Biochemistry
Team 434

# *Vitamin B6 and B12*

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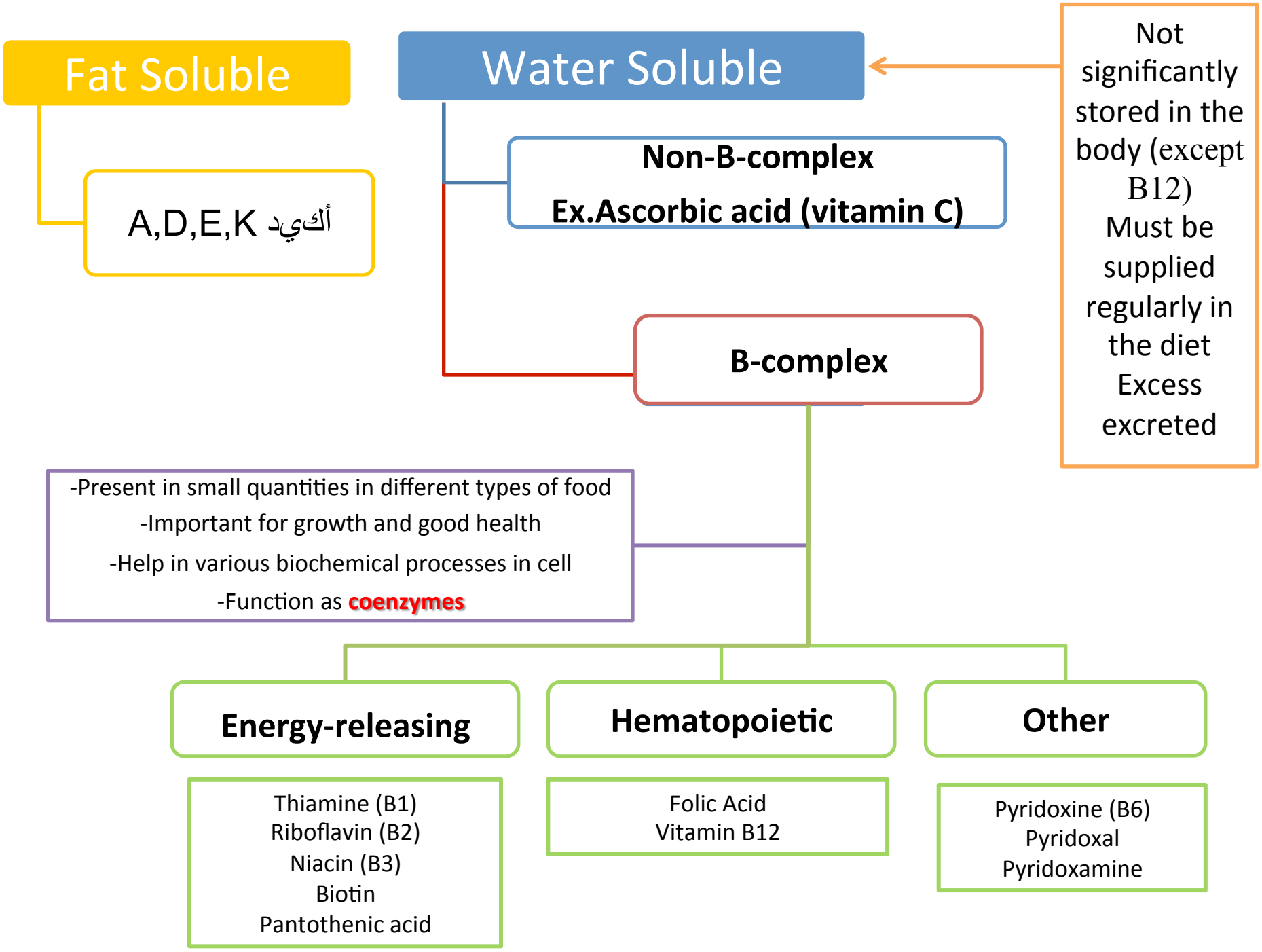

