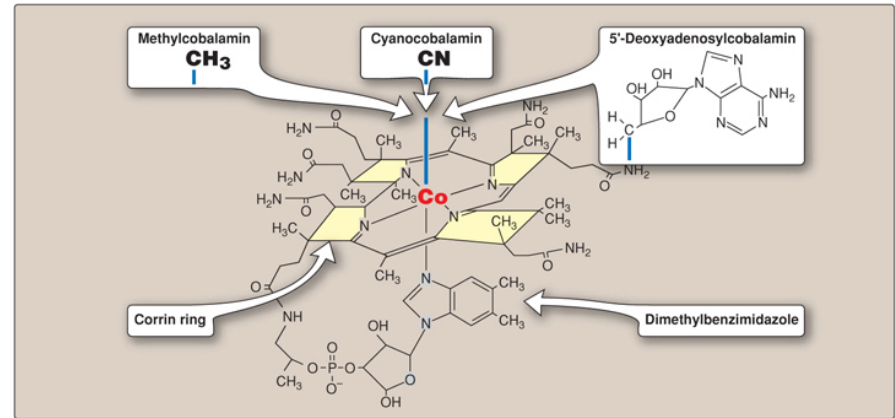


Vitamins

B₆ and B₁₂



Copyright © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins

Neuropsychiatry Block
Dr. Usman Ghani
Biochemistry

Objectives

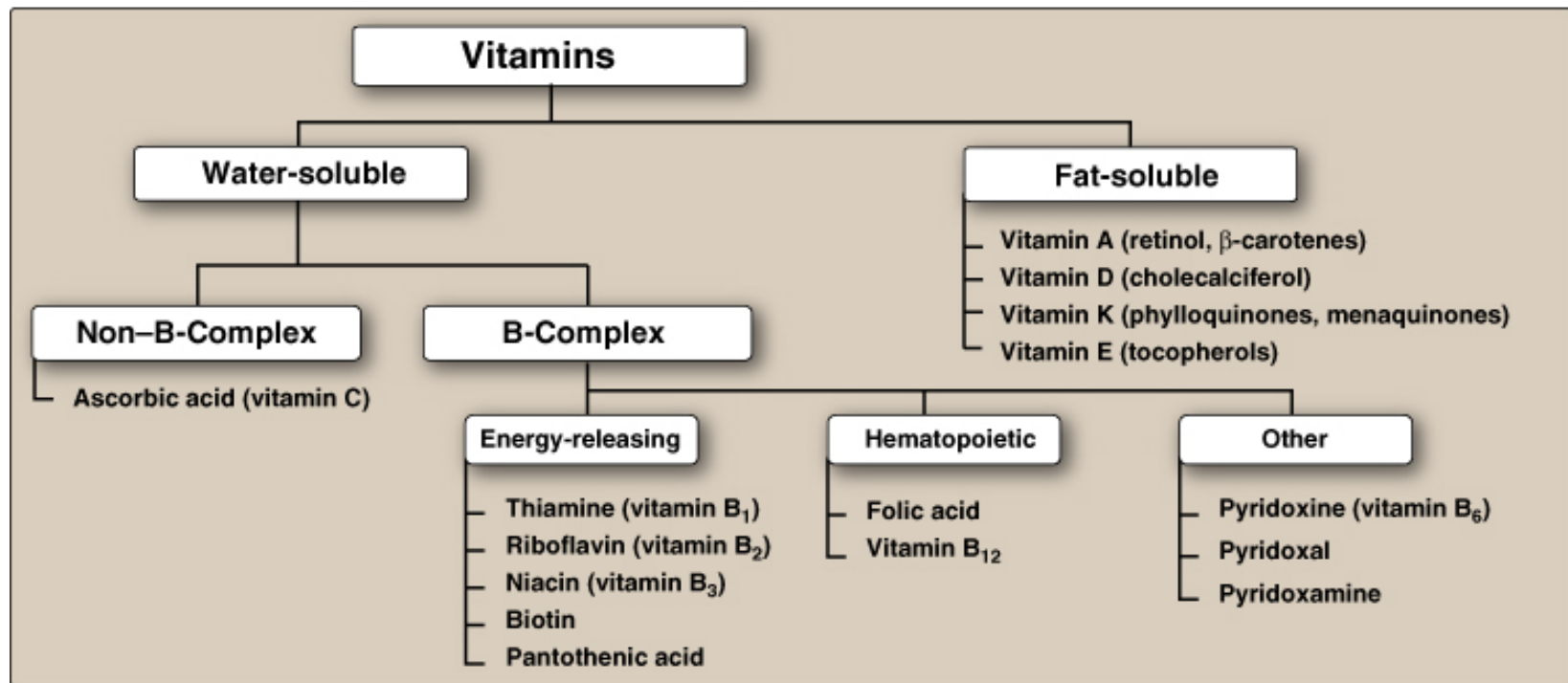
By the end of this lecture the Second Year students will be able to:

- Understand the types and functions of vitamins B₆ and B₁₂
 - Recognize the role of these vitamins in maintaining the myelin sheath of nerves and their function
 - Discuss the consequences of vitamin B₆ and B₁₂ deficiency that can lead to nerve degeneration and irreversible neurological damage
-

Overview

- Types and functions of vitamins B₆ and B₁₂
- Disorders due to Vitamins B₆ and B₁₂ deficiency
- Vitamin B₁₂ deficiency and folate trap
- Demyelination, neuropathy and neuropsychiatric symptoms of vitamin B₁₂ deficiency

Classification of Vitamins



Water-Soluble Vitamins

■ B vitamins

- Thiamin (B₁), riboflavin (B₂), niacin (B₃), pantothenic acid (B₅), pyridoxine (B₆), biotin (B₇), cobalamin (B₁₂), folate

- Not significantly stored in the body
 - Must be supplied regularly in the diet
 - Excess excreted
-

Vitamin B Complex

- Present in small quantities in different types of food
 - Important for growth and good health
 - Help in various biochemical processes in cell
 - **Function as coenzymes**
-

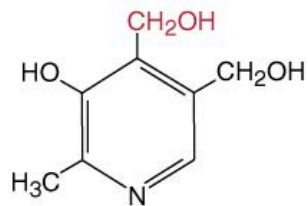
Vitamin B₆

- **Three forms**

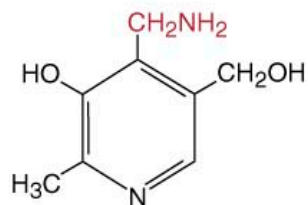
- Pyridoxine
- Pyridoxal
- Pyridoxamine

- **Active form**

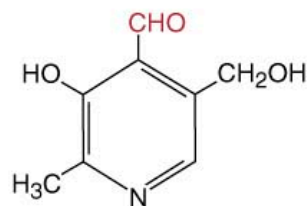
- All 3 are converted to **pyridoxal phosphate (PLP)**
-



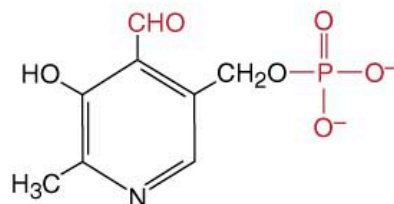
Pyridoxine



Pyridoxamine



Pyridoxal



Pyridoxal phosphate

Figure 28.11. Structures of vitamin B₆.

Functions of Vitamin B₆

- **As coenzyme for**
 - ❑ **Transamination**
 - ❑ **Deamination**
 - ❑ **Decarboxylation**
 - ❑ **Condensation reactions**
-

