Conversion of amino acids to Specialized products

Department of Biochemistry

Specific Learning Objectives

- Conversion of aa to Specialized products
- Describe roles of arginine and ornithine in metabolic pathways other than urea cycle (in NO and synthesis, respectively)

Introduction

- In addition to serving as building blocks for proteins, aa are precursors of many nitrogen-containing compounds that have important physiologic functions
- These molecules include porphyrins (involved in heme biosynthesis), hormones, purines, and pyrimidines, neurotransmitters.

Conversion of arginine, ornithine & proline to specialized products

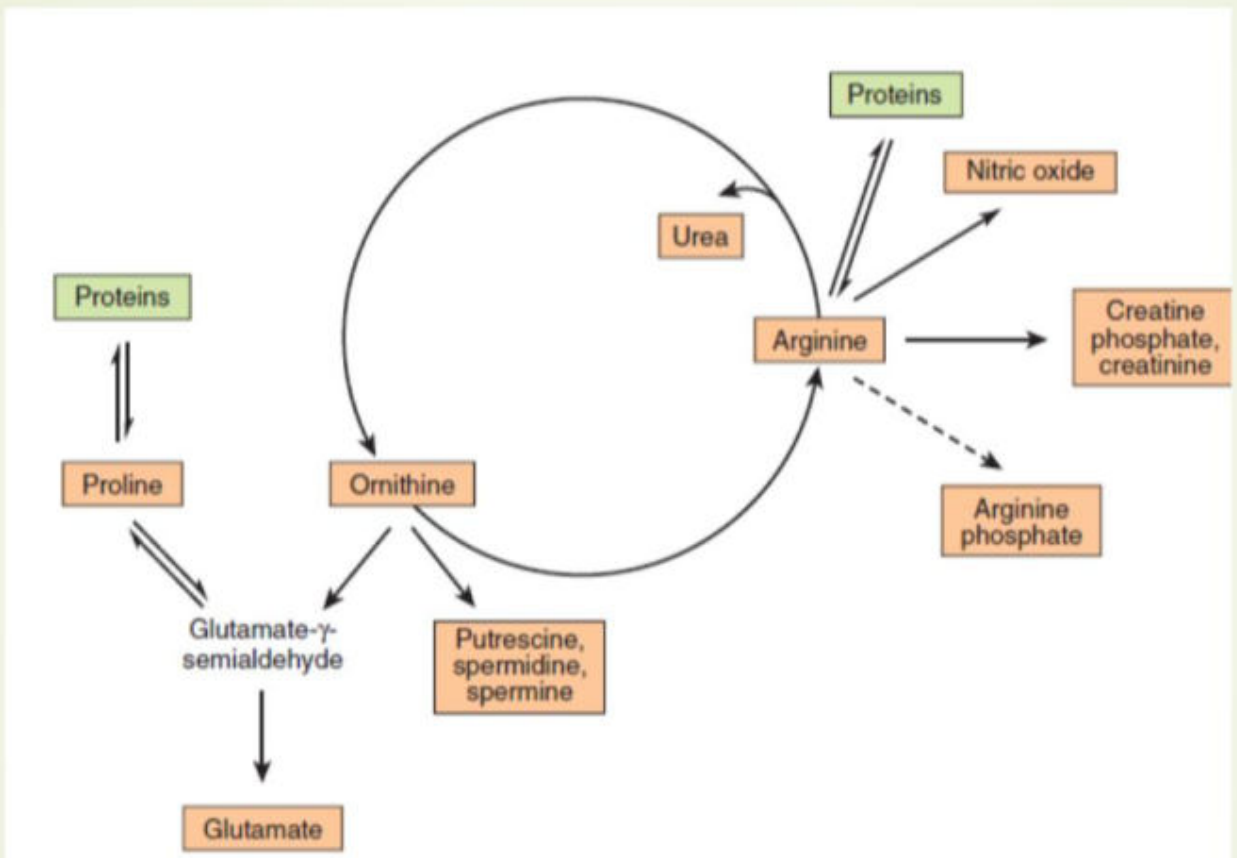

FIGURE 30–1 Arginine, ornithine, and proline metabolism. Reactions with solid arrows all occur in mammalian tissues. Putrescine and spermine synthesis occurs in both mammals and bacteria. Arginine phosphate of invertebrate muscle functions as a phosphagen analogous to creatine phosphate of mammalian muscle. Fig 30.1. Harper's Illustrated Biochemistry 30th Edition

Creatine & Creatinine

- Creatinine is formed in muscle from creatine phosphate by irreversible, non-enzymatic dehydration, and loss of phosphate