Fat Soluble
A,D,E,K أكيد
Water Soluble
Not significantly stored in the body (except B12)
Must be supplied regularly in the diet
Excess excreted
Non-B-complex
Ex.Ascorbic acid (vitamin C)
B-complex
-Present in small quantities in different types of food
-Important for growth and good health
-Help in various biochemical processes in cell
-Function as coenzymes
Energy-releasing
Hematopoietic
Other
Thiamine (B1)
Riboflavin (B2)
Niacin (B3)
Biotin
Pantothenic acid
Folic Acid
Vitamin B12
Pyridoxine (B6)
Pyridoxal
Pyridoxamine

# Vitamin $B_6$

**Forms..?**
- Pyridoxine (plants)
- Pyridoxal (animal source)
- Pyridoxamine (animal)

**Active form..?**
All 3 are converted to **pyridoxal phosphate (PLP)** 90% in muscles.
(next slide)

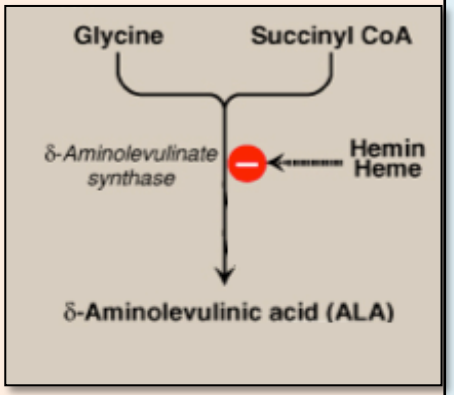
(PLP) acts as a coenzyme for the following reactions:

## 1. Condensation Reaction.

Formation of aminolevulinic acid (ALA) by ALA synthase..

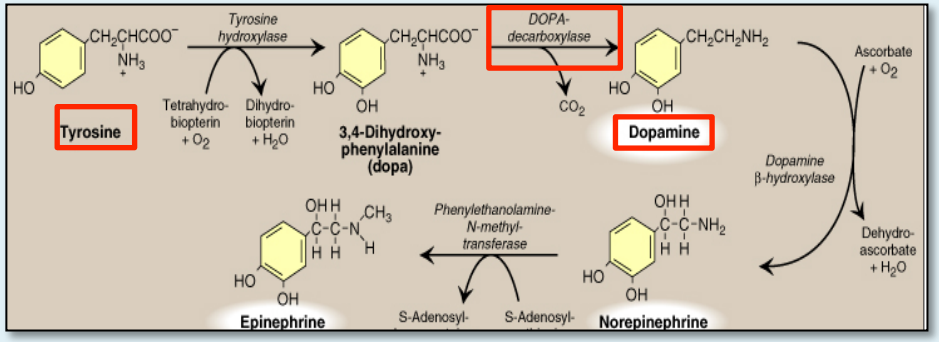
**The regulatory step in hemoglobin synthesis**

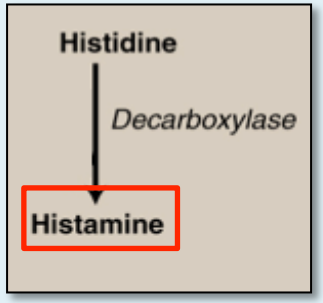
It requires pyridoxal phosphate for formation of (ala)



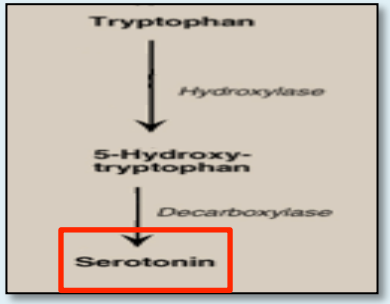

## 2. Decarboxylation Reaction:

- Formation of Chatecholamines: Dopamine, norepinephrine and epinephrine.
- Formation of Histamine and Serotonin.

