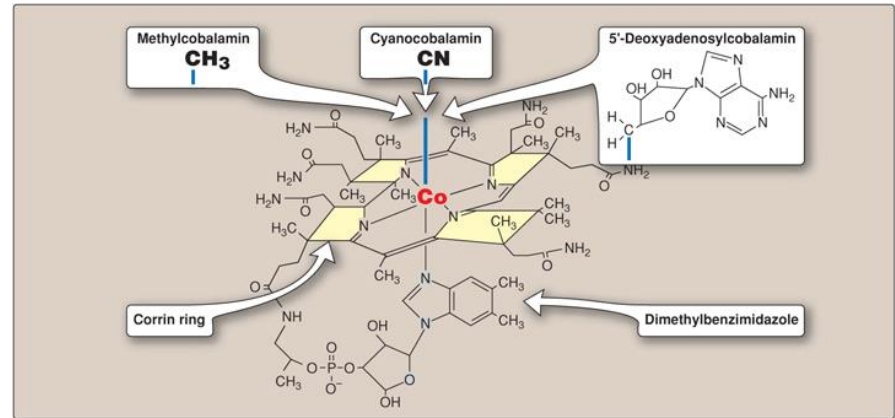


# *Vitamins*

## *B<sub>6</sub> and B<sub>12</sub>*



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Neuropsychiatry Block

1 Lecture

Dr. Usman Ghani

Biochemistry

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# *Objectives*

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

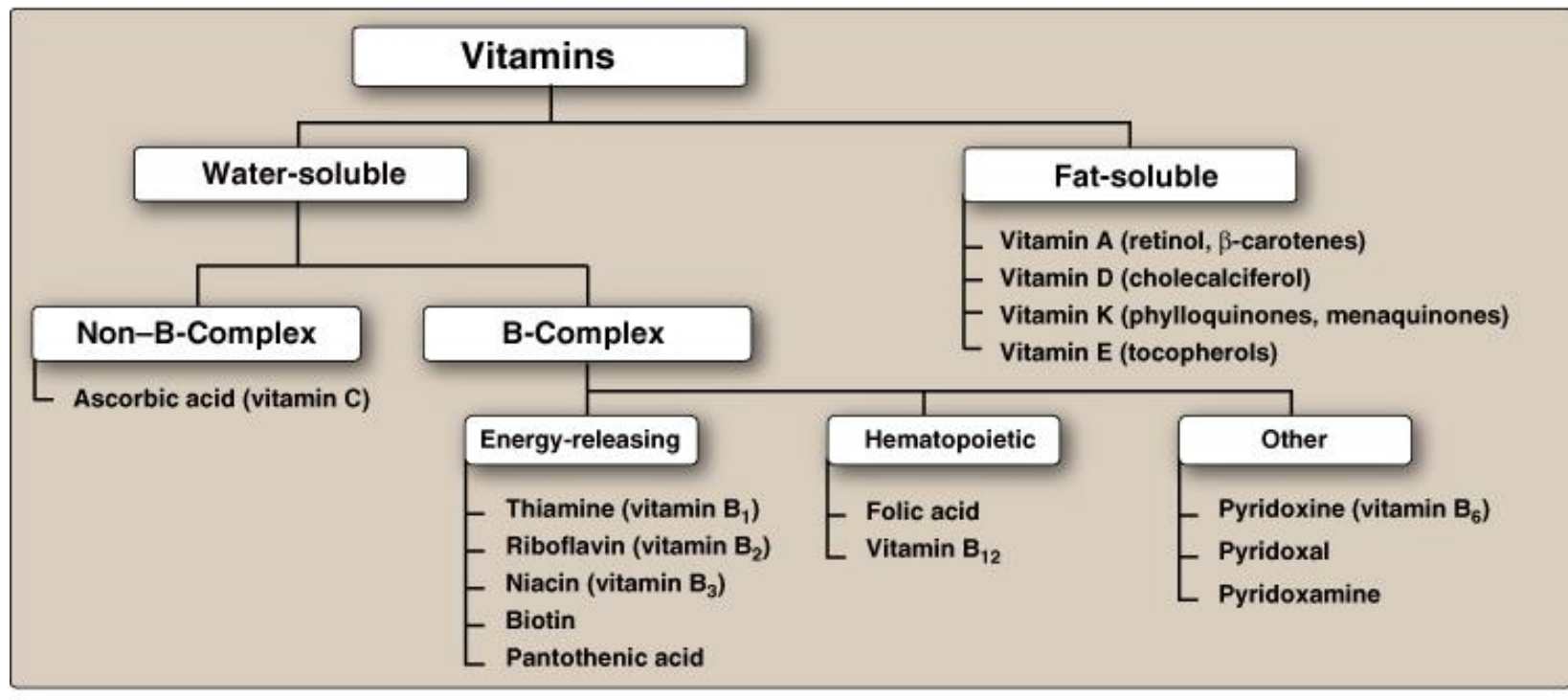
- Understand the types and functions of vitamins B<sub>6</sub> and B<sub>12</sub>
  - Recognize the role of these vitamins in maintaining the myelin sheath of nerves and their function
  - Discuss the consequences of vitamin B<sub>6</sub> and B<sub>12</sub> deficiency that can lead to nerve degeneration and irreversible neurological damage
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# *Overview*

