Biochemistry For Pharmacy College Students

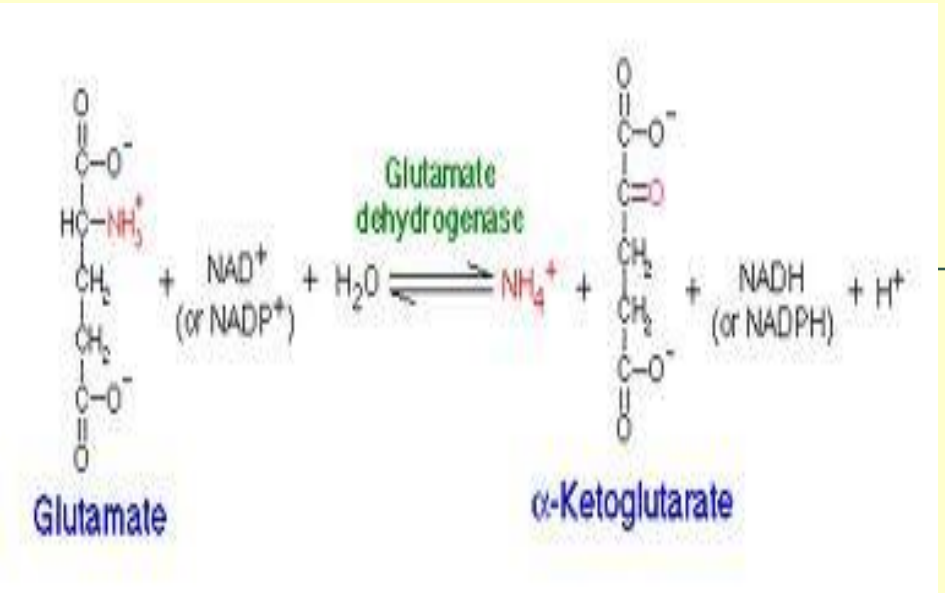
Metabolism Of Amino Acids & Proteins

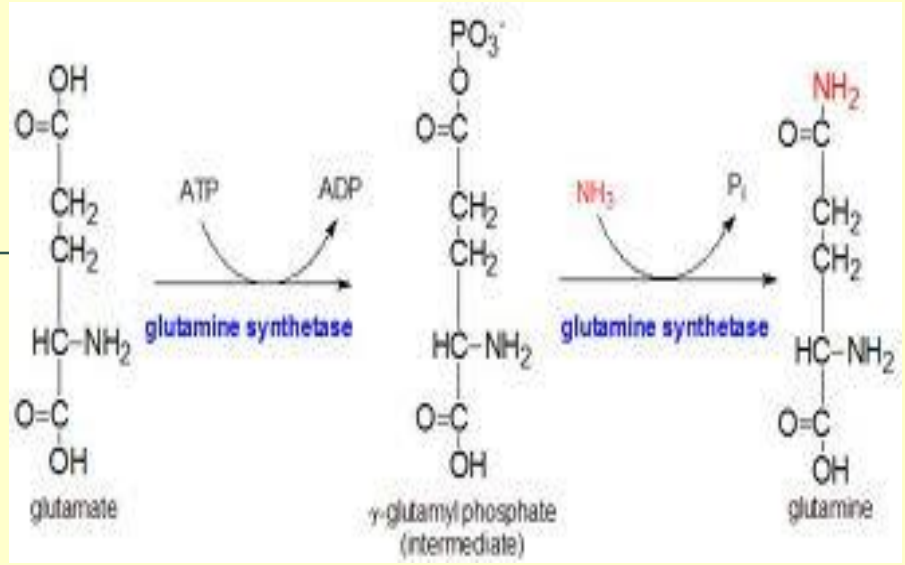
Dr. Yaser A.M Sulaiman

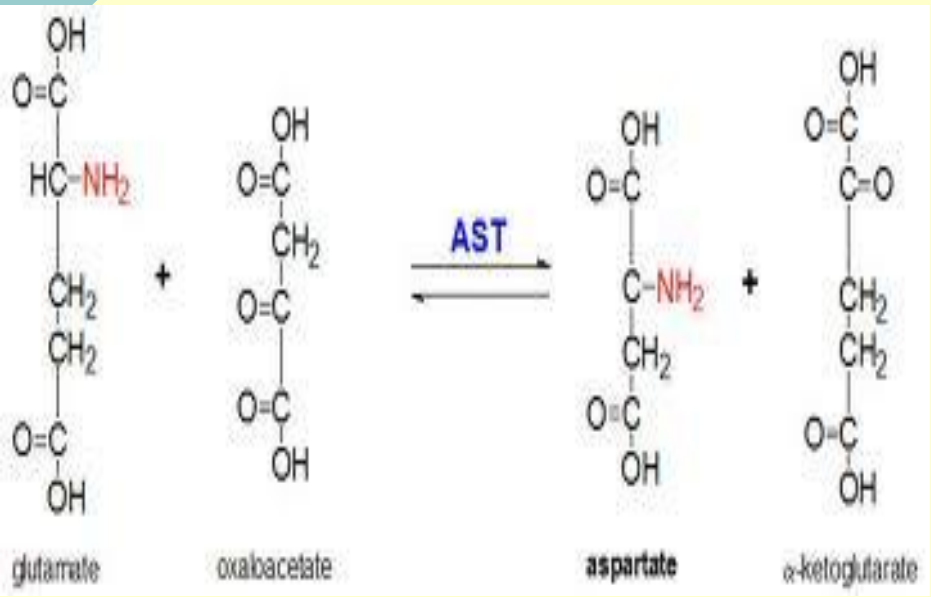
Biosynthesis of the Nutritionally Nonessential Amino Acids

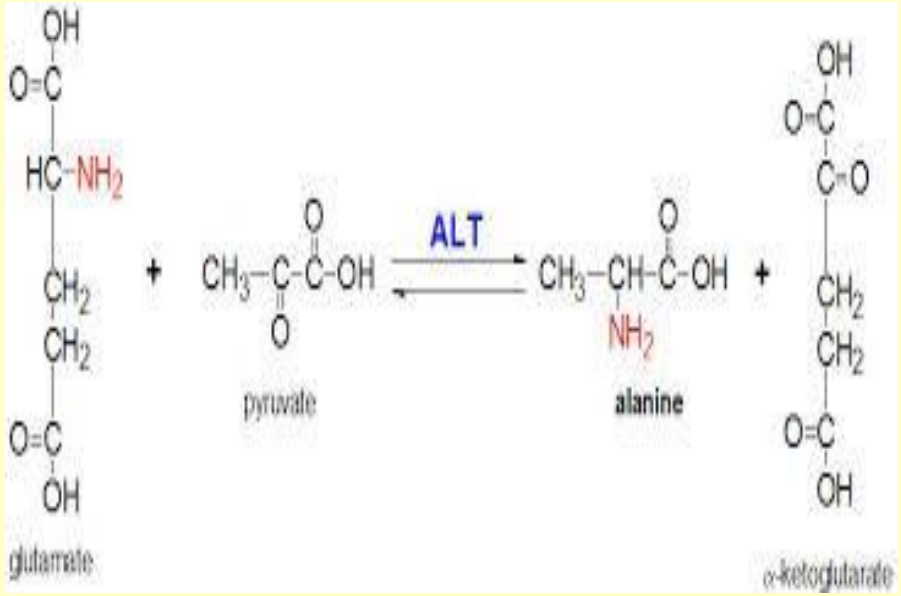
- Although all 20 of the amino acids present in proteins are essential for health, humans can synthesize 12 (nonessential) of the 20 common amino acids from the intermediates of glycolysis and of the citric acid cycle except three A.A. (cysteine, tyrosine and hydroxylysine) from nutritionally essential amino acids.
- The enzymes (1)glutamate dehydrogenase, (2)glutamine synthetase, and (3)aminotransferases occupy central positions in A.A. biosynthesis.
- e. g. Glutamate and Glutamine. Reductive amination of α-ketoglutarate is catalyzed by glutamate dehydrogenase, then Amination of glutamate to glutamine is catalyzed by glutamine synthetase.
- To form Alanine. Transamination of pyruvate forms alanine.
- Aspartate and Asparagine. Transamination of oxaloacetate forms aspartate. The conversion of aspartate to asparagine is catalyzed by asparagine synthetase (resembles glutamine synthetase).