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

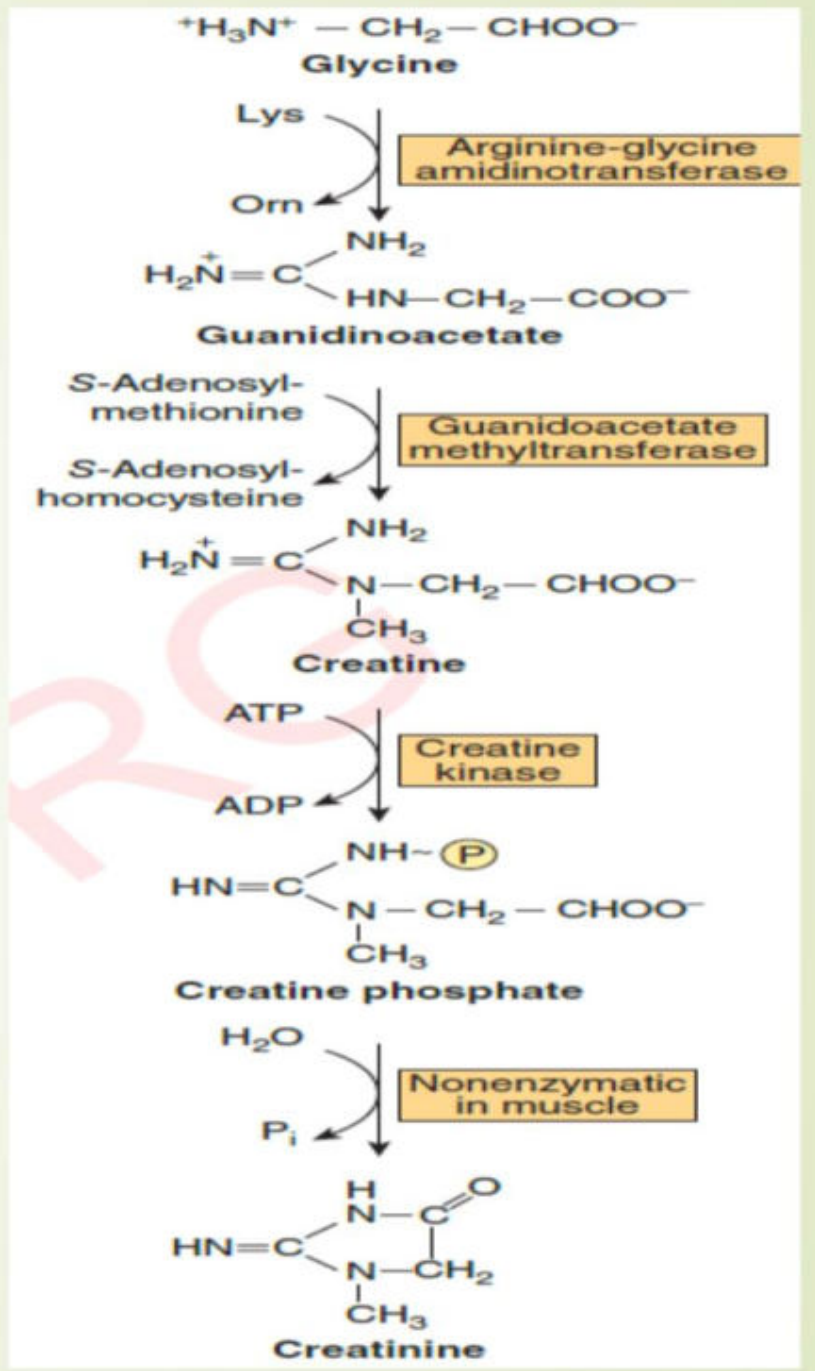

Fig 30.13. Harper's Illustrated Biochemistry 30th Edition

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- Creatine converted into creatine phosphate by creatine kinase using ATP as a phosphate donor

- Presence of creatine kinase in plasma is indicative of heart damage and is used in diagnosis of myocardial infarction

Conversion of cysteine to Taurine

- Three enzyme catalyzed reactions convert cysteine to taurine
- Taurine displace coenzyme A moiety of cholyl-CoA to form bile acid taurocholic acid

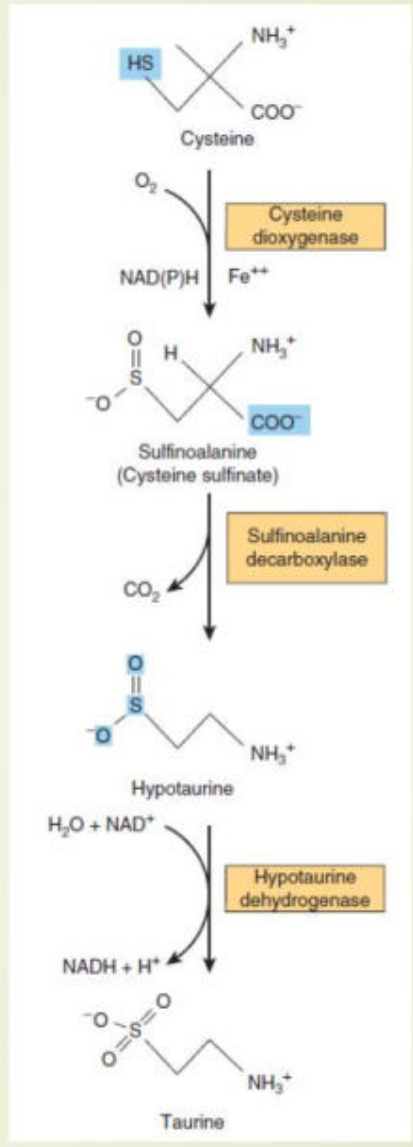

Fig 30.4. Harper's Illustrated Biochemistry 30th Edition

Biosynthesis of hippurate from glycine

- Many metabolites and pharmaceuticals are excreted as water soluble glycine conjugates
- Ex. include glycocholic acid and hippuric acid formed from food additive benzoate
- Many drugs, drug metabolites, and other compounds with carboxyl groups are conjugated with glycine, which makes them more water-soluble and thereby facilitates their excretion in urine

