[lecture 5]

Vitamins B6 and B12

Biochemistry Team

Teams

The Objectives

- General biochemistry
- Functions
- Deficiency diseases

Red = Import-ant

Blue = explain

Green = addition notes

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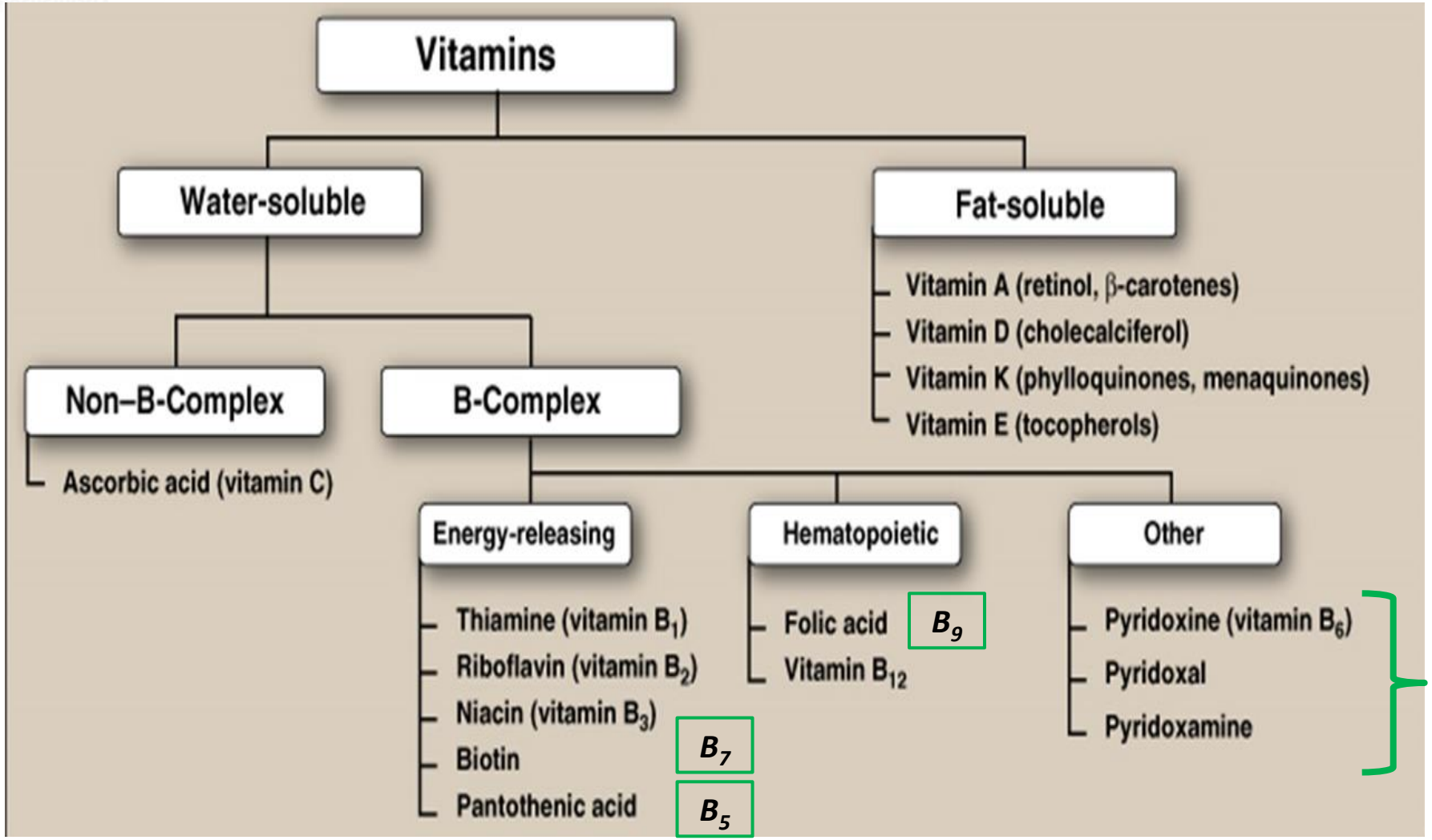
Mind Map



Different forms of vitamin B_6

Water-Soluble Vitamins:

- Not significantly stored in the body (Unusual to get toxicity)
- Must be supplied regularly in the diet
- Excess excreted