- Types and functions of vitamins B<sub>6</sub> and B<sub>12</sub>
  - Disorders due to Vitamins B<sub>6</sub> and B<sub>12</sub> deficiency
  - Vitamin B<sub>12</sub> deficiency and folate trap
  - Demyelination, neuropathy and neuropsychiatric symptoms of vitamin B<sub>12</sub> deficiency
-

# Classification of Vitamins



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# Water-Soluble Vitamins

- **B vitamins**

- **Thiamin (B<sub>1</sub>), riboflavin (B<sub>2</sub>), niacin (B<sub>3</sub>), pantothenic acid (B<sub>5</sub>), pyridoxine (B<sub>6</sub>), biotin (B<sub>7</sub>), cobalamin (B<sub>12</sub>), folate**

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

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## *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**
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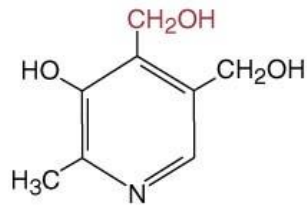
# *Vitamin B<sub>6</sub>*

- **Three forms**

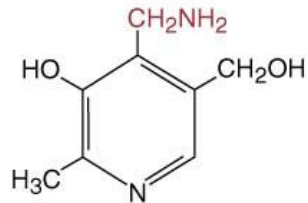
- Pyridoxine
- Pyridoxal
- Pyridoxamine

- **Active form**

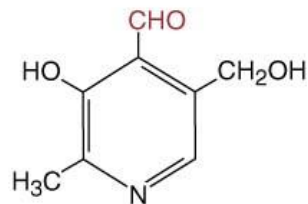
- All 3 are converted to **pyridoxal phosphate (PLP)**
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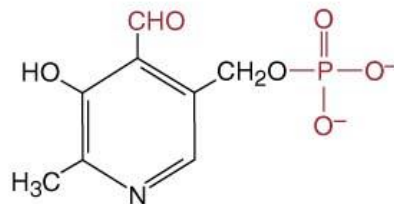
**Pyridoxine**



**Pyridoxamine**



**Pyridoxal**



**Pyridoxal phosphate**

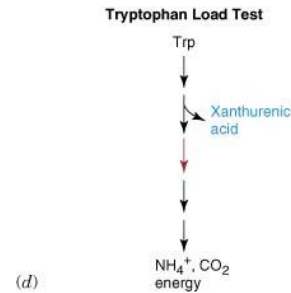
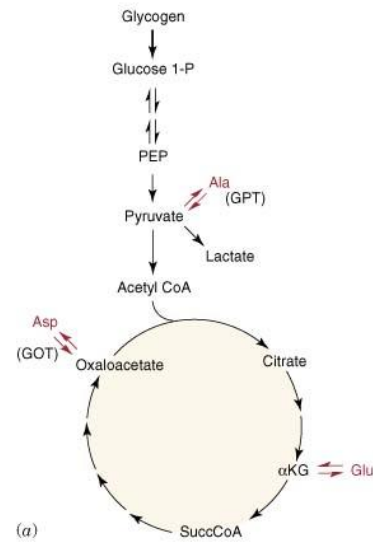
**Figure 28.11. Structures of vitamin B<sub>6</sub>.**



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# *Functions of Vitamin B<sub>6</sub>*