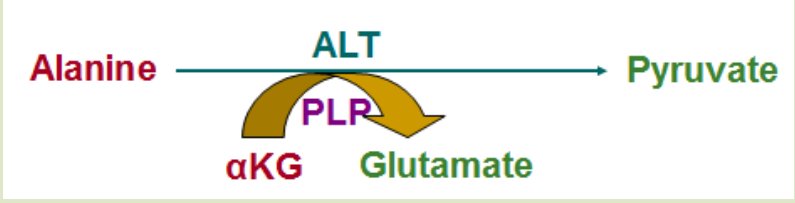



Allergy mediator

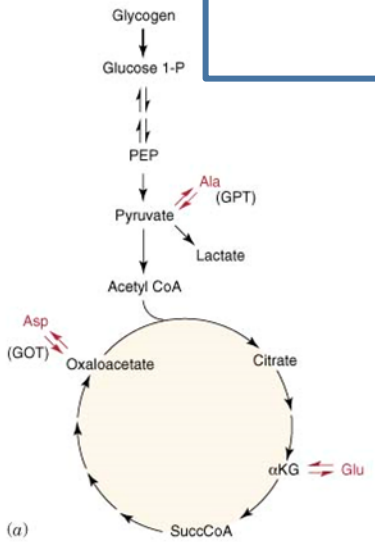


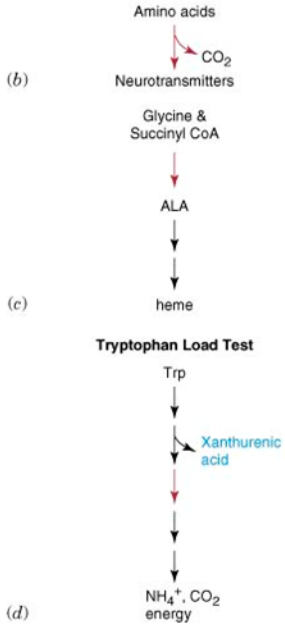

## 3. Transamination Reaction.

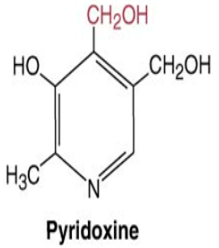



## 4. Deamination.

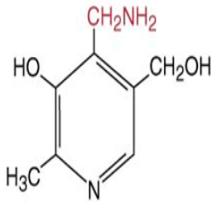
# Vitamin $B_6$



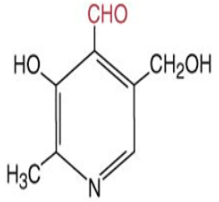



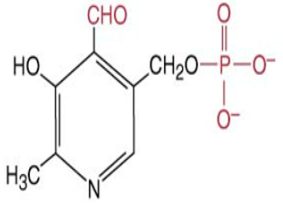

Pyridoxine




Pyridoxamine




Pyridoxal




Pyridoxal phosphate

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

*:hemistry With Clinical Correlations, Sixth Edition*, Edited by Thomas M. Devlin. Copyright © 2006 John W

**Figure 28.11. Structures of vitamin $B_6$**

*Correlations, Sixth Edition*, Edited by Thomas M. Devlin. C

# Vitamin $B_6$

## *Disorders of Vitamin $B_6$ Deficiency..*

### *Causes..?*

-Dietary deficiency is rare, but it was observed in: (more common in females)

1. **Newborn infants fed on formulas low in B6**
2. **Women on oral contraceptives**
3. **Alcoholics**

-*Isoniazid treatment for tuberculosis can lead to vitamin $B_6$ deficiency by forming inactive derivative with PLP.*

### *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)]

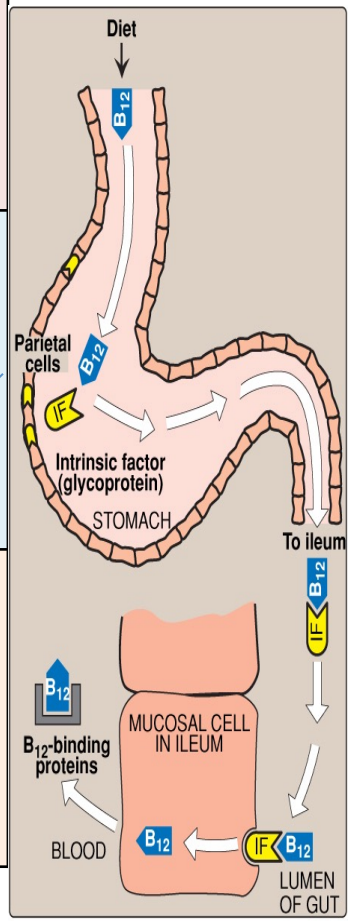
-PLP is involved in the synthesis of sphingolipids, Its deficiency leads to demyelination of nerves and consequent peripheral neuritis

| Mild deficiency leads to: | Severe deficiency leads to: |
|---|---|
| Irritability<br>Nervousness<br>Depression | Peripheral neuropathy<br>Convulsions |