Vitamin B complex

Note: no vitamin B4 , B8,B10, B11

B_1	Thiamin
B_2	Riboflavin
B_3	Niacin
B_5	Pantothenic acid
B_6	Pyridoxine
B_7	Biotin (Vitamin H)
B_9	Folic Acid (Folate)
B_{12}	cobalamin

- Present in small quantities in different types of food and must be supplied regularly.
- Not significantly stored in the body and Important for growth and good health.
- Help in various biochemical processes in cell
- **Function as coenzymes** (Explained later)

Note: ***Coenzymes:*** Loosely bind to an enzyme (not permanent)

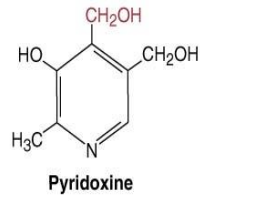
Prosthetic groups: Tightly bind to an enzyme (permanent)

Vitamin B6:

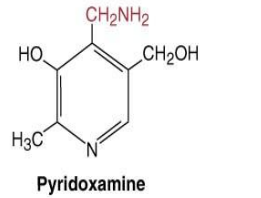
Form	Source
Pyridoxine	(Plant)
Pyridoxal	(Animal) Such as eggs & meat
Pyridoxamine	(Animal) Such as eggs & meat

Active form

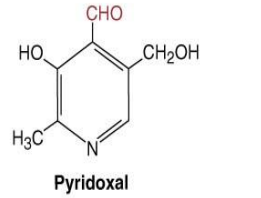
All 3 are converted to pyridoxal phosphate *(PLP)*



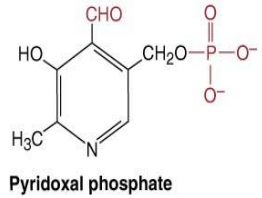
Pyridoxine



Pyridoxamine



Pyridoxal



Pyridoxal phosphate

We don't have to know the structures

Figure 28.11. Structures of vitamin B_6.

Functions of Vitamin B6: (As coenzymes)

Transamination	**The transfer of amino groups** Important when a non-essential amino acid is converted into an essential amino acid e.g. Alanine —(ALT, PLP)→ Pyruvate αKG → Glutamate
Deamination	**The removal of an amine group from a molecule**
Decarboxylation	**The removal of a carboxyl group** Important to convert an amino acid to a neurotransmitter *next slid
Condensation reactions	**The combination of two molecules to form a larger molecule** e.g. Formation of ALA* by ALA synthase, the regulatory step in hemoglobin synthesis.

ALA: δ-Aminolevulinic acid

Reminder: Essential amino acids are those that are "essential" in the diet. In other words, we cannot create them through our own metabolism

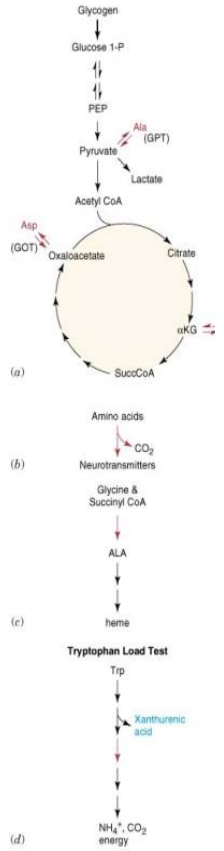


Figure 28.12. Some important metabolic roles of pyridoxal phosphate.

Dr. Sumbul said we don't have to know this pathway, just the main reactions which are explained in the table

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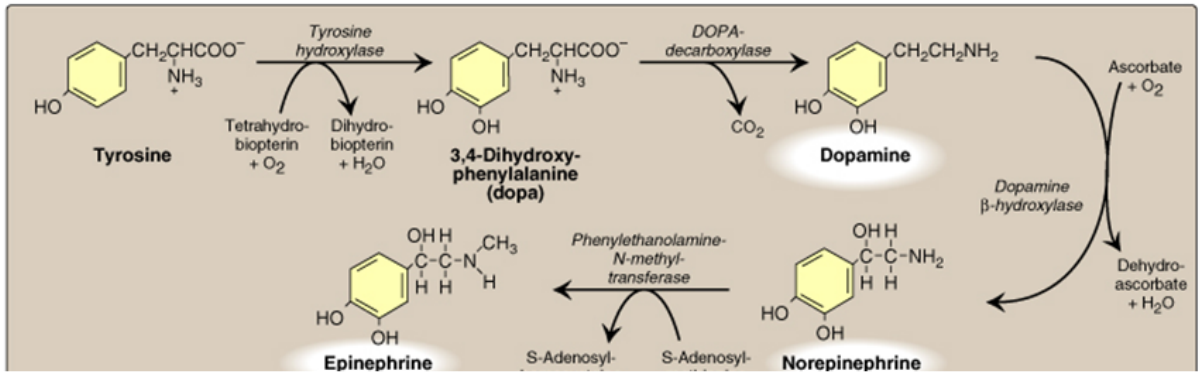
Functions of Vitamin B6: (As coenzymes)

