinate. The reaction needs ATP and has been catalysed by the *arginosuccinate synthetase.* Arginosuccinate gets cleaved reversibly to a mixture of fumarate and arginine by the enzyme *arginosuccinase.* Finally, arginine gets cleaved by the enzyme *arginase* into urea and ornithine. This has completed the cycle. Now ornithine molecule accepts another molecule of carbamyl phosphate to repeat this cycle.

In summary, two ammonia (from glutamate and asparate) and one CO_2 gives urea. In the process, 3 moles of ATP are consumed.

Ornithine cycle of urea synthesis is shown in Fig. 16.2.

(v) *Creatine and creatinine :* Creatinine is the anhydride of creatine. Its constant amount (related to muscle mass) is excreted daily. Formation of these have been described elsewhere in this chapter because these are formed only from three amino acids, namely, glycine, arginine and methionine rather the entire group of amino acids, However, the relationship of these compounds to each other has been depicted as follows :

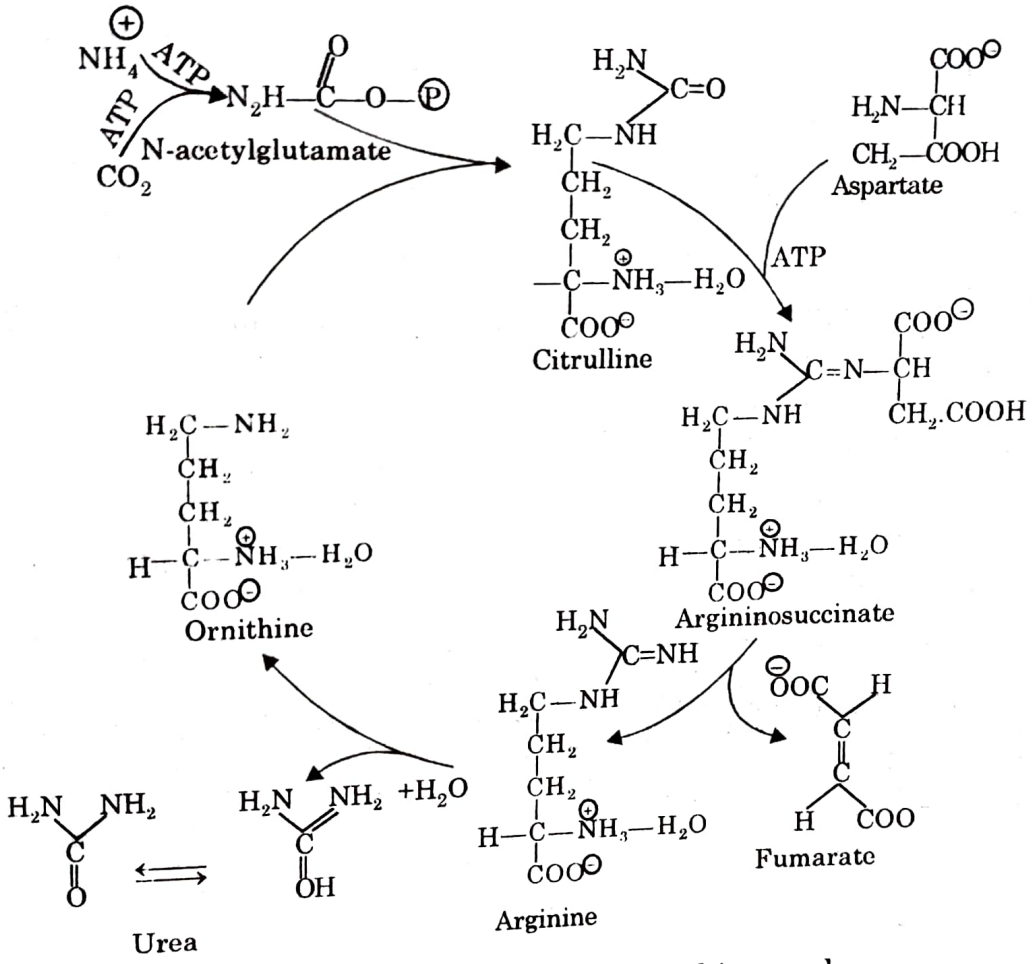
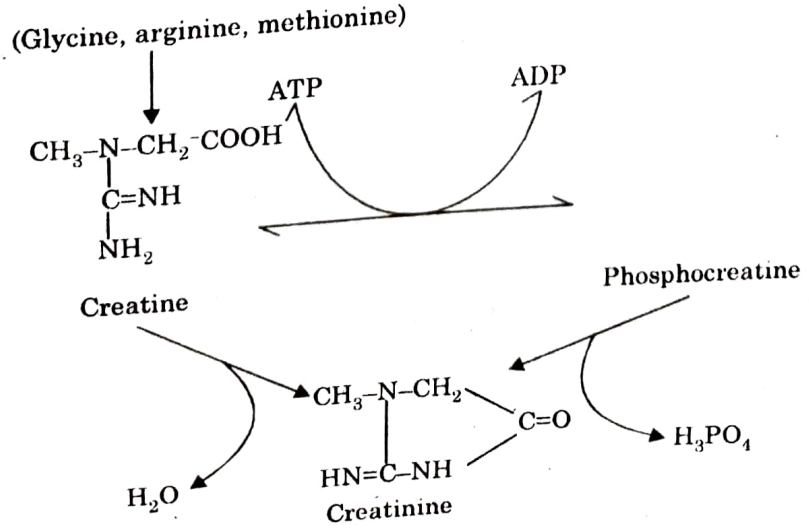


Fig. 16.2. Urea synthesis by the ornithine cycle.