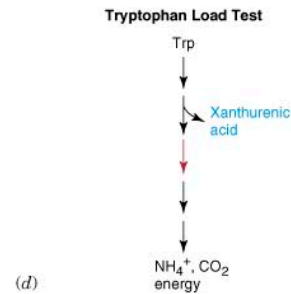
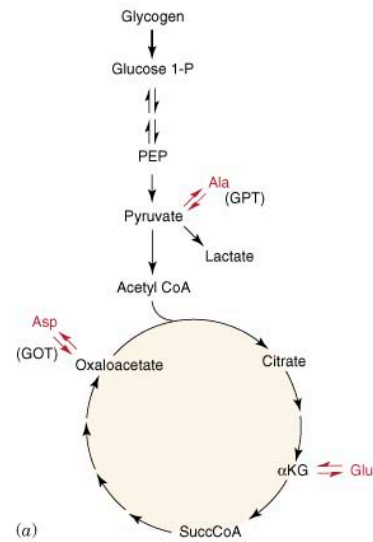
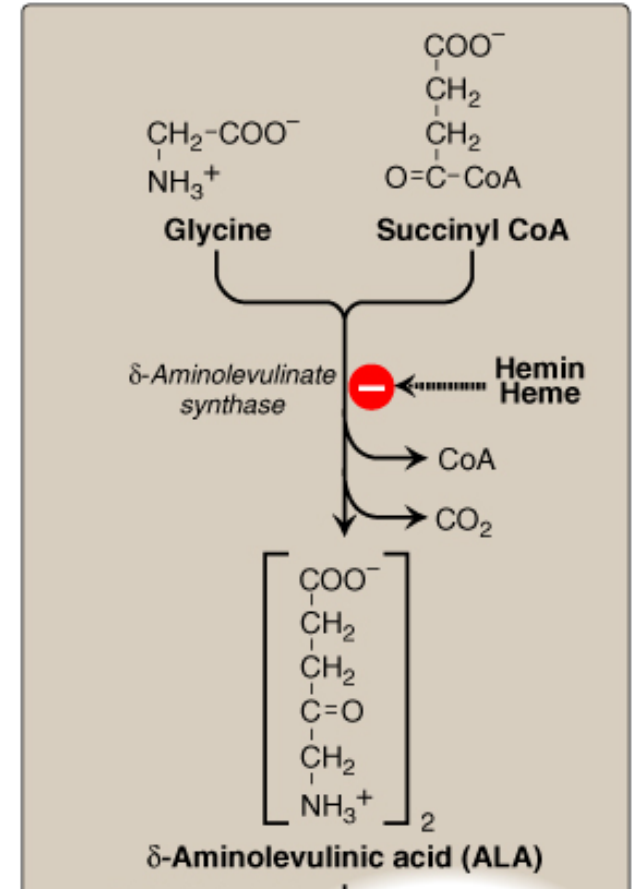


Figure 28.12. Some important metabolic roles of pyridoxal phosphate.