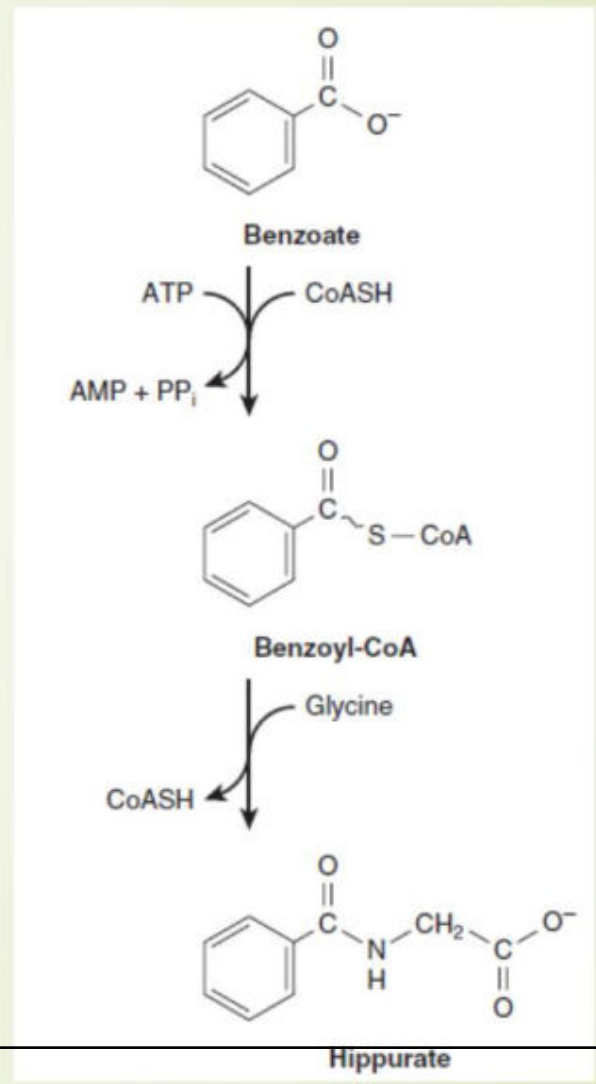

Fig 30.5. Harper's Illustrated Biochemistry 30th Edition

Derivatives of Histidine

- Decarboxylation of histidine to histamine is catalyzed by pyridoxal 5′-phosphate-dependent enzyme histidine decarboxylase
- Histamine functions in allergic reactions and gastric secretion

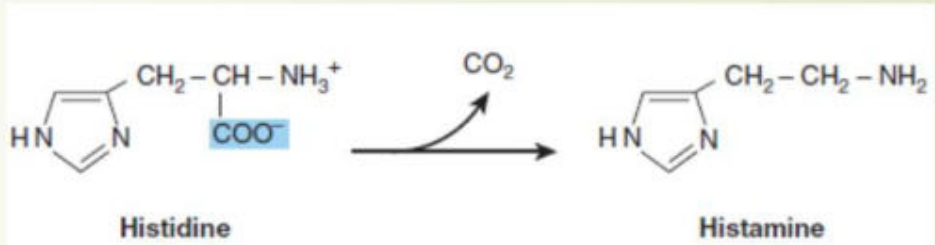

FIGURE 30–6 The reaction catalyzed by histidine decarboxylase.

Fig 30.6. Harper's Illustrated Biochemistry 30th Edition

Derivatives of Methionine

- These polyamines function in cell proliferation and growth, are growth factors for cultured mammalian cells, and stabilize intact cells, subcellular organelles, and membranes
- They bear multiple positive charges, polyamines readily associate with DNA and RNA