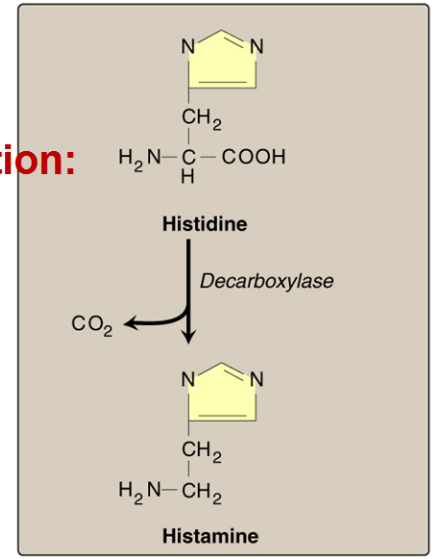
Decarboxylation Reaction:

Formation of Chatecholamines:
Dopamine, norepinephrine and epinephrine



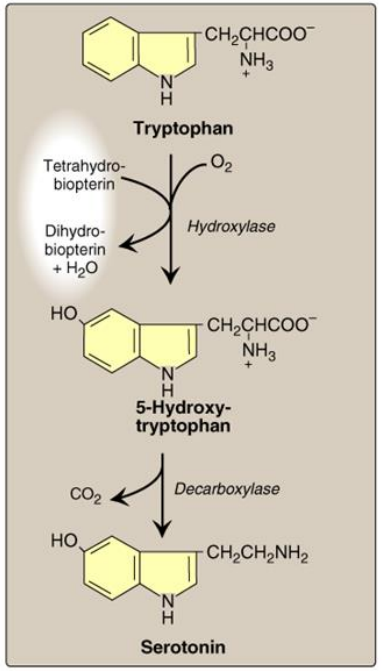
Decarboxylation Reaction:

Formation of Histamine



Decarboxylation Reaction:

Formation of Serotonin



In All these graphs we only have to know the *Path way, *Enzyme or Co-Enzymes

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Disorders of Vitamin B6 Deficiency:

Dietary deficiency is **rare**, but it was observed in:

1. Newborn infants fed on formulas low in B_6
2. Women on oral contraceptives
3. Alcoholics (Alcohol reduces the absorption of nutrients)
4. **Isoniazid** treatment for **tuberculosis** can lead to vitamin B_6deficiency by forming inactive derivative with PLP*

Deficiency leads to poor activity of PLP-dependent enzymes causing:

1. Deficient amino acid metabolism
2. Deficient lipid metabolism
3. Deficient neurotransmitter synthesis [serotonin, epinephrine, noradrenaline 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 involves:

1. Irritability
2. Nervousness
3. Depression

Severe deficiency involves:

1. Peripheral neuropathy
2. Convulsions

*PLP: Pyridoxal phosphate.

Vitamin B12 (Cobalamin)

Forms of Vitamin B_{12}:

1-Cyanocobalamin

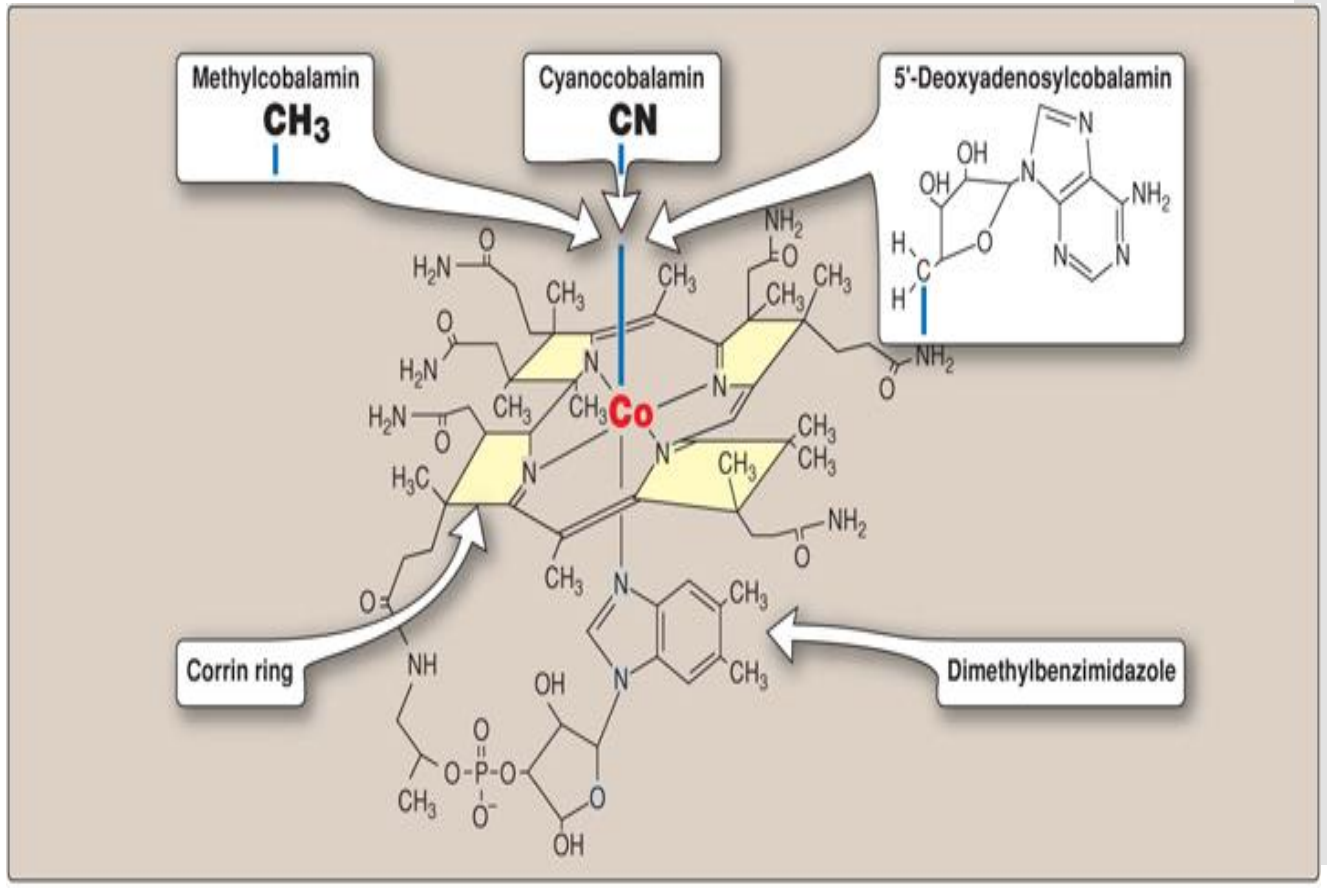
2-Hydroxycobalamin

These 2 forms which is given to patient as supplement + it can be converted into active coenzymes with help of different enzymes

3-Adenosylcobalamin (major storage form in the liver)

4-Methylcobalamin (mostly found in blood circulation)

*Coenzymes for metabolic reactions



About vit.B12

•It is mainly found in animal liver bound to protein as

Methylcobalamin or 5'-deoxyadenosylcobalamin

The only way to get it is from the animal sources ,(synthesized by bacteria and normal flora in our bodies)

Curd is a good source because of the present of lactic acid bacteria.

•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

•Deficiency of b12 could be due to diet or if intrinsic factor* is not there

Its storage

•Vitamin B_{12} Storage

-Liver stores vitamin B_{12} (4-5 mg)

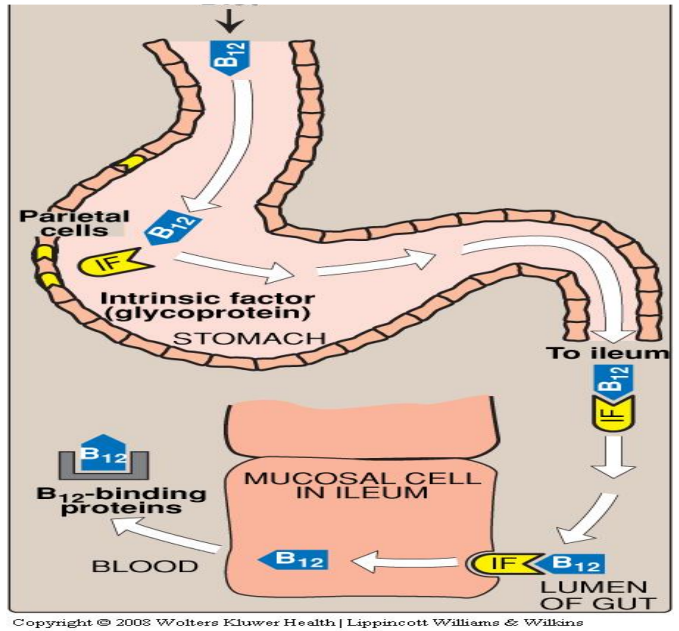
-Other B vitamins are not stored in the body