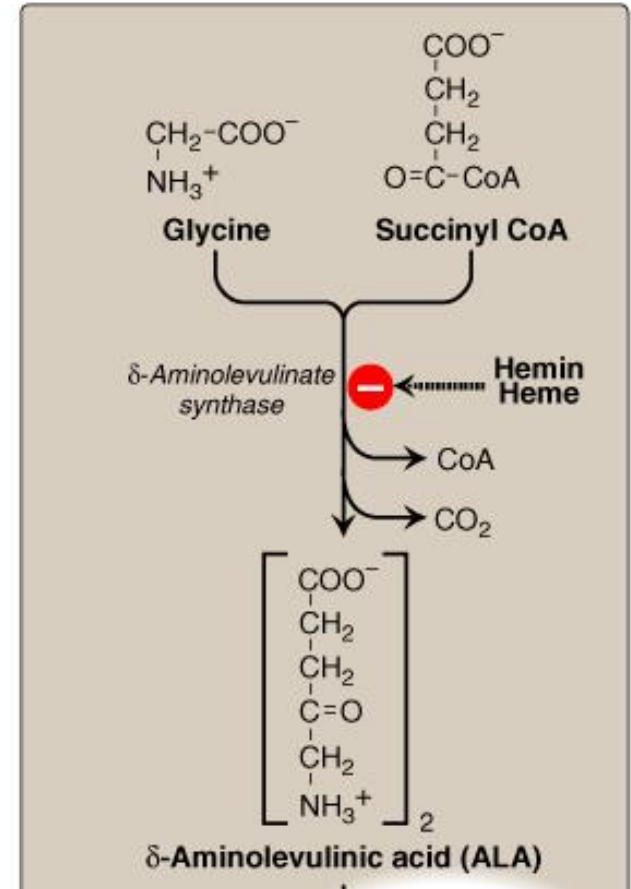
- **As coenzyme for**
    - **Transamination**
    - **Deamination**
    - **Decarboxylation**
    - **Condensation reactions**
-