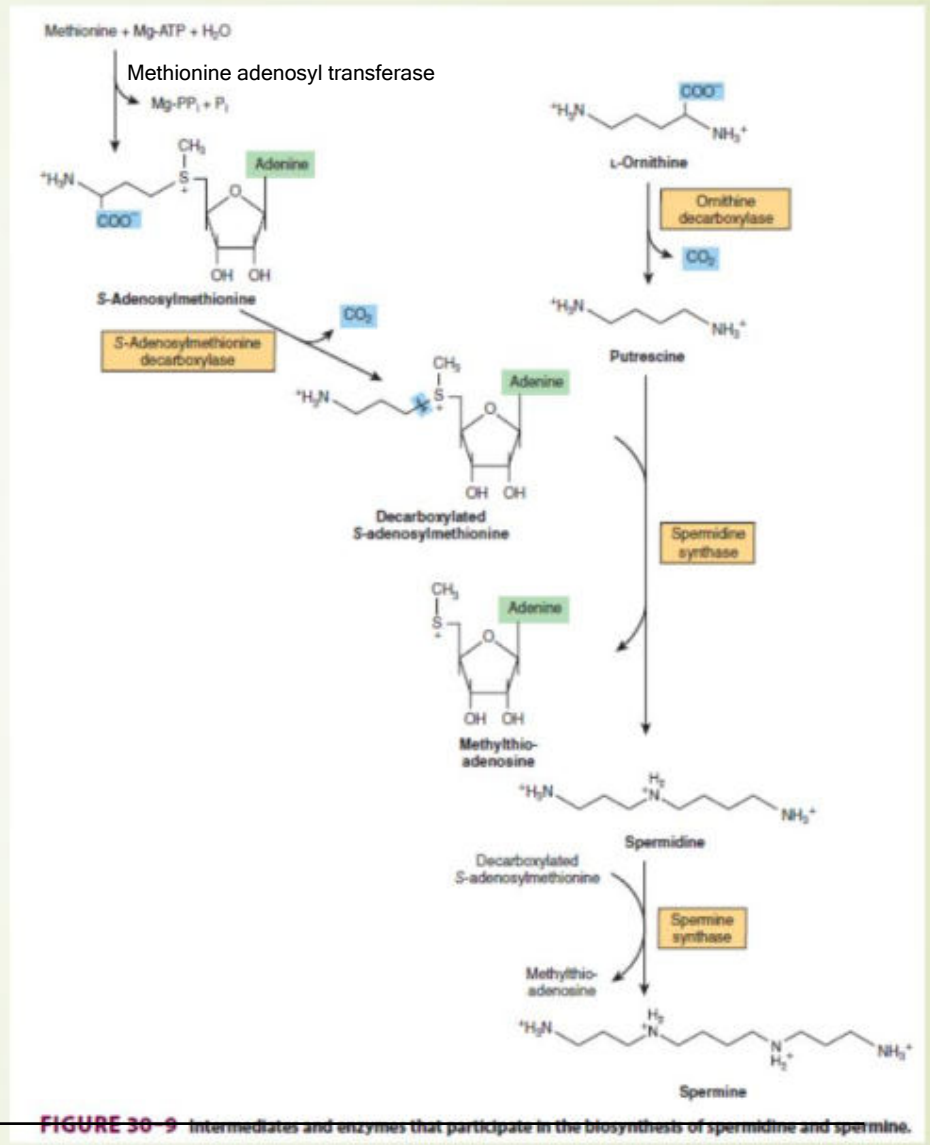

FIGURE 30–9 Intermediates and enzymes that participate in the biosynthesis of spermidine and spermine.

Fig 30.9. Harper's Illustrated Biochemistry 30th Edition

Derivatives of Tryptophan

- Hydroxylation of tryptophan to 5-hydroxytryptophan by liver tryptophan hydroxylase subsequent decarboxylation forms serotonin a potent vasoconstrictor and stimulator of smooth muscle contraction.

- Catabolism of serotonin is initiated by deamination to 5-hydroxyindole-3-acetate, a reaction catalyzed by monoamine oxidase

Cont--

- N-Acetylation of serotonin, followed by its O-methylation in pineal body, forms melatonin

- Kidney tissue, liver tissue, and fecal bacteria all convert tryptophan to tryptamine, then to indole 3-acetate

- Normal urinary catabolites of tryptophan are 5-hydroxyindoleacetate and indole 3-acetate.