Nutritionally Essential	Nutritionally Nonessential
Arginine[1]	Alanine
Histidine	Asparagine
Isoleucine	Aspartate
Leucine	Cysteine
Lysine	Glutamate
Methionine	Glutamine
Phenylalanine	Glycine
Threonine	Hydroxyproline[2]
Tryptophan	Hydroxylysine[2]
Valine	Proline
	Serine
	Tyrosine


Glutamate dehydrogenase
NAD+ (or NADP+)
H2O
NH4+
NADH (or NADPH)
+ H+
Glutamate
α-Ketoglutarate


ATP
ADP
glutamine synthetase
NH3
Pi
glutamine synthetase
glutamate
γ-glutamyl phosphate (intermediate)
glutamine


AST
glutamate
oxalacetate
aspartate
α-ketoglutarate


ALT
pyruvate
alanine
glutamate
α-ketoglutarate

Catabolism of Proteins & of Amino Acid Nitrogen

The continuous degradation and synthesis of cellular proteins occur in all forms of life. Each day humans turn over 1–2% of their total body protein, principally muscle protein. High rates of protein degradation occur in tissues undergoing structural rearrangement.

e.g., skeletal muscle in starvation, uterine tissue during pregnancy, etc.

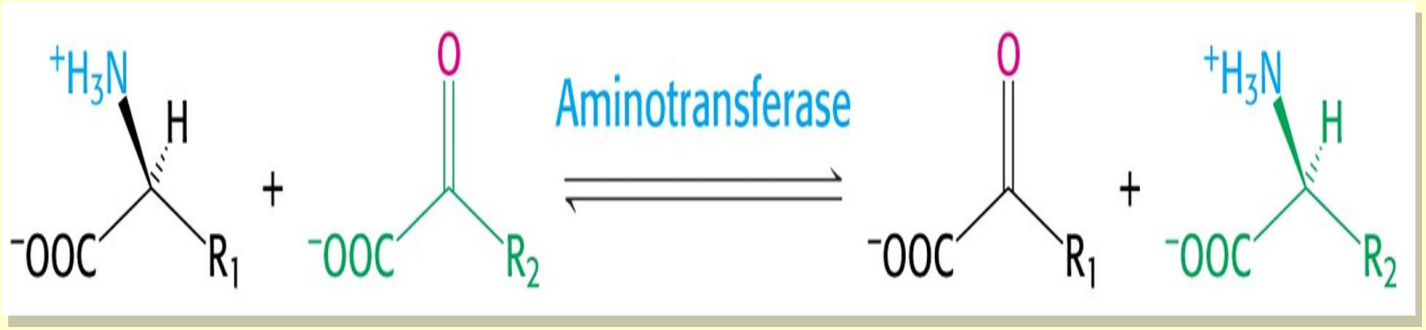
the liberated amino acids, approximately 75% are reutilized.

Unlike glucose and fatty acids, which can be stored, excess amino acids are not stored, those not immediately incorporated into new protein are rapidly degraded.

While ammonia, derived mainly from the α-amino nitrogen of amino acids, is highly toxic, in most mammals, tissues convert ammonia to the amide nitrogen of nontoxic glutamine. Subsequent deamination of glutamine in the liver releases ammonia (NH3), which is then converted to nontoxic urea ($(NH_2)_2CO$) (through urea cycle in the liver) and excreted.