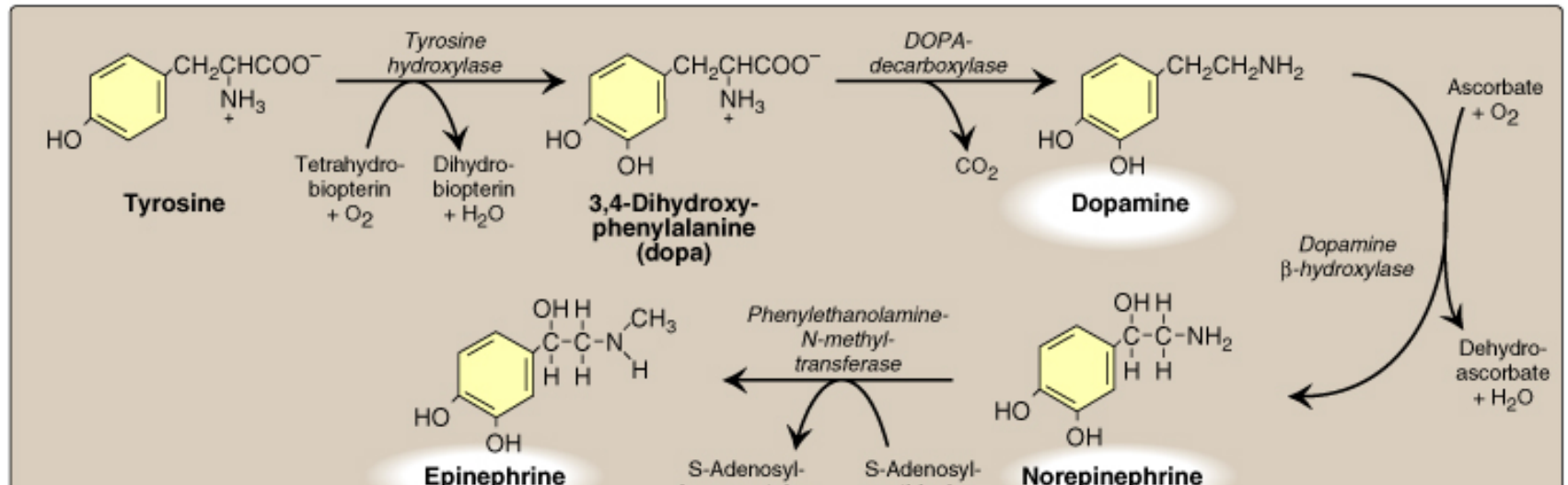
Condensation Reaction

Formation of ALA by ALA synthase,
The regulatory step in hemoglobin synthesis



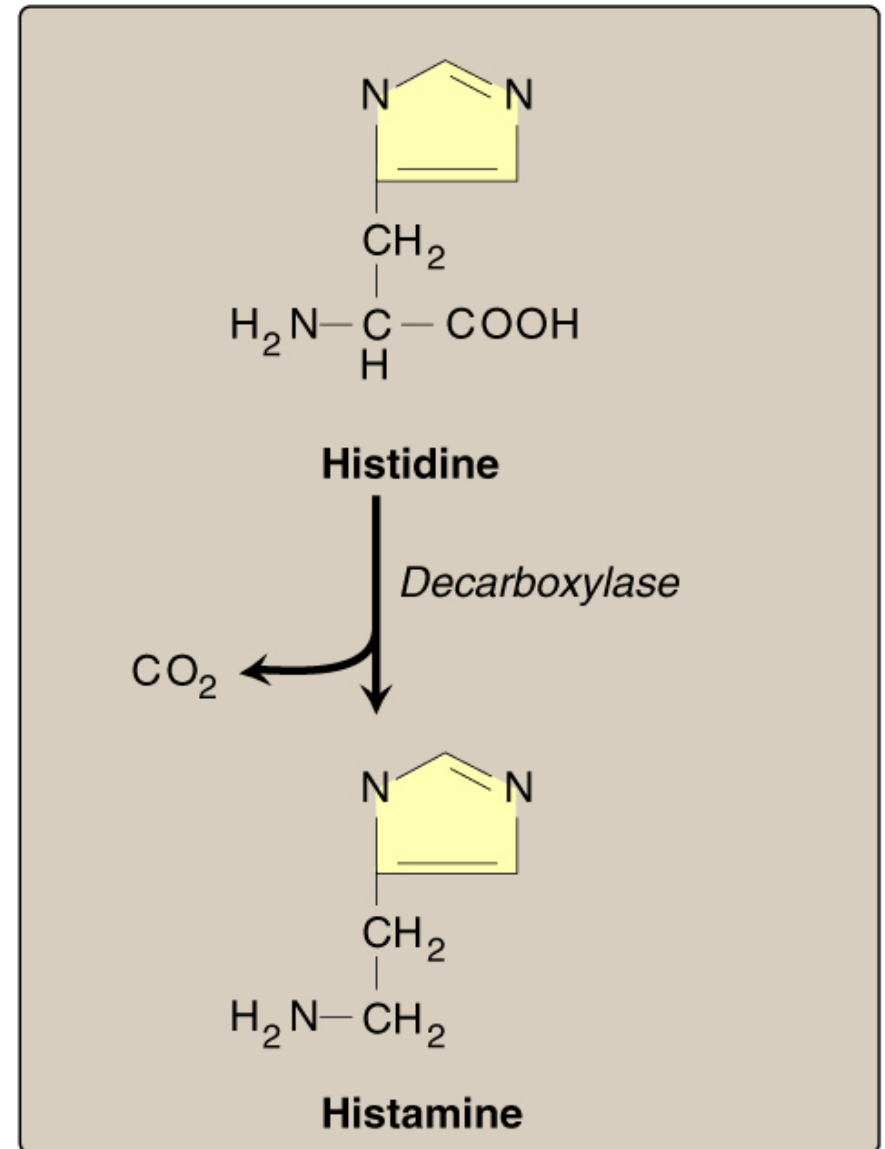
Decarboxylation Reaction:

Formation of Chatecholamines: Dopamine, norepinephrine and epinephrine



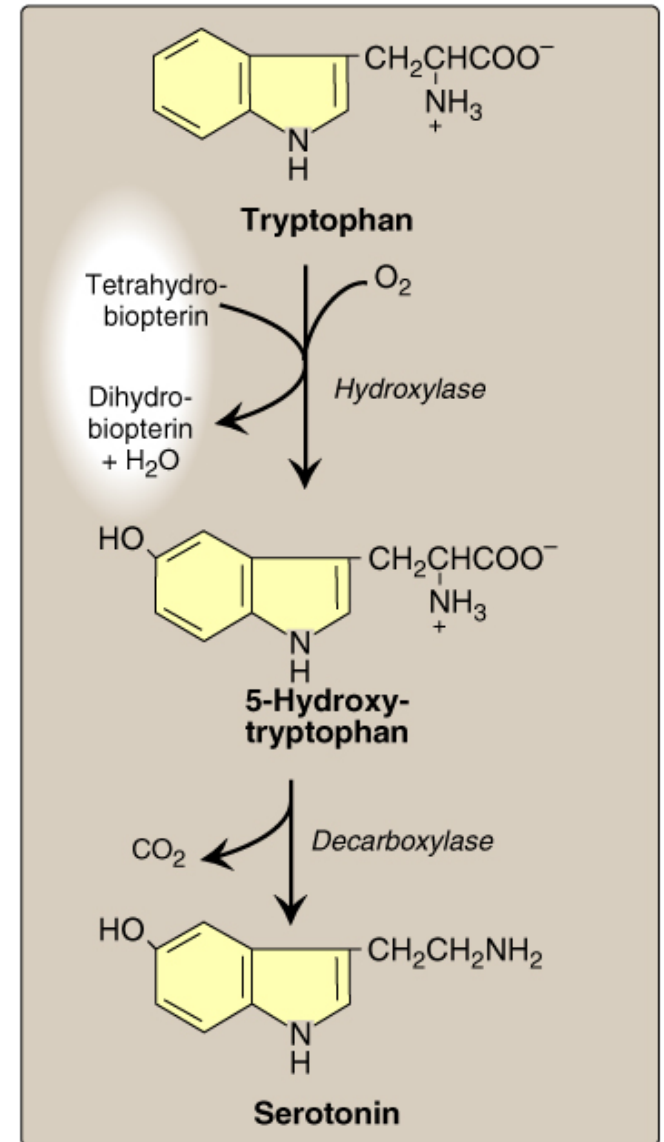
Decarboxylation Reaction:

Formation of histamine

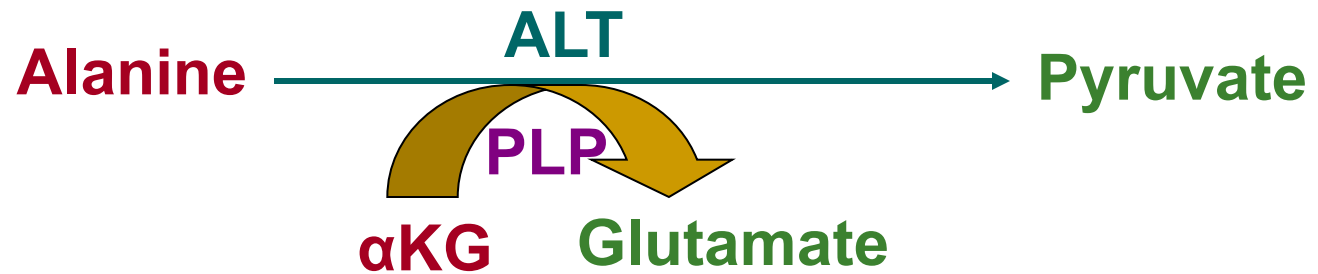


Decarboxylation Reaction:

Formation of Serotonin



Transamination Reaction



Disorders of Vitamin B₆

Deficiency

- **Dietary deficiency is rare, but it is observed in:**
 - Newborn infants fed on formulas low in B₆
 - Women on oral contraceptives
 - Alcoholics
 - **Isoniazid treatment for tuberculosis can lead to vitamin B₆ deficiency by forming inactive derivative with PLP**
-

Disorders of Vitamin B₆

Deficiency

- Deficiency leads to poor activity of PLP-dependent enzymes causing:
 - Deficient amino acid metabolism
 - Deficient lipid metabolism
 - Deficient neurotransmitter synthesis:
 - Serotonin, epinephrine, norepinephrine and gamma-aminobutyric acid (GABA)
-

Disorders of Vitamin B₆

Deficiency

- PLP is involved in the synthesis of sphingolipids
 - Its deficiency leads to demyelination of nerves and consequent peripheral neuritis
-