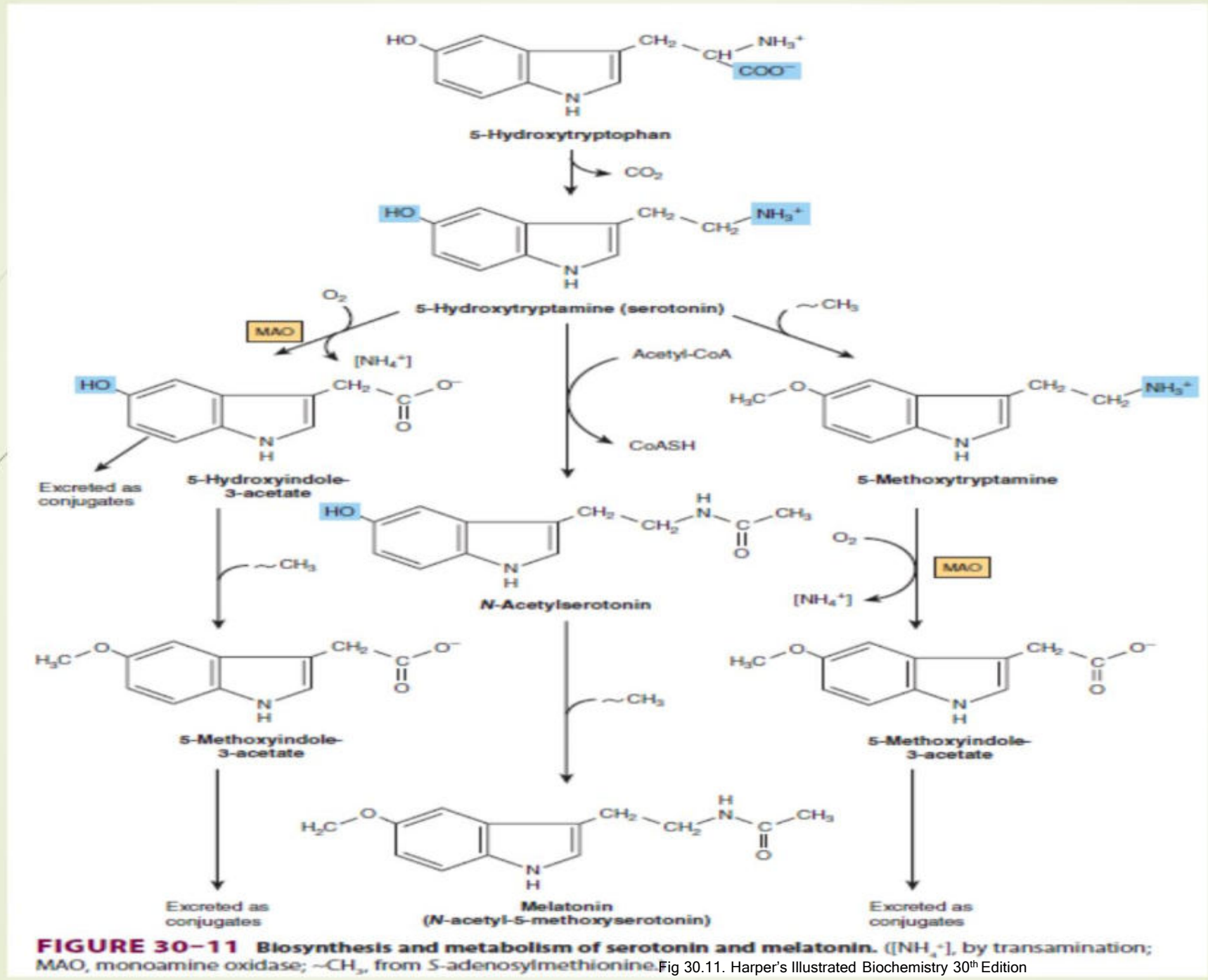

FIGURE 30–11 **Biosynthesis and metabolism of serotonin and melatonin.** ([NH_4^+], by transamination; MAO, monoamine oxidase; ~CH_3, from S-adenosylmethionine.

Fig 30.11. Harper's Illustrated Biochemistry 30th Edition

Derivatives of Tyrosine

Melanin: Tyrosine form DOPA by Tyrosinase in melanocytes, L-Dopa can be converted, via tyrosinase, into dopaquinone followed melanin synthesis

- Tyrosine forms DOPA by Tyrosine Hydroxylase in adrenal chromaffin cells

Nor-Epinephrine and Epinephrine:

- Neural cells convert tyrosine to epinephrine and norepinephrine

- Dopa decarboxylase, a PLP-dependent enzyme, forms dopamine

Cont--

- Subsequent hydroxylation, catalyzed by dopamine β-oxidase forms norepinephrine
- In adrenal medulla, phenylethanolamine-N-methyltransferases utilizes S-adenosylmethionine to methylate the primary amine of norepinephrine, forming epinephrine