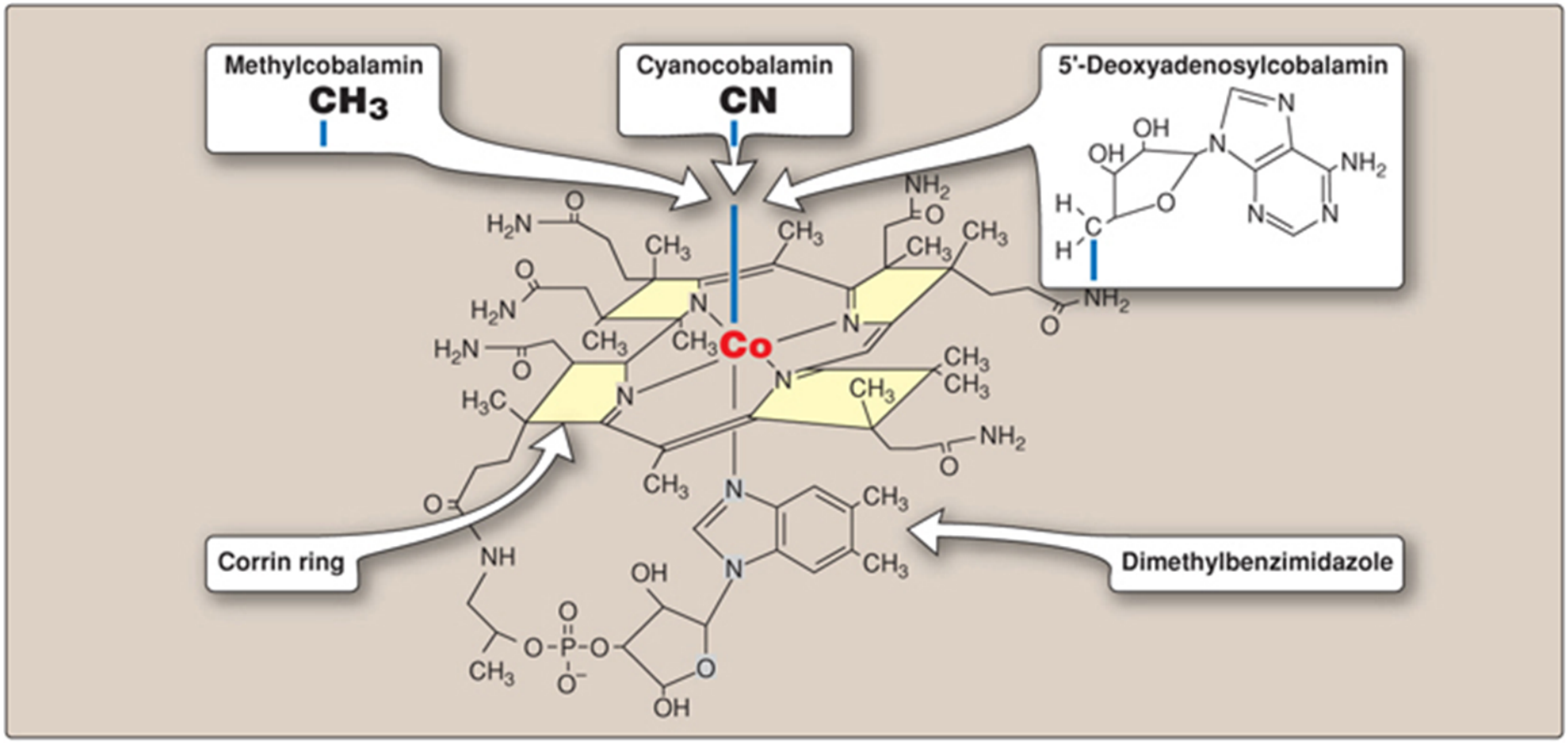
-Cyanocobalamin and Hydroxycobalamin is commercially available form found as supplementary form
-Adenosylcobalamin the most active