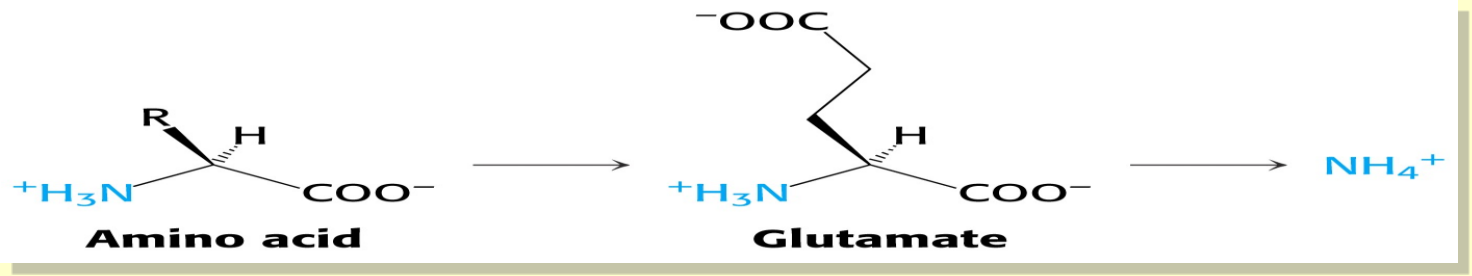
Catabolism of Proteins & of Amino Acid Nitrogen

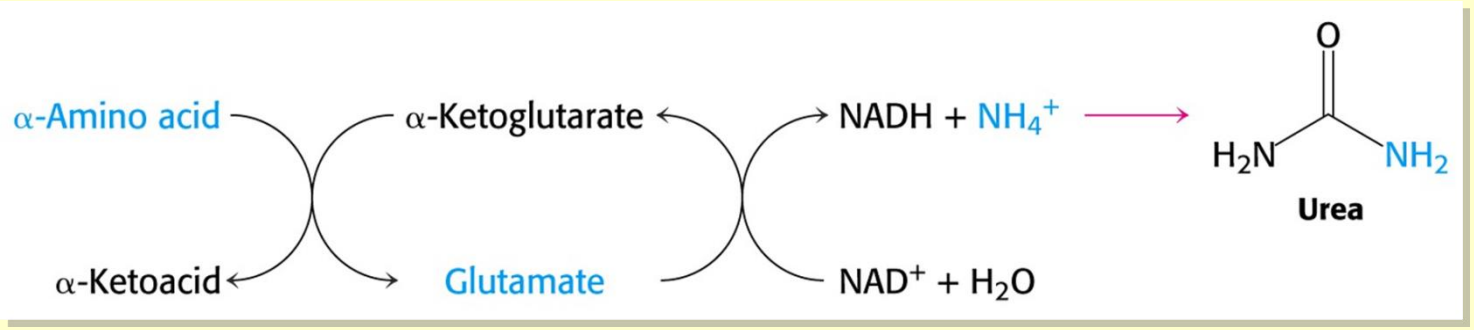
- While Carbon skeleton is converted to:
- Acetyl–CoA, Acetoacetyl–CoA, Pyruvate &Citric ac cycle intermediate.
- The Deamination produces α-keto acids, which are degraded to other metabolic intermediates.
- Generally Aspartate transaminase and Alanine transaminase enzymes funnel amino groups to α–ketoglutarate.