T3 and T4: Tyrosine is also a precursor of triiodothyronine and thyroxine

Derivatives of Tyrosine: Melanin

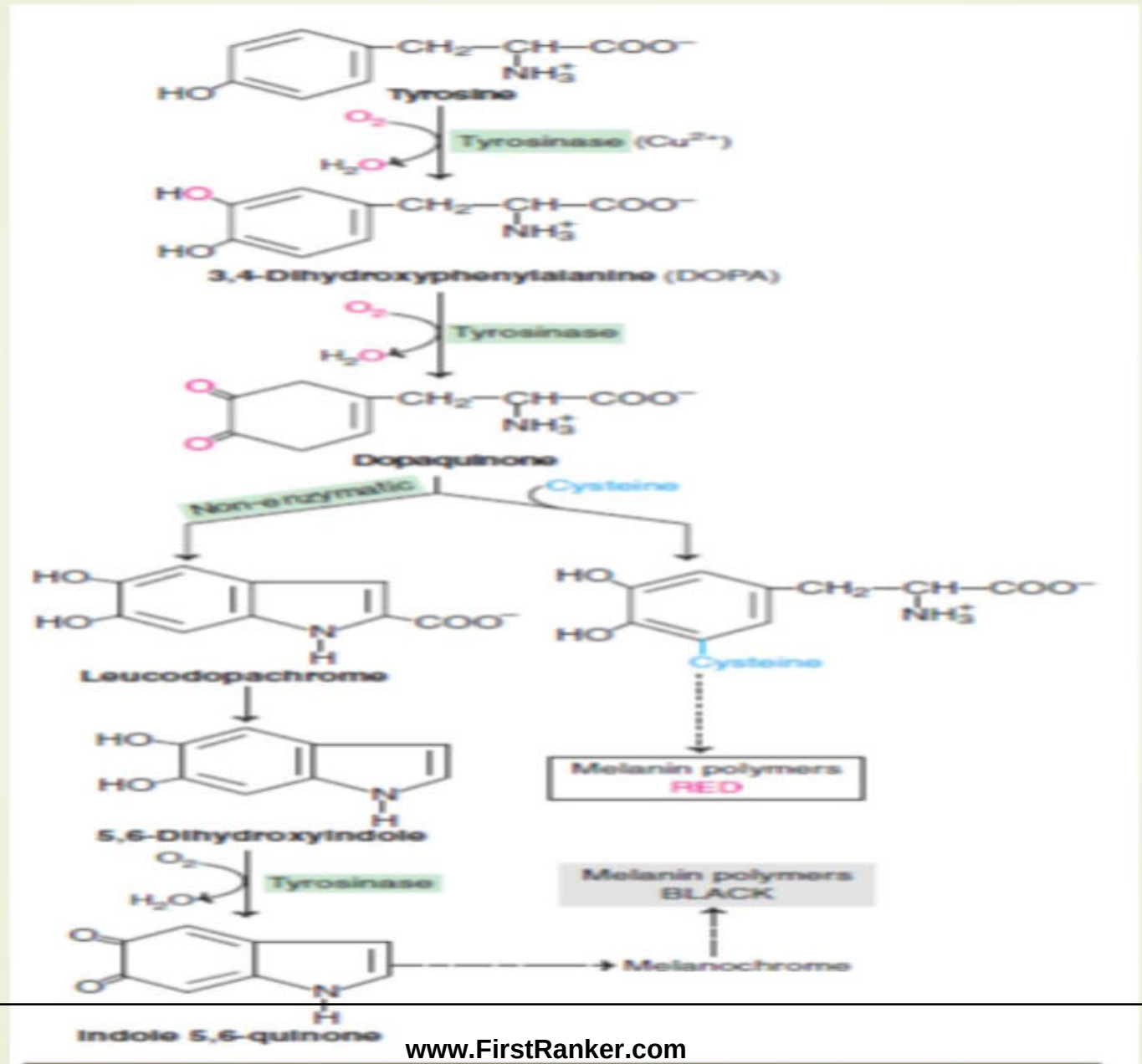

Fig. 15.20 : Metabolism of tyrosine—biosynthesis of melanin (Defect in tyrosinase causes albinism).