Disorders of Vitamin B₆

Deficiency

- **Mild deficiency leads to:**
 - Irritability
 - Nervousness
 - Depression

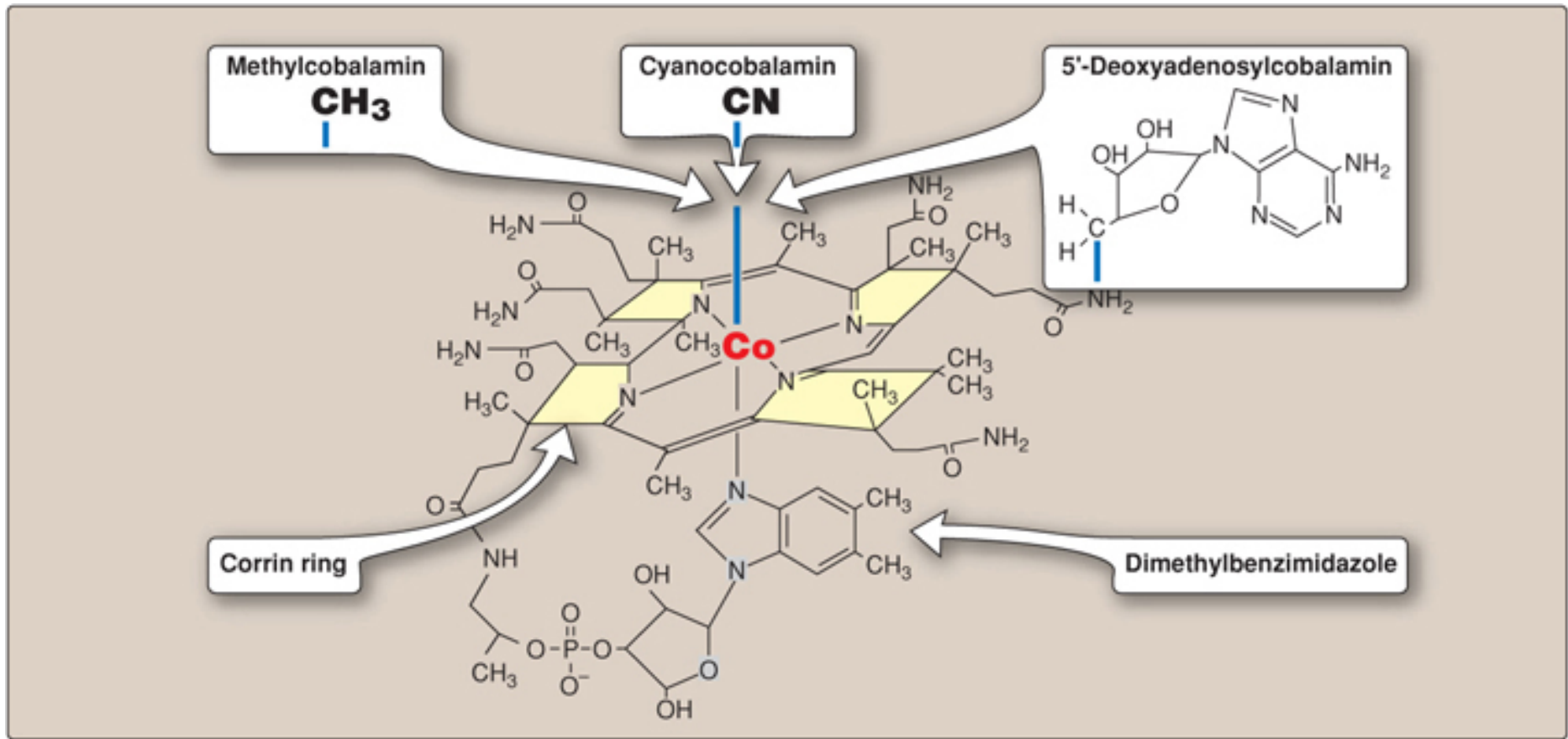
 - **Severe deficiency leads to:**
 - Peripheral neuropathy
 - Convulsions
-

Forms of Vitamin B₁₂

- Cyanocobalamin
 - Hydroxycobalamin
 - Adenosylcobalamin (major storage form in the liver)
 - Methylcobalamin (mostly found in blood circulation)
-

Coenzyme forms of B_{12}

- Adenosylcobalamin and Methylcobalamin
 - Coenzymes for metabolic reactions
 - Body can convert other cobalamins into active coenzymes
-