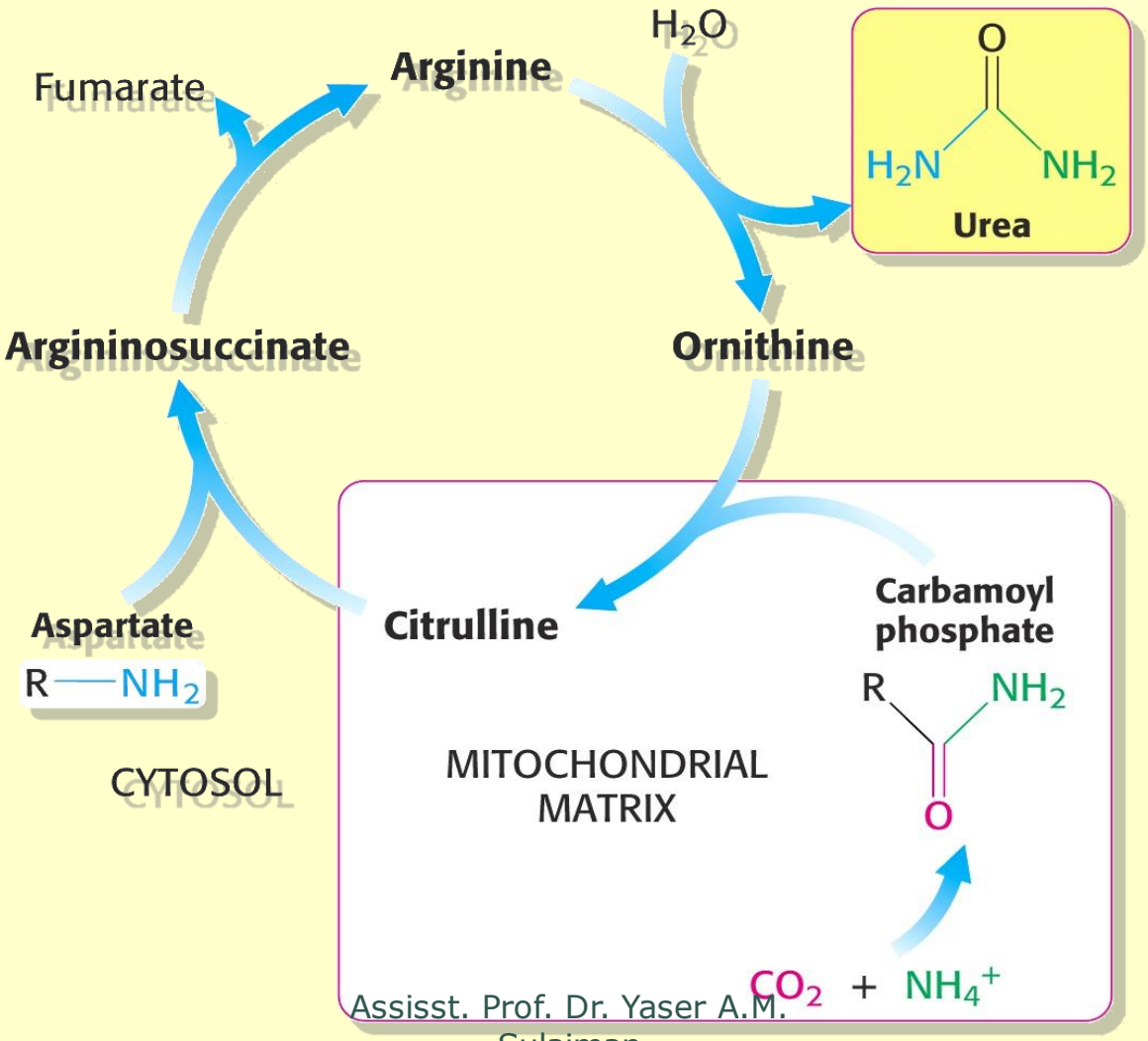
The Conversion to Ammonium Ions

- α–Amino groups are converted to ammonium ions by the oxidative deamination of glutamate.