**Figure 28.12. Some important metabolic roles of pyridoxal phosphate.**

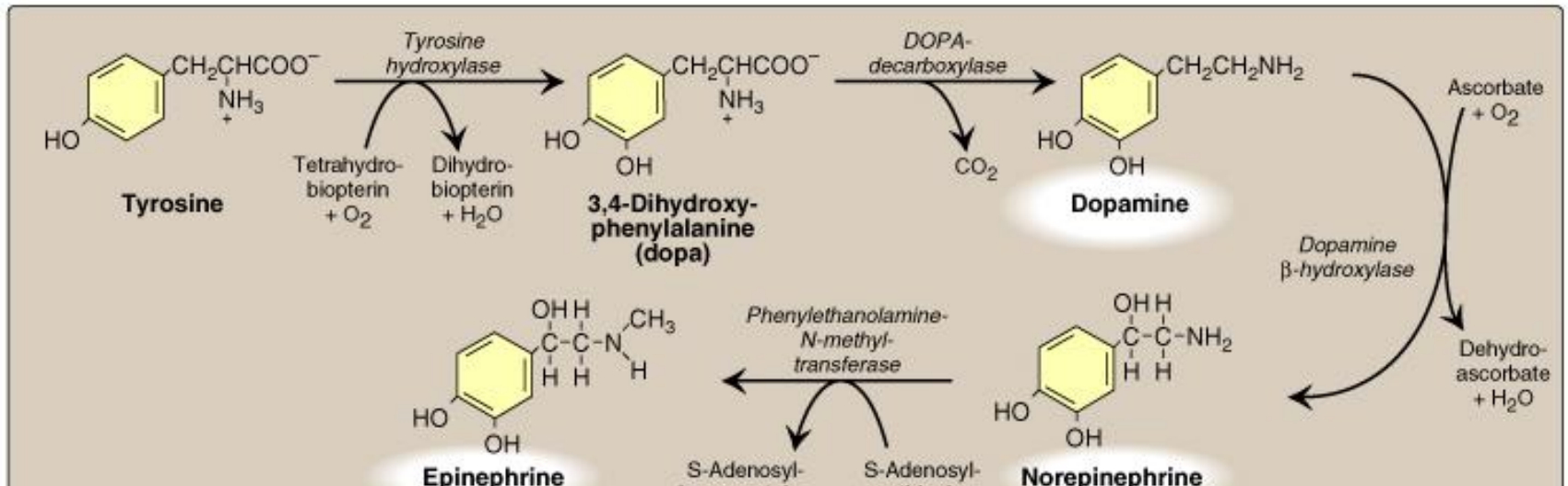
# Condensation Reaction

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



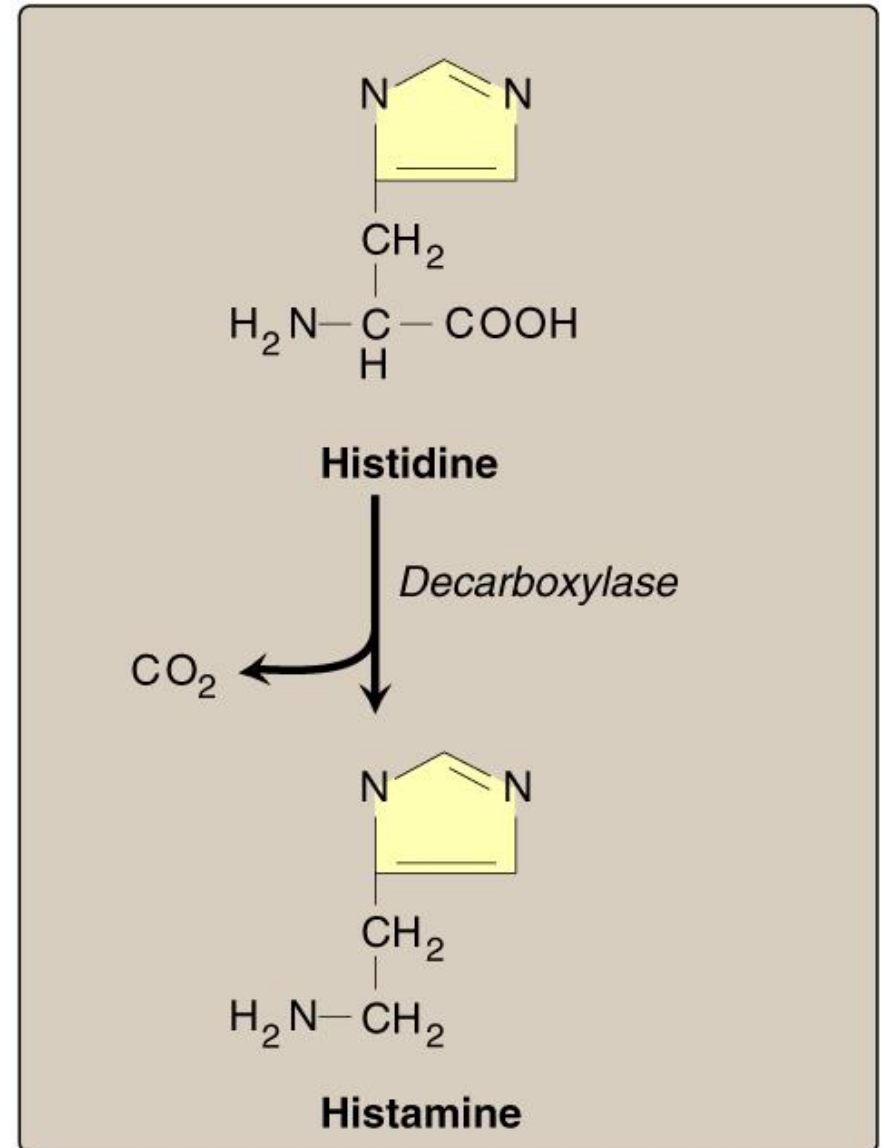
# Decarboxylation Reaction:

## Formation of Chatecholamines: Dopamine, norepinephrine and epinephrine



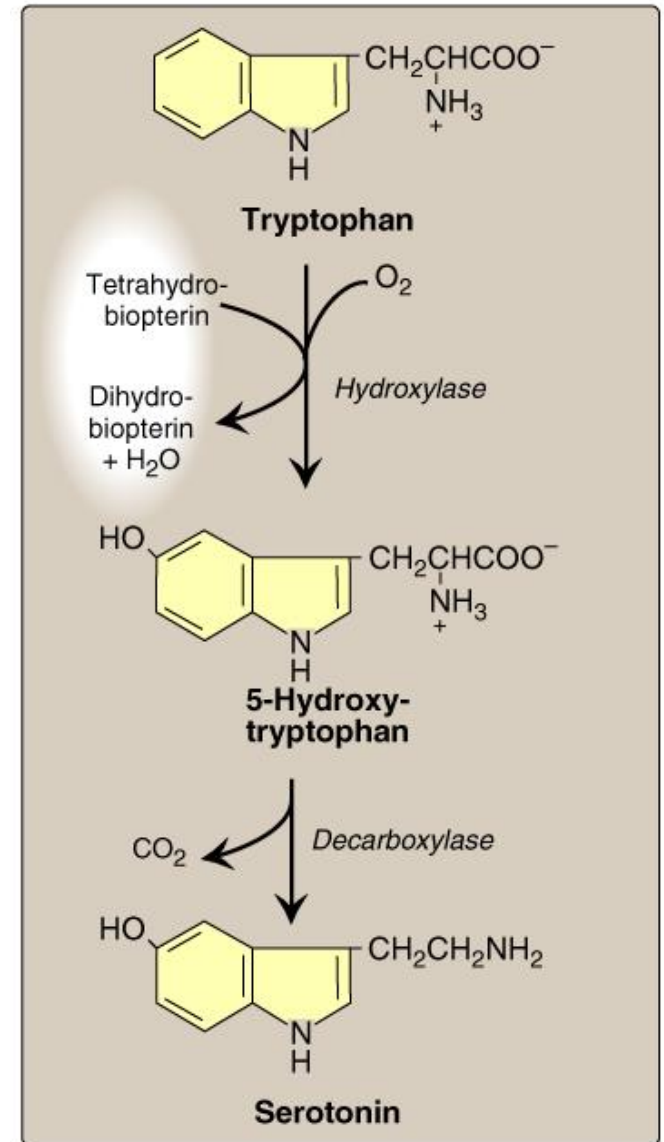
## Decarboxylation Reaction:

### Formation of histamine

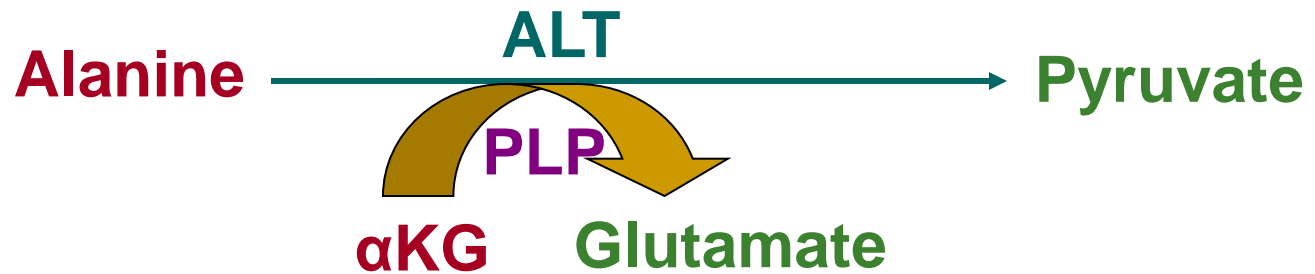


# Decarboxylation Reaction:

## Formation of Serotonin



# Transamination Reaction



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# *Disorders of Vitamin B<sub>6</sub>*

## *Deficiency*

- **Dietary deficiency is rare, but it is observed in:**
    - Newborn infants fed on formulas low in B<sub>6</sub>
    - Women on oral contraceptives
    - Alcoholics
  - **Isoniazid treatment for tuberculosis can lead to vitamin B<sub>6</sub> deficiency by forming inactive derivative with PLP**
-



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# *Disorders of Vitamin B<sub>6</sub>*

## *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 amino butyric acid (GABA)
-

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# *Disorders of Vitamin B<sub>6</sub>* *Deficiency*

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

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# *Disorders of Vitamin B<sub>6</sub>*

## *Deficiency*

- **Mild deficiency leads to:**
    - Irritability
    - Nervousness
    - Depression
  
  - **Severe deficiency leads to:**
    - Peripheral neuropathy
    - Convulsions
-