B12 is the only water soluble vit. stored in body

-Vitamin B_{12} deficiency is observed in patients with IF deficiency due to autoimmunity or by partial or total gastrectomy

Clinical deficiency symptoms develop in several years because it is stored in the liver

Intrinsic factor *



*Intrinsic factor is a glycoprotein secreted by cells in the stomach. So when we take B12(extrinsic factor) in the diet, the parietal cells of the stomach release the intrinsic factor and binds it to B12 and carries it to the ileum. When it reaches the ileum, the mucosal cells of the ileum absorbs b12,then B12 is unloaded inside the mucosal cells of the ileum then it goes to the circulation.

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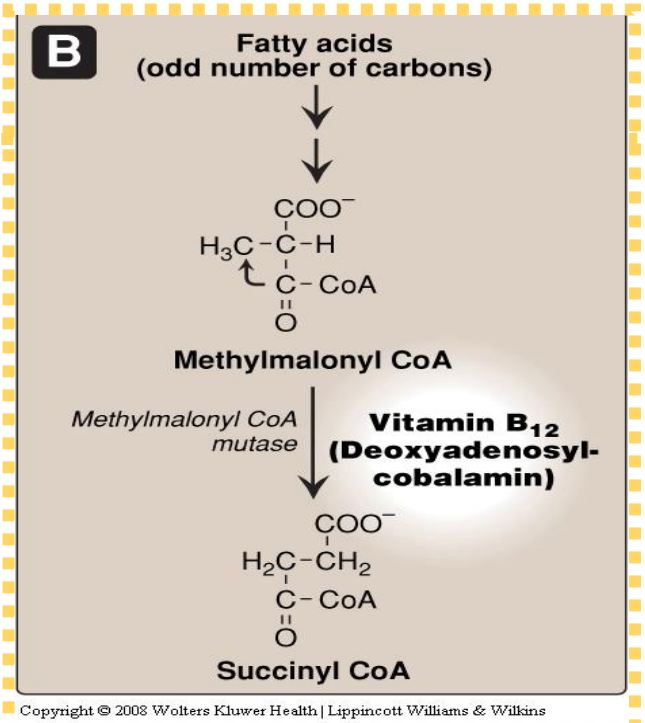
Functions of Vitamin B12:

- Two reactions require B12:

(1) **Conversion of propionyl-CoA to succinyl-CoA:**

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

So, in deficiency of vitamin B12 the patient will have Excess ***methyl-malonyl-CoA leading to demylination***



(2) **Conversion of homocysteine to methionine:**

Methionine synthesis requires B12 and N5 –methyltetrahydrofolate by methionine synthase.

N5-methyltetrahydrofolate will converted into ***tetrehydrofolate*** (which is the functional form of folic acid.)

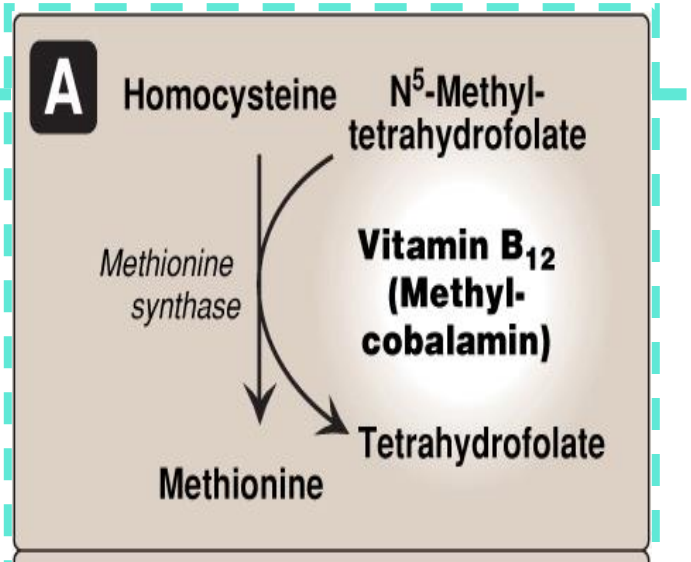
Tetrehydrofolate carrier for 1 carbon unit.