The Urea Cycle

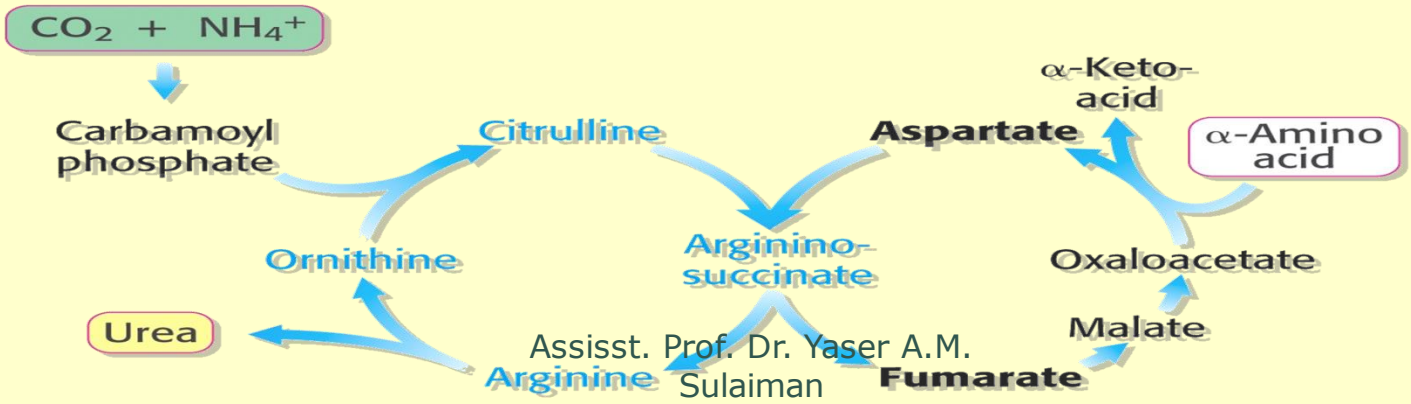


The Urea Cycle

- First two reactions (the formation of NH_4^+ from glutamate in the presence of glutamate dehydrogenase and the subsequent incorporation into the citrulline) occurs in the mitochondrial matrix
-The other 3 reactions of the urea cycle take place in the cytosol
-Citrulline is transported to the cytosol.

The Urea cycle cost of four "high-energy" phosphate bonds (3 ATP hydrolyzed to 2 ADP and one AMP)

The urea cycle is linked to the citric acid cycle: Kreb's Bi-cycle.



Catabolism of the Carbon Skeletons of Amino Acids

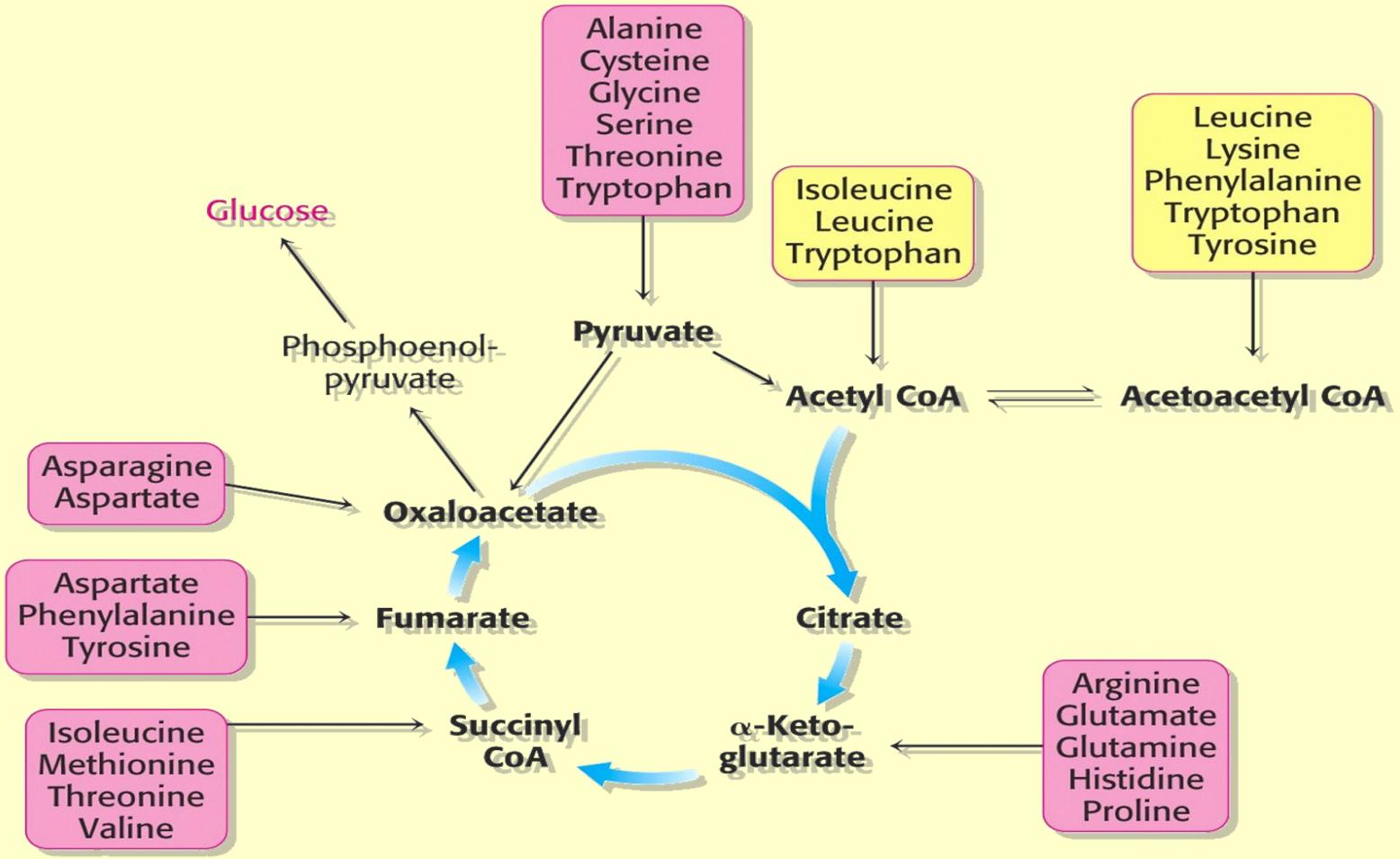
The carbon atoms of degraded amino acids emerge as major metabolic intermediates.