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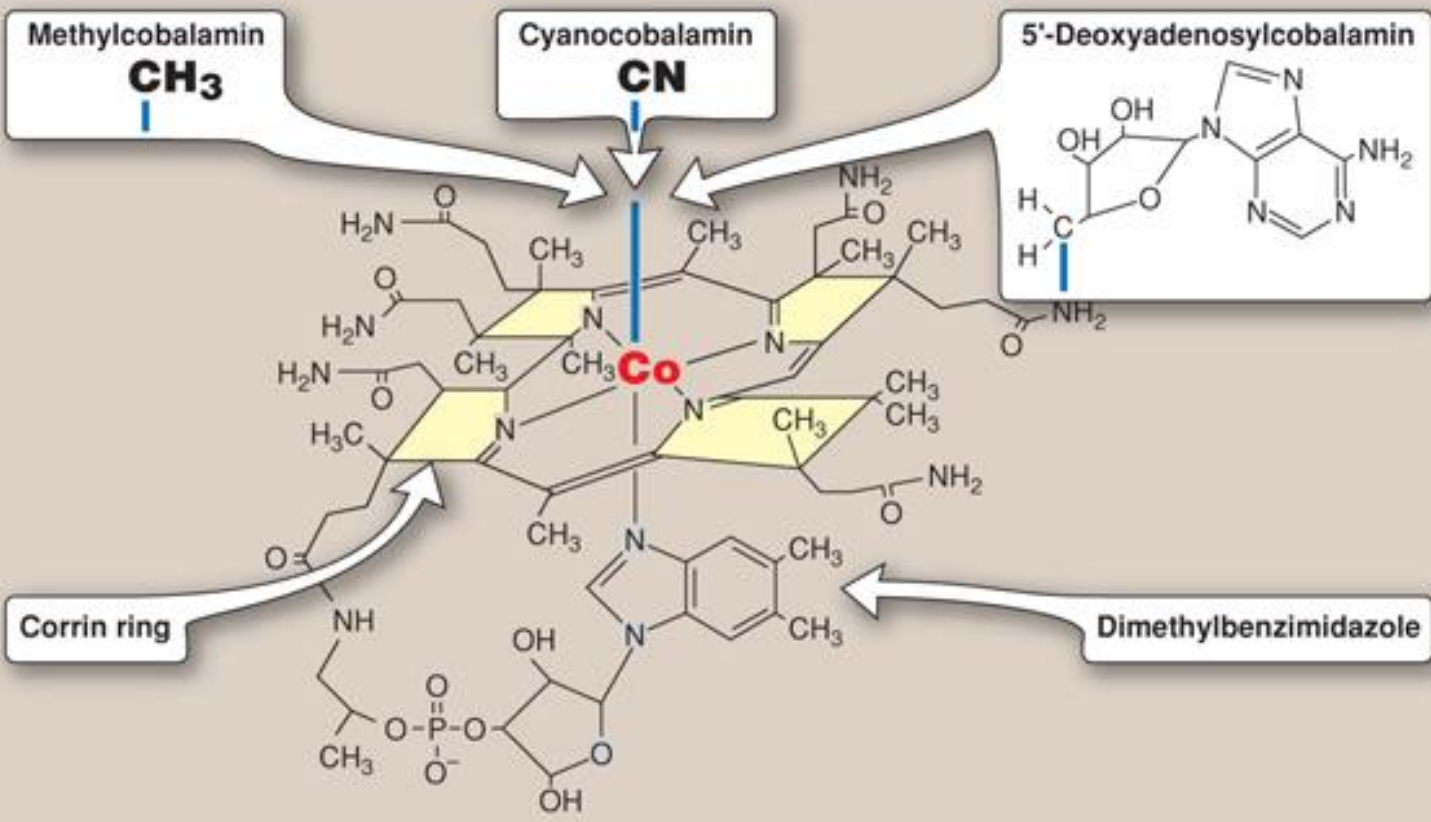
# *Forms of Vitamin B<sub>12</sub>*

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

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# Coenzyme forms of $B_{12}$

- Adenosylcobalamin and Methylcobalamin
    - Coenzymes for metabolic reactions
  - Body can convert other cobalamins into active coenzymes
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# *Vitamin B<sub>12</sub>*

(Cobalamin)