# Vitamin $B_{12}$

| | |
|---|---|
| **Forms** | • Cyanocobalamin<br>• Hydroxycobalamin<br>• Adenosylcobalamin (major storage form in the liver)<br>• Methylcobalamin (mostly found in blood circulation) |
| **Coenzyme** | -Adenosylcobalamin and Methylcobalamin (Coenzymes for metabolic reactions)<br>-Body can convert other cobalamins into active coenzymes<br>see next slide.. |
| **Sources** | • Mainly found in animal liver bound to protein as<br>➢ Methylcobalamin<br>➢ 5'-deoxyadenosylcobalamin<br>• Not synthesized in the body and must be supplied in the diet |
| **Absorption + Stores** | • Binds to intrinsic factor and absorbed by the ileum<br>• **Intrinsic factor is a protein secreted by cells in the stomach**<br>• Liver stores vitamin $B_{12}$ (4-5 mg)<br>• Only water soluble vitamin that is stored in the body |



# Vitamin $B_{12}$



# *Vitamin $B_{12}$*

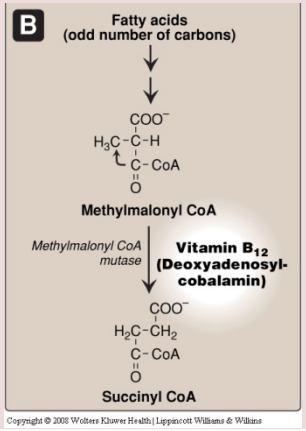
## Importance..?

1-Essential for normal nervous system function and red blood cell maturation.

2-Required in 2 reactions:

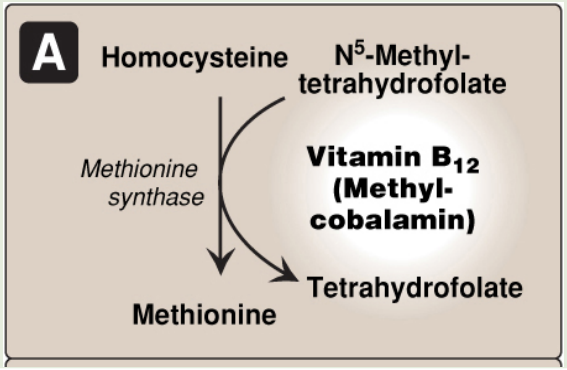
### Conversion of propionyl-CoA to succinyl-CoA

•The enzyme in this pathway, methyl-malonyl-CoA mutase, requires $B_{12}$




### Conversion of homocysteine to methionine

- Methionine synthase requires $B_{12}$ in converting homocysteine to methionine




Tetrahydrofolate is the active form found in the body

# *Vitamin $B_{12}$*

**Homocysteine re-methylation reaction** is the only pathway where $N^5$-methyl TH4 can be returned back to tetrahydrofolate pool..

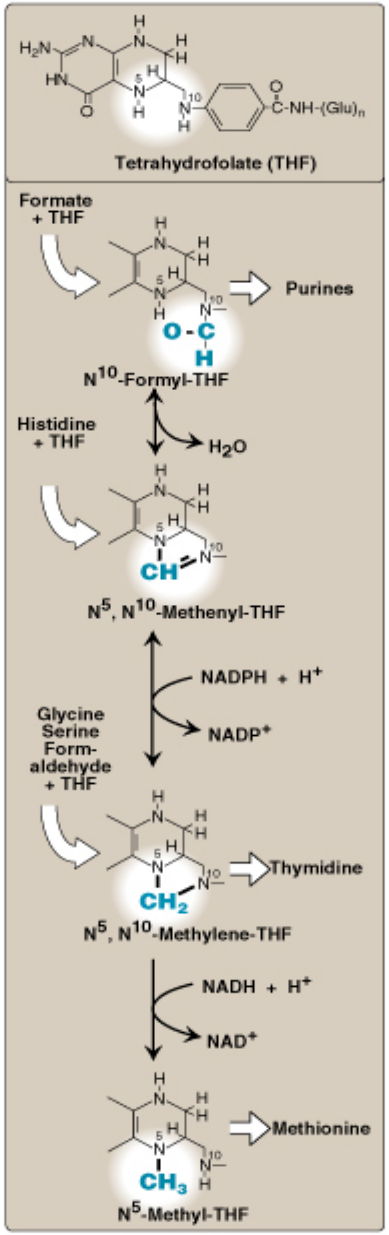
**Hence folate is trapped as ➔ $N^5$-methyltetrahydrofolate (folate trap)**