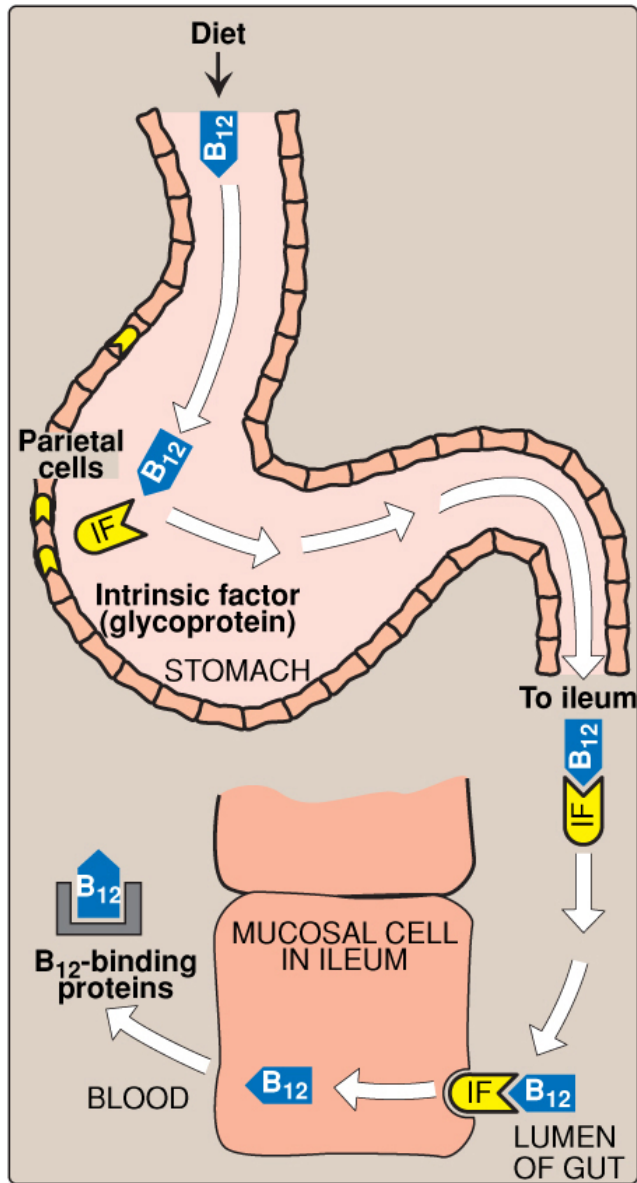
Vitamin B₁₂

(Cobalamin)

- Mainly found in animal liver
 - Bound to protein as
 - Methylcobalamin or
 - 5'-deoxyadenosylcobalamin
-

Vitamin B₁₂

- Essential for normal nervous system function and red blood cell maturation
 - Not synthesized in the body and must be supplied in the diet
 - Binds to intrinsic factor and absorbed by the ileum
 - Intrinsic factor is a protein secreted by cells in the stomach
-



Vitamin B₁₂ Storage

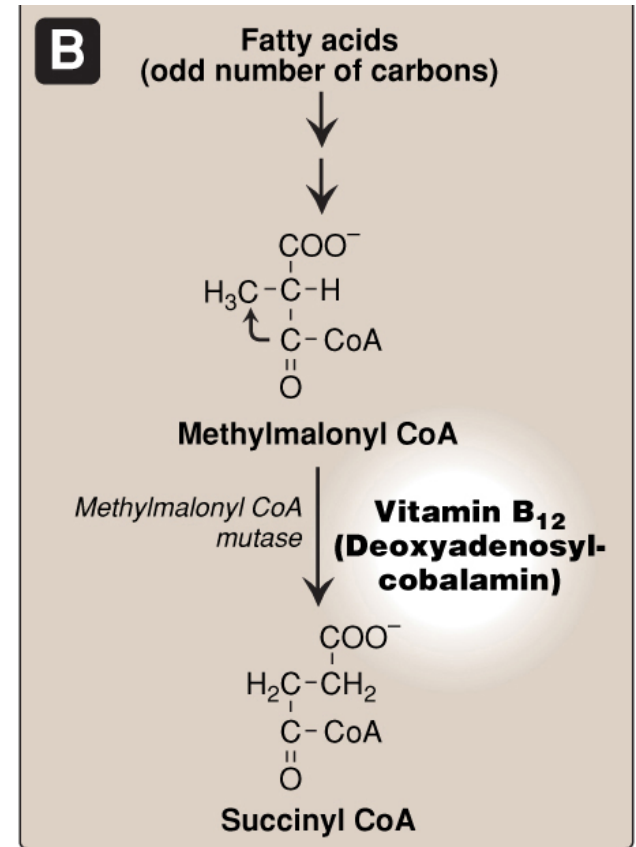
- Liver stores vitamin B₁₂ (4-5 mg)
 - Other B vitamins are not stored in the body
 - Vitamin B₁₂ deficiency is observed in patients with IF deficiency due to autoimmunity or by partial or total gastrectomy
 - Clinical deficiency symptoms develop in several years
-

Functions of Vitamin B₁₂

Two reactions require B₁₂

1. Conversion of methylmalonyl-CoA to succinyl-CoA

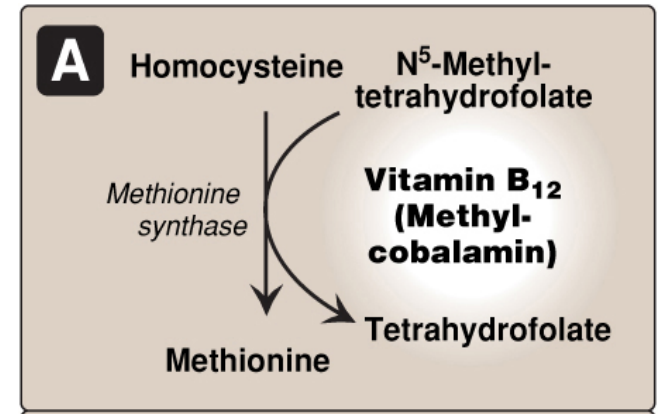
- The enzyme in this pathway, **methylmalonyl-CoA mutase**, requires B₁₂