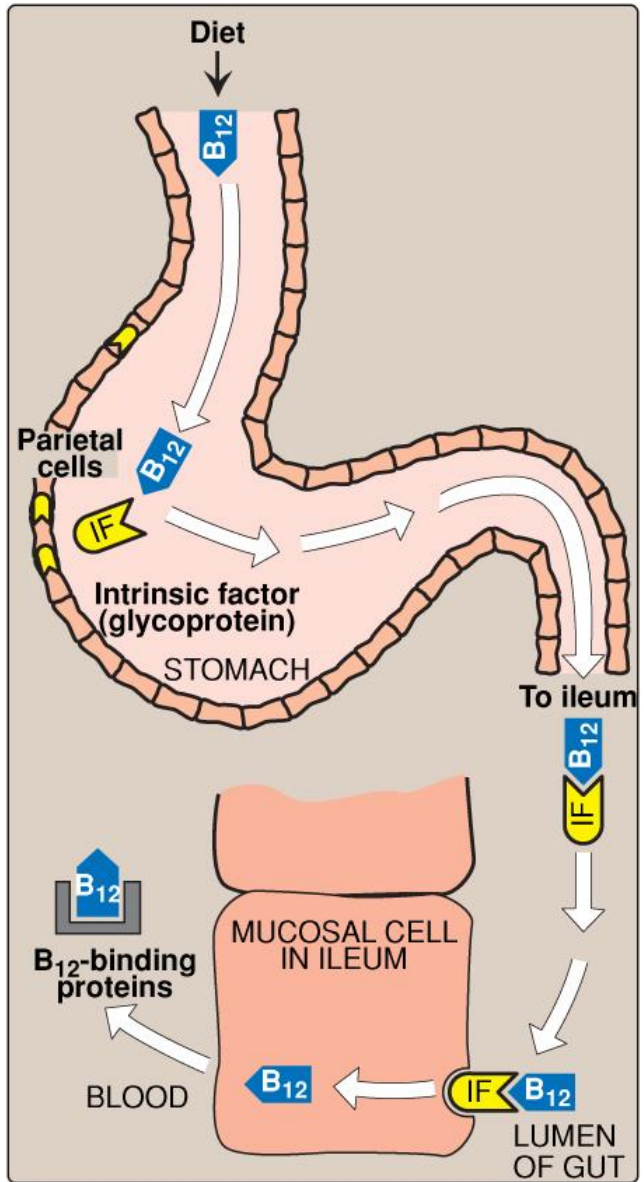
- Mainly found in animal liver
  - Bound to protein as
    - Methylcobalamin or
    - 5'-deoxyadenosylcobalamin
-

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# *Vitamin B<sub>12</sub>*

- 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
-





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# *Vitamin B<sub>12</sub> Storage*

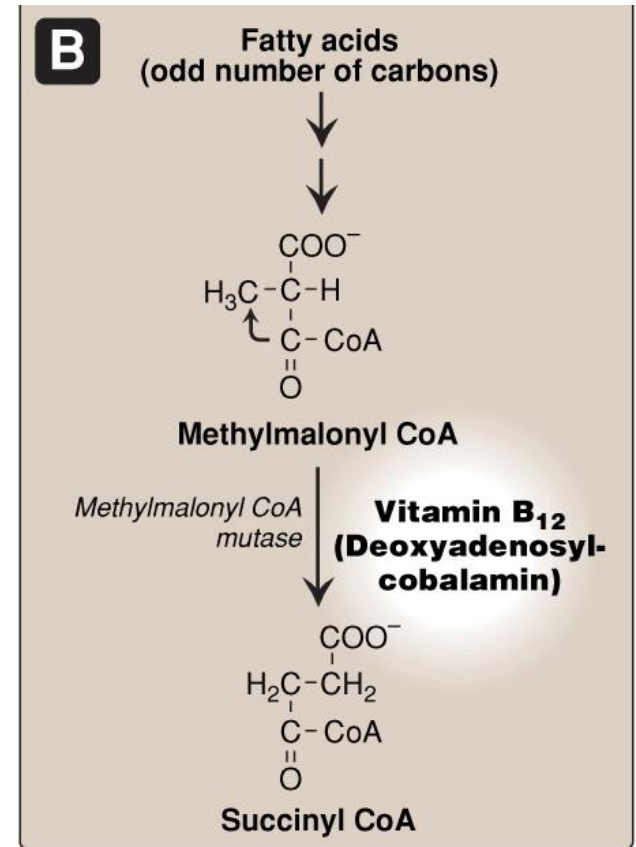
- Liver stores vitamin B<sub>12</sub> (4-5 mg)
  - Other B vitamins are not stored in the body
  - Vitamin B<sub>12</sub> deficiency is observed in patients with IF deficiency due to autoimmunity or by partial or total gastrectomy
    - Clinical deficiency symptoms develop in several years
-