Derivatives of Tyrosine: Epinephrine

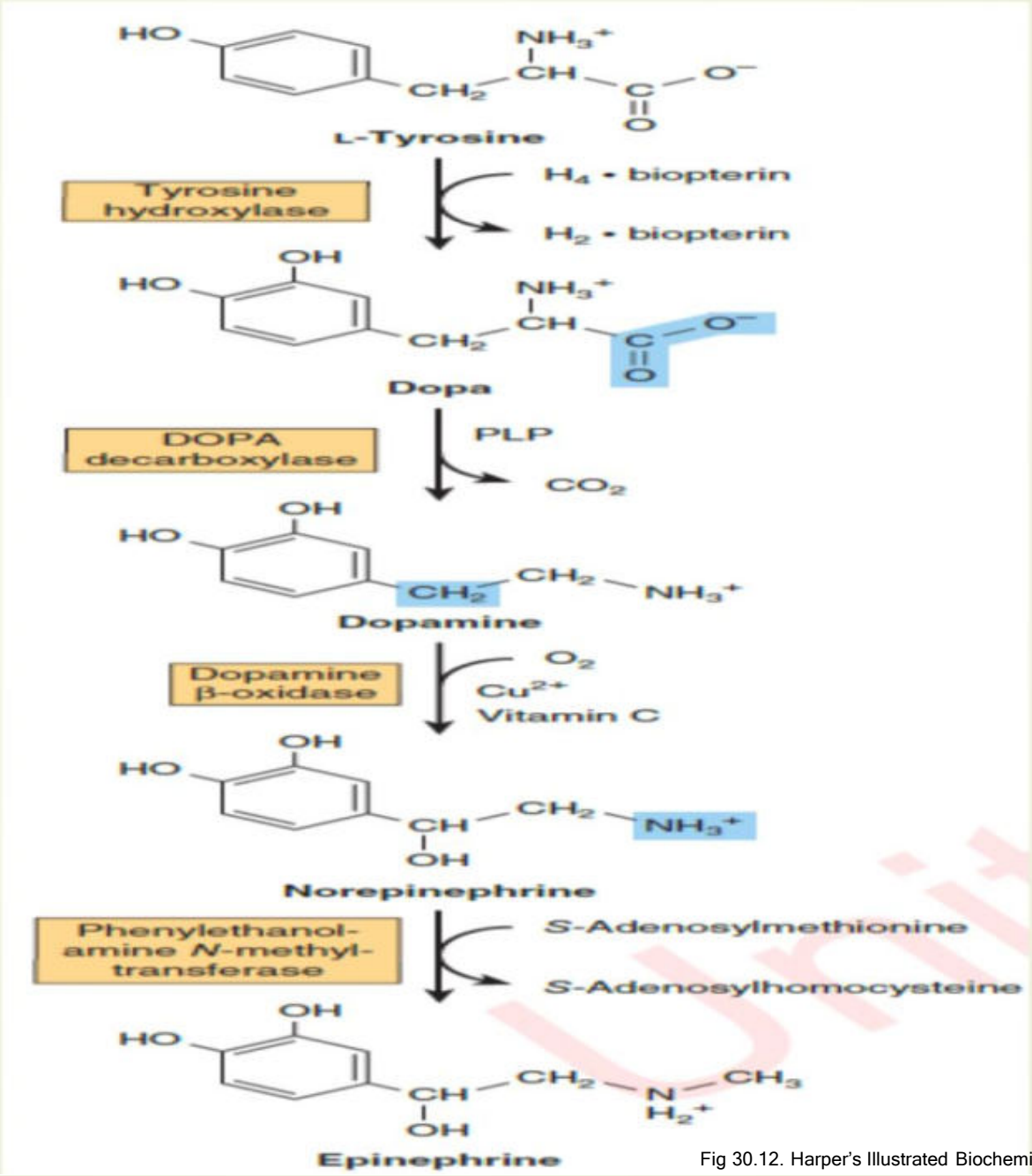

Fig 30.12. Harper's Illustrated Biochemistry 30th Edition

Derivatives of Tyrosine: T3 and T4

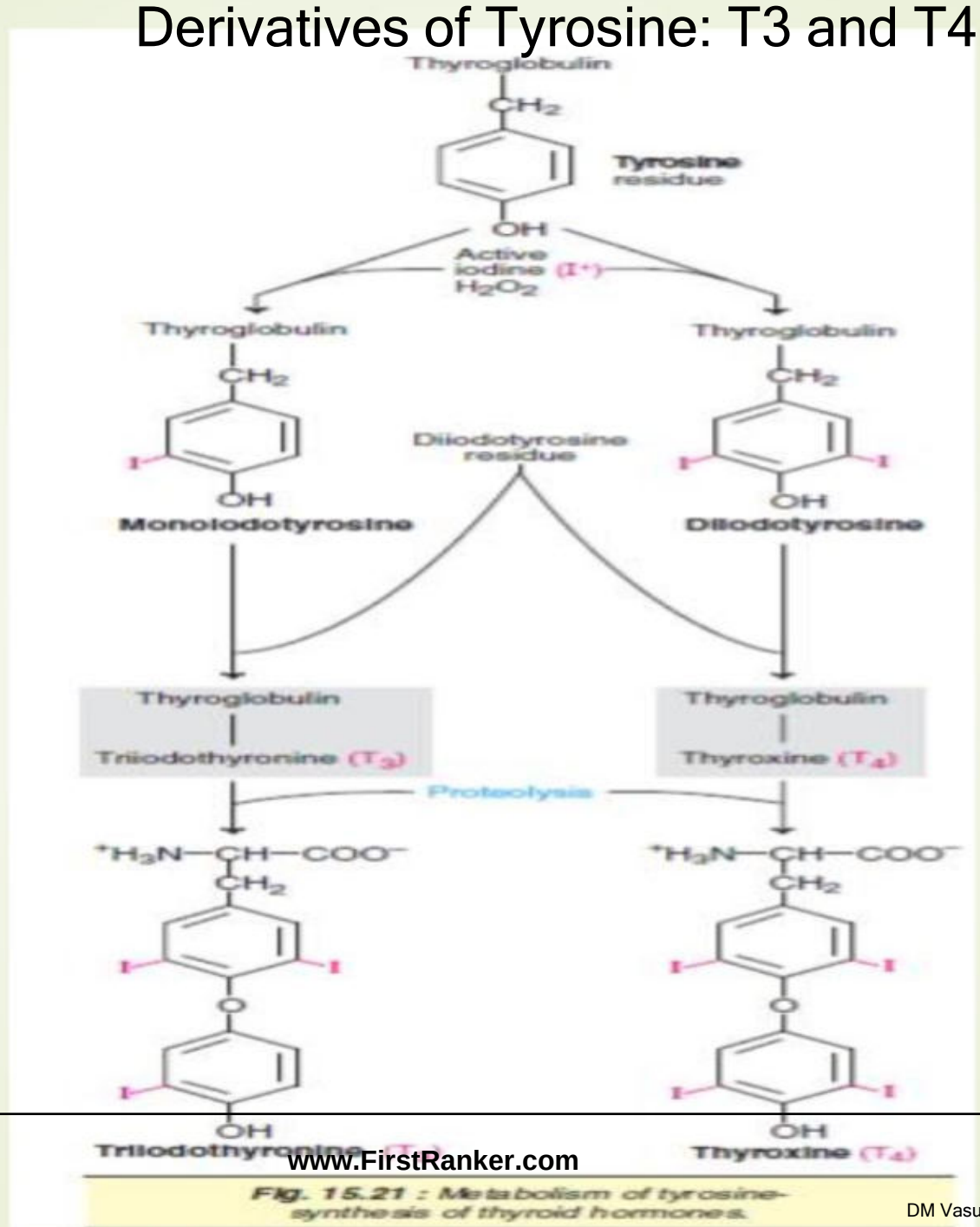

Fig. 15.21 : Metabolism of tyrosine-synthesis of thyroid hormones.