Functions of Vitamin B₁₂

2. Conversion of homocysteine to methionine

- **Methionine synthase** requires B₁₂ in converting homocysteine to methionine

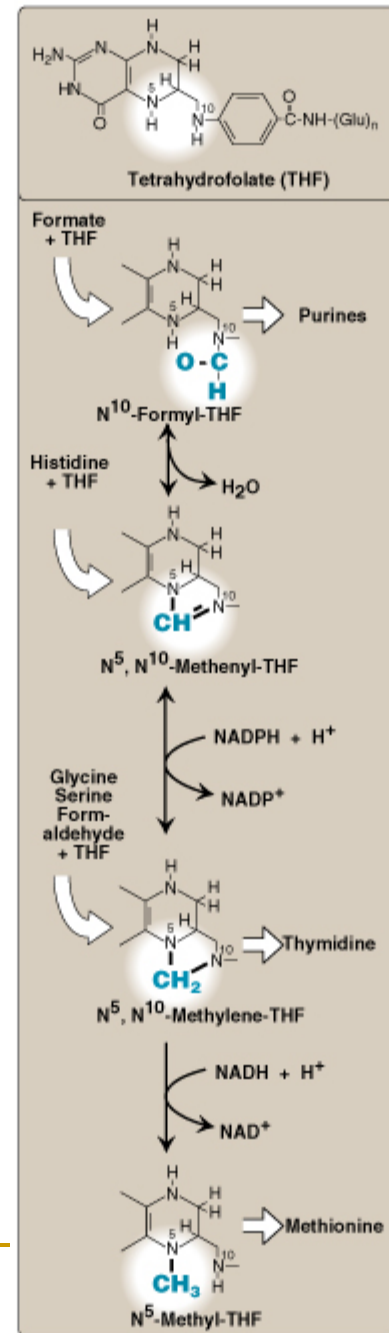


B₁₂ Deficiency and Folate Trap

- Homocysteine re-methylation reaction is the only pathway where N⁵-methyl TH4 can be returned back to tetrahydrofolate pool
- Hence folate is trapped as
N⁵-methyltetrahydrofolate (folate trap)
- This leads to folate deficiency and deficiency of other TH4 derivatives (N⁵-N¹⁰ methylene TH4 and N¹⁰ formyl TH4) required for purine and pyrimidine syntheses

TH4: Tetrahydrofolate

Interconversion between TH4 carrier of “one-carbon units”



Disorders of Vitamin B₁₂ Deficiency

Pernicious anemia

- ❑ Megaloblastic anemia
 - ❑ Vitamin B₁₂ deficiency is mainly due to the deficiency of intrinsic factor
-

Disorders of Vitamin B₁₂ Deficiency

Demyelination

- Myelin sheath of nerves is chemically unstable and damaged

Neuropathy

- Peripheral nerve damage
-

Disorders of Vitamin B₁₂ Deficiency

Causes of neuropathy

- Deficiency of vitamin B₁₂ leads to accumulation of methylmalonyl CoA
 - High levels of methylmalonyl CoA are used instead of malonyl CoA for fatty acid synthesis
 - Myelin synthesized with these abnormal fatty acids is unstable and degraded causing neuropathy
-

Neuropsychiatric symptoms of Vitamin B₁₂ Deficiency

Neurological symptoms

- Paraesthesia (abnormal sensation) of hands and feet
 - Reduced perception of vibration and position
 - Absence of reflexes
 - Unsteady gait and balance (ataxia)
-

Neuropsychiatric symptoms of Vitamin B₁₂ Deficiency

Psychiatric symptoms

- Confusion and memory loss
 - Depression
 - Unstable mood
-

Take home message

- Vitamins B₆ and B₁₂ are essential in maintaining the nerve function and the central nervous system
 - Various neurological symptoms have been associated with their deficiency
-

References

- Lippincott's Biochemistry. 5th Edition, pp 375-376, 378, Lippincott Williams & Wilkins, New York, USA
-