# Functions of Vitamin B<sub>12</sub>

## Two reactions require B<sub>12</sub>

1. Conversion of methylmalonyl-CoA to succinyl-CoA

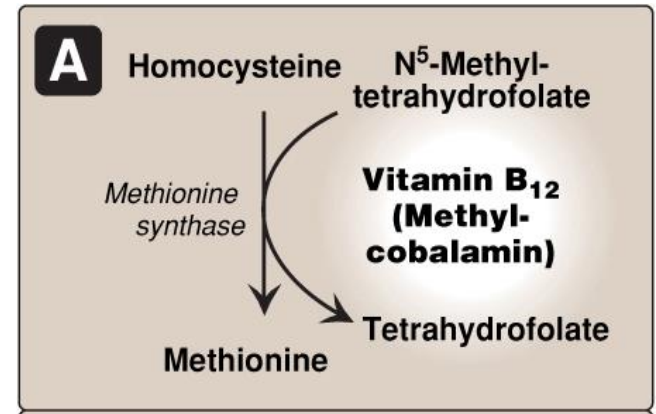
- The enzyme in this pathway, methylmalonyl-CoA mutase, requires B<sub>12</sub>



# *Functions of Vitamin B<sub>12</sub>*

## 2. Conversion of homocysteine to methionine

- Methionine synthase requires B<sub>12</sub> in converting homocysteine to methionine



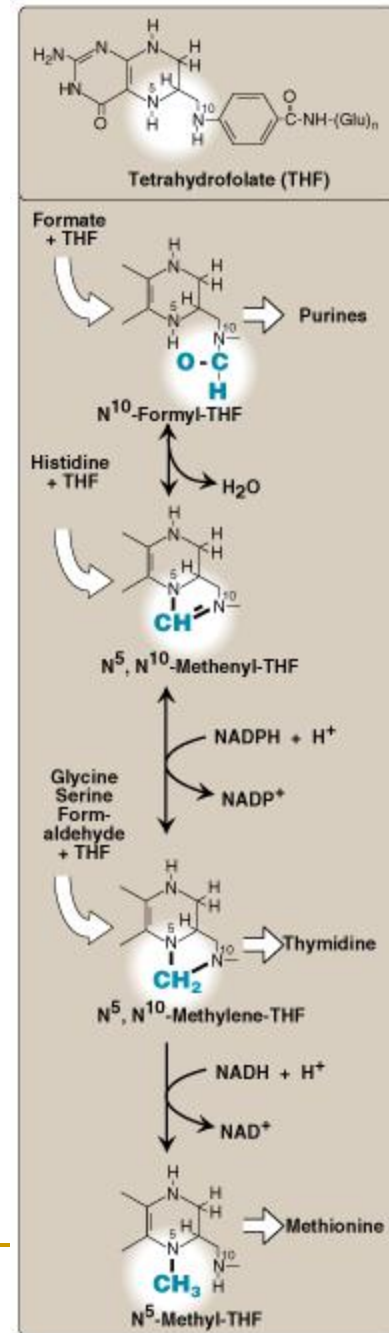
# *B<sub>12</sub> Deficiency and Folate Trap*

- Homocysteine re-methylation reaction is the only pathway where N<sup>5</sup>-methyl TH4 can be returned back to tetrahydrofolate pool
- Hence folate is trapped as  
N<sup>5</sup>-methyltetrahydrofolate (folate trap)
- This leads to folate deficiency and deficiency of other TH4 derivatives (N<sup>5</sup>-N<sup>10</sup> methylene TH4 and N<sup>10</sup> formyl TH4) required for purine and pyrimidine syntheses

**TH4: Tetrahydrofolate**

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# *Interconversion between TH4 carrier of “one-carbon units”*



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# *Disorders of Vitamin B<sub>12</sub> Deficiency*

## Pernicious anemia

- ❑ Megaloblastic anemia
  - ❑ Vitamin B<sub>12</sub> deficiency is mainly due to the deficiency of intrinsic factor
-

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# *Disorders of Vitamin B<sub>12</sub> Deficiency*

## Demyelination

- Myelin sheath of nerves is chemically unstable and damaged

## Neuropathy

- Peripheral nerve damage
-



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# *Disorders of Vitamin B<sub>12</sub> Deficiency*

## Causes of neuropathy

- Deficiency of vitamin B<sub>12</sub> 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
-

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# *Neuropsychiatric symptoms of Vitamin B<sub>12</sub> Deficiency*

## Neurological symptoms

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

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# *Neuropsychiatric symptoms of Vitamin B<sub>12</sub> Deficiency*

## Psychiatric symptoms

- Confusion and memory loss
  - Depression
  - Unstable mood
-

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## *Take home message*

- Vitamins B<sub>6</sub> and B<sub>12</sub> are essential in maintaining the nerve function and the central nervous system
  - Various neurological symptoms have been associated with their deficiency
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# *References*

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