This leads to folate **deficiency** and deficiency of other TH4 derivatives ($N^5$-$N^{10}$ methylene TH4 and $N^{10}$ formyl TH4) required for purine and pyrimidine syntheses

***TH4: Tetrahydrofolate**

## *Interconversion between TH4 carrier of "one-carbon units"*

**We don't have to memorize the structure**



# *Vitamin $B_{12}$*

## *Disorders of Vitamin $B_{12}$ Deficiency*

**Pernicious anemia**

**Megaloblastic anemia**

Vitamin $B_{12}$ deficiency is mainly due to the deficiency of intrinsic factor

**Demyelination**

Myelin sheath of neurons is chemically unstable and damaged

**Neuropathy**

Peripheral nerve damage

break down the lipid for this myelination, and nerves will be affected.

# *Vitamin $B_{12}$*

***Neuropsychiatric symptoms of Vitamin $B_{12}$ Deficiency..?***

affect both sensory and motor

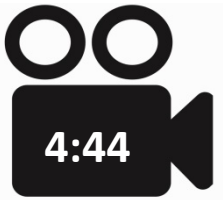
## Neurological symptoms

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

## Psychiatric symptoms

- Confusion and memory loss
- Depression
- Unstable mood

# SUMMARY




| Vitamins | B6 | B12 |
|---|---|---|
| Forms | 1. Pyridoxine<br>2. Pyridoxal<br>3. Pyridoxamine | 1. Cyanocobalamin<br>2. Hydroxycobalamin<br>3. Adenosylcobalamin (in liver)<br>4. Methylcobalamin (in blood circulation) |
| Active Form | Pyridoxal phosphate | Adenosylcobalamin, Methylcobalamin |
| Function | Work as coenzyme for:<br>1. Transamination 2. Deamination<br>3. Decarboxylation 4. Condensation reactions | 1. Conversion of Propionyl-CoA to succinyl-CoA<br>2. Conversion of Homocysteine to methionine |
| Dietary deficiency observed in | *Rare<br>• Newborn infants fed on formulas low in B6<br>• Women on oral contraceptives<br>• Alcoholics<br>• Isoniazid treatment for tuberculosis | patients with IF* such as:<br>• Autoimmunity<br>• Partial or total gastrectomy |
| Deficiency diseases | • Deficient amino acid metabolism<br>• Deficient lipid metabolism<br>• Deficient neurotransmitter synthesis<br>• Demyelination of nerves and consequent peripheral neuritis | • Pernicious anemia<br>• Demyelination<br>• Neuropathy |
| Symptoms | Mild deficiency leads to:<br>Irritability, Nervousness, Depression<br><br>Severe deficiency leads to:<br>Peripheral neuropathy, Convulsions | Neurological symptoms:<br>Paraesthesia of hands and feet<br>Reduced perception of vibration and position<br>Absence of reflexes, ataxia.<br>Psychiatric symptoms:<br>Confusion, memory loss, Depression, Unstable mood |