- Degradation of the 20 amino acids funnel into 7 metabolic intermediates
  - Acetyl-CoA
  - Acetoacetyl-CoA — Ketogenic
  - Pyruvate
  - α-Ketoglutarate
  - Succinyl–CoA — Glucogenic
  - Fumarate
  - Oxaoloacetate

Catabolism of the Carbon Skeletons of Amino Acids

Ketogenic	Glucogenic	Both
leucine	serine	isoleucine
lysine	threonine	phenylalanine
	aspartic acid	tryptophan
	glutamic acid	tyrosine
	asparagine	
	glutamine	
	glycine	
	alanine	
	valine	
	proline	
	histidine	
	arginine	
	methionine	
	cysteine	

Catabolism of the Carbon Skeletons of Amino Acids



Conversion of Amino Acids to Specialized Products

BIOMEDICAL IMPORTANCE

Important products derived from amino acids include heme, purines, pyrimidines, hormones, neurotransmitters, and biologically active peptides. In addition, many proteins contain amino acids that have been modified for a specific function such as binding calcium or as intermediates that serve to stabilize proteins—generally structural proteins—by subsequent covalent cross-linking.

Histamine plays a central role in many allergic reactions. Neurotransmitters derived from amino acids include γ-aminobutyrate, 5-hydroxytryptamine (serotonin), dopamine, norepinephrine, and epinephrine. Many drugs used to treat neurologic and psychiatric conditions affect the metabolism of these neurotransmitters.

Conversion of Amino Acids to Specialized Products

Tyrosine

Neural cells convert tyrosine to epinephrine and norepinephrine. While dopa is also an intermediate in the formation of melanin, different enzymes hydroxylate tyrosine in melanocytes. Dopa decarboxylase, a pyridoxal phosphate-dependent enzyme, forms dopamine. Subsequent hydroxylation by dopamine β-oxidase then forms norepinephrine.

Tyrosine is also a precursor of triiodothyronine and thyroxine.

Creatinine

Creatinine is formed in muscle from creatine phosphate by irreversible, nonenzymatic dehydration and loss of phosphate. The 24-hour urinary excretion of creatinine is proportionate to muscle mass.

Glycine, arginine, and methionine all participate in creatine biosynthesis.