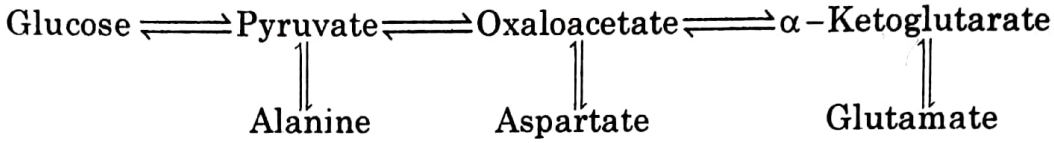


Disposal of Carbon Skeleton

The fate of keto acids, which are obtained by the removal of amino group as ammonia, may be either of the following types :

(i) Synthetic pathways : The α-keto acids which are formed by deamination may also undergo amination reductively by reversing transdeamination mechanism, thus reforming the original amino acids. This process is continuous.

(ii) Glucogenic pathway : The carbon skeleton of most of the amino acids may be converted into carbohydrates (gluconeogenesis from protein). Such amino acids are termed as *glucogenic or antiketogenic amino acids.* A few amino acids involving in carbohydrate metabolism directly, are depicted below :



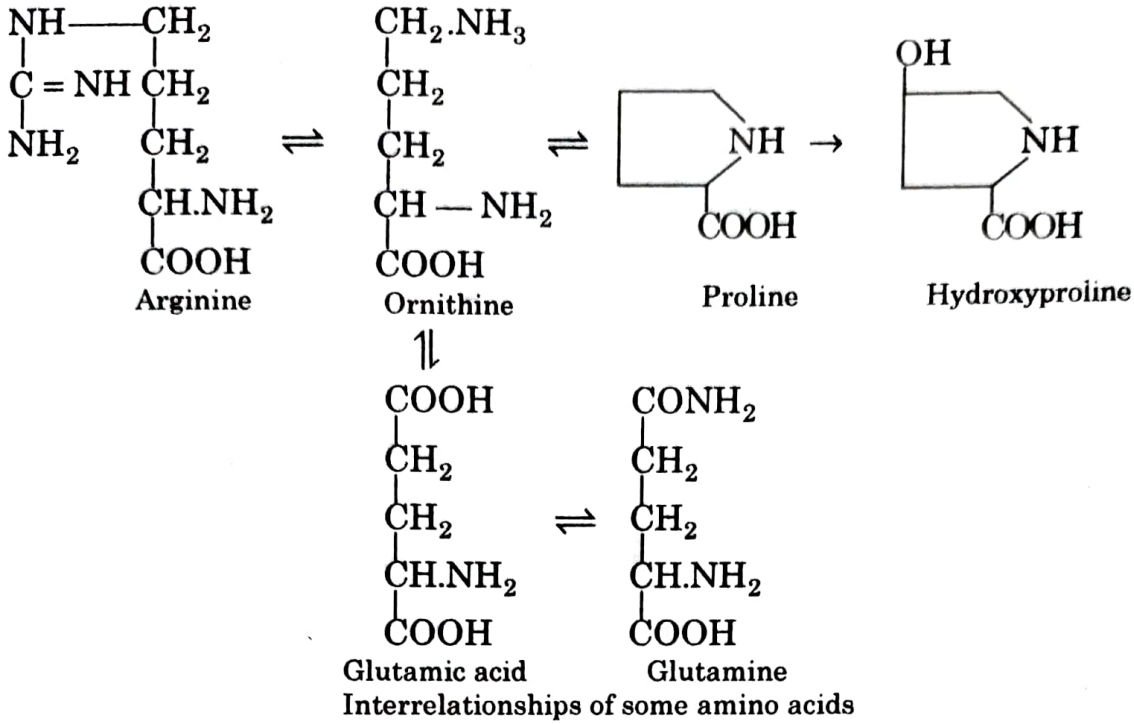
The routes for the conversion of various keto acids to carbohydrates have been found to depend upon the compound concerned (for details see metabolism of individual amino acids). The various glucogenic amino acids are given in Table 16.2.

The keto acids derived from these amino acids may also directly enter the tricarboxylic acid cycle and thus get oxidised ultimately to CO_2 and H_2O. For example, pyruvic acid obtained by the deamination of alanine gets oxidised to CO_2 and H_2O *via* TCA cycle.

Table 16.2
AMINO ACIDS ACCORDING TO THE FATE OF THEIR CARBON SKELETON

Glycogen forming (Glycogenic amino acid)	*Fat forming (Ketogenic amino acid)*	*Both glycogen and fat forming (Glycogenic as well as ketogenic amino acids)*
Alanine Hydroxyproline	Leucine	Isoleucine
Arginine Methionine		Lysine
Asparate Proline		Phenylalanine
Cystine Serine		Tyrosine
Glutamic acid Threonine		Tryptophan
Glycine Valine		
Histidine		

(iii) Ketogenic pathway : The α-keto acid (isovaleryl formic acid) derived from the deamination of leucine, on its oxidation to CO_2 and H_2O has to pass through the stage of acetoacetic acid and thus ketone bodies instead of glucose are formed. Such amino acids are termed as *ketogenic amino acids.*



Interrelationships of some amino acids

(iv) Glucogenic as well as ketogenic pathway : The keto acids derived from certain amino acids may enter the above-mentioned glucogenic as well as ketogenic pathways, thereby forming both glucose and ketone bodies. Such amino acids are isoleucine, lysine, phenylalanine, tyrosine and tryptophan.

(v) Other pathways : The metabolic pathways of certain amino acids do not correspond with either of the above pathways. These routes are highly specific and have been described in the appropriate sections.

Interrelationships of amino acids : Isotopic experiments show that arginine, ornithine, proline and glutamic acid could be interconverted by keeping the carbon chain intact.