**1.The active form of vitamin B6 is:**

A.pyridoxine
B.hydroxycobalamin
C.pyridoxal phosphate
D.pyridoxamine

**2.Vitamin B6 is involved in the formation of heme by which of the following reactions ?**

A. decarboxylation
B. condensation
C. aminotransduction
D. deamination

**3.Vit B6 deficiency could results in :**

A. bleeding
B. night blindness
C. neural tube defects
D. anexity

**4.An other name of vitamin B12 :**

A. riboflavin
B. ascorbic acid
C. retinol
D. cobalamin

**5.Vit B12 is mainly stored in liver in the form of :**

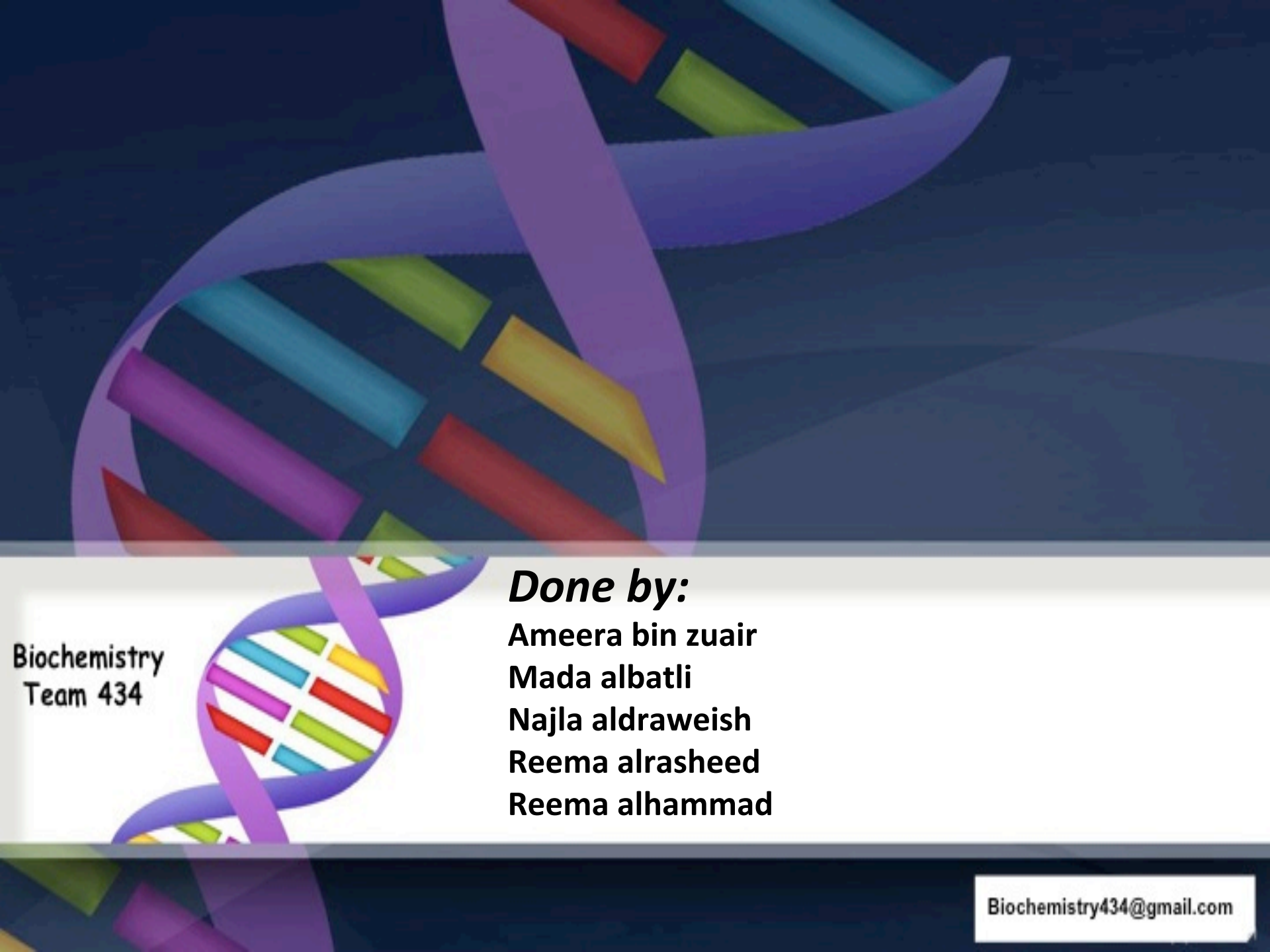
A. adenosylcobalamin
B. methylcobalamin
C. cyanocobalamin
D. phylloquinone

**6.Which of the following is a result of folate trapping ?**

A. neuropathy
B. ataxia
C. depression
D. pernicious anemia

**7.Accumulatin of malonyl coA leads to :**

A. abnormal myelin synthesis
B. decrease intrinsic factor levels
C. inability to synthesize Pyrimidine
D. abnormal cell division

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