DM Vasudevan' s Textbook of Biochemistry for Medical Students-6th Ed

Disorder related to Tyrosine derivative

Albinism: A deficiency of tyrosinase in melanocytes causes one form of albinism; it is inherited as an autosomal recessive disorder

- Pigmentation of skin, hair and iris is reduced and eyes may appear pink
- Reduced pigmentation of iris causes photosensitivity and decreased skin pigmentation associated with increased incidence of certain skin cancers
- Tyrosinase involved in catecholamine synthesis is a different isoenzyme, controlled by different gene; consequently, adrenaline (epinephrine) metabolism is normal

Metabolism of γ-AminoButyrate (GABA)

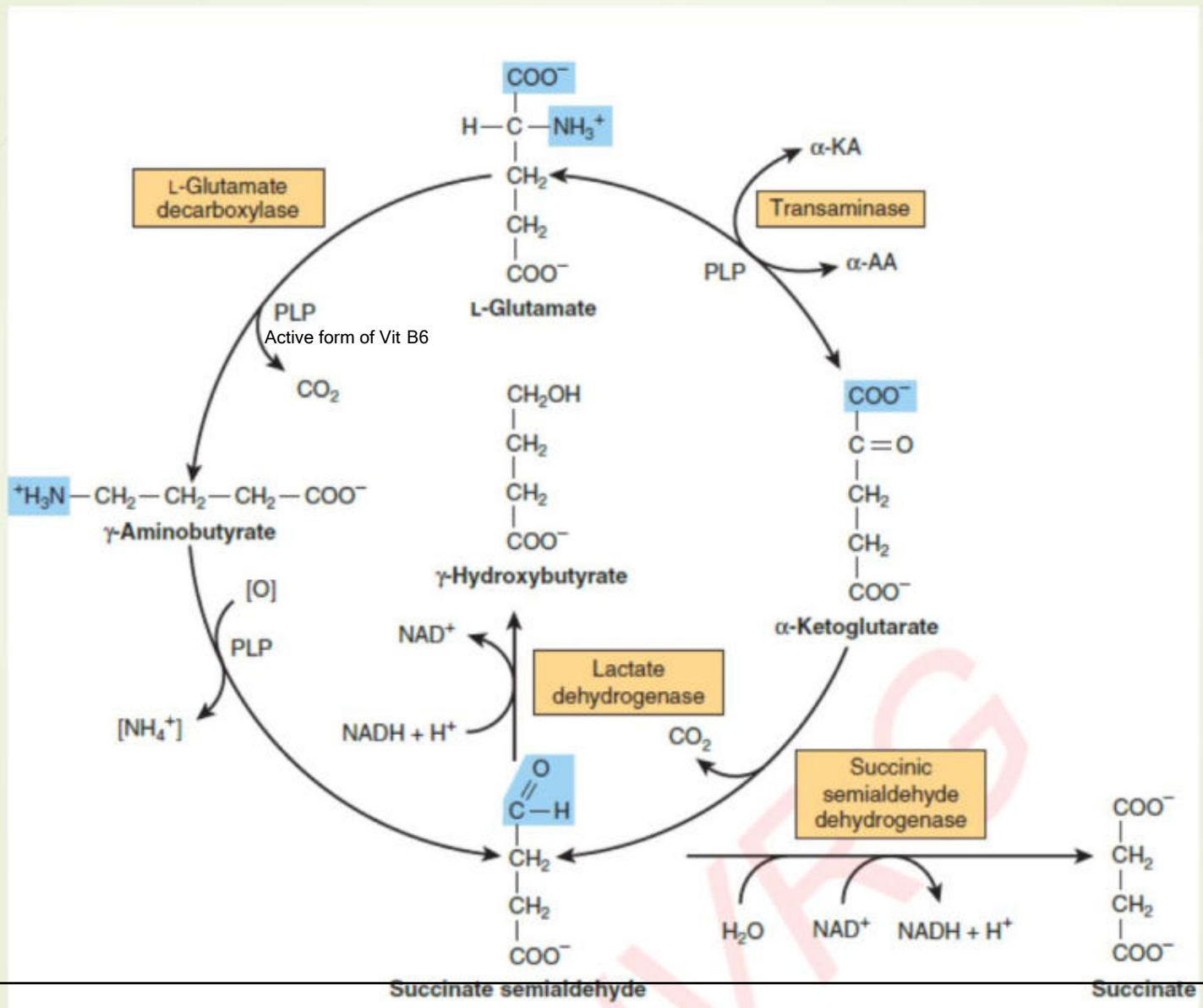

FIGURE 30–14 Metabolism of γ-aminobutyrate. (α-AA, α-amino acids; α-KA, α-keto acids; PLP, pyridoxal phosphate.) Fig 30.14. Harper's Illustrated Biochemistry 30th Edition

Disorder related to GABA

4-hydroxybutyric aciduria

- Defects in succinic semialdehyde dehydrogenase, are responsible for 4-hydroxybutyric aciduria a rare metabolic disorder of γ-aminobutyrate catabolism

- Characterized by presence of 4-hydroxybutyrate in urine, plasma and cerebrospinal fluid

- No present treatment is available for accompanying mild to severe neurologic symptoms.

Clinical-cases discussed

Reference Books

1) Lehninger Principles of Biochemistry, 6th Ed.
2) Harper's Illustrated Biochemistry-30th edition
3) Biochemistry, Lippincott's Illustrated Reviews, 6th Ed
4) Gregory S. Ducker and Joshua D Rabinowitz. Cell Metab. 2017 Jan 10;25(1):27-42

Thank you