Deficiency of B12 will cause acuumlation of **N5-methyltetrahydrofolat** → folate trap.

also it will cause accumulation of homocysteine

Causes cardiovascular disorder

The exact mechanism is notknown.



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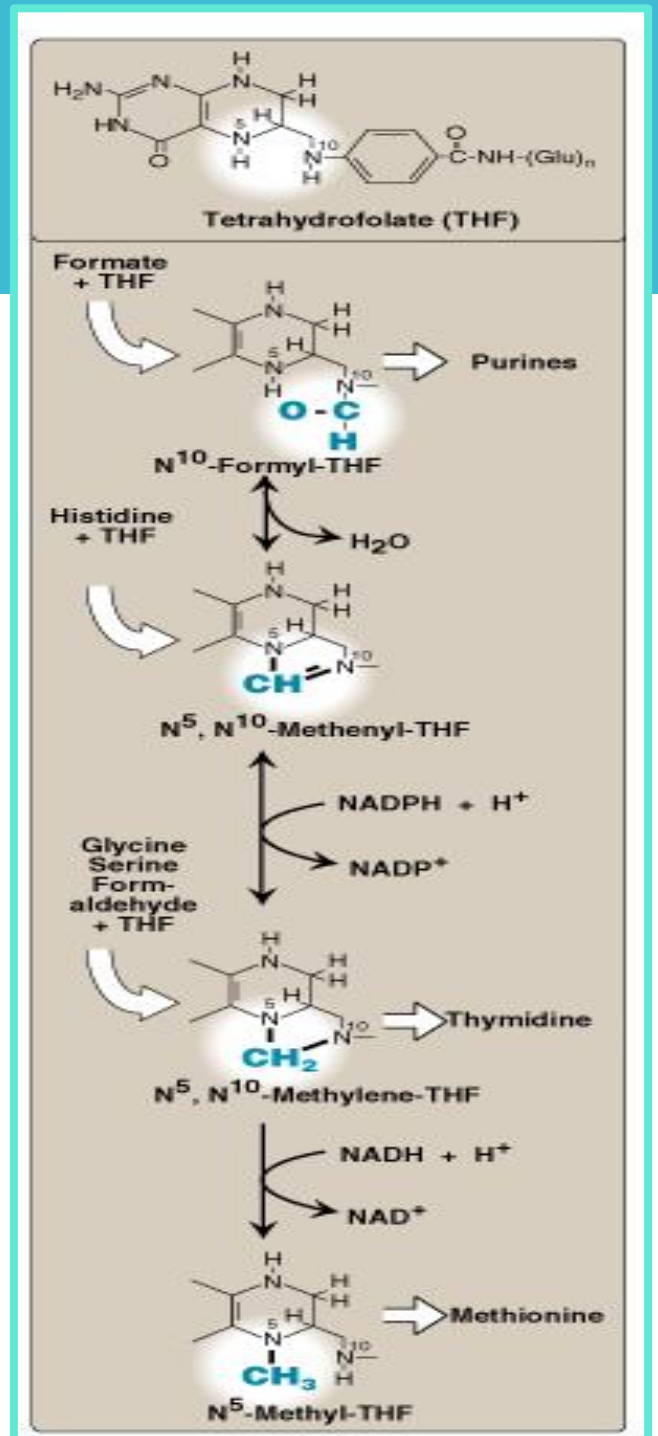
B12 Deficiency and Folate Trap

- Homocysteine re-methylation reaction is the only pathway where N^5-methyl TH_4* 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 TH_4 derivatives (N^5-N^{10} methylene TH_4 and N^{10} formyl TH_4) required for purine and pyrimidine syntheses



*TH_4: Tetrahydrofolate

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Disorders of Vitamin B_{12} Deficiency

1-Pernicious anemia
*Megaloblastic anemia.
*Vitamin B_{12} deficiency is mainly due to the deficiency of intrinsic factor.
2-Demyelination
*Myelin sheath of neurons is chemically unstable and damaged. (because of the presence of ***methyl-malonyl-CoA.)***
3-Neuropathy
*Peripheral nerve damage.

•Causes of neuropathy

1-Deficiency of vitamin B_{12} leads to accumulation of methylmalonyl CoA.
2-High levels of methylomalonyl CoA is used instead of malonyl CoA for fatty acid synthesis.
3-Myelin synthesized with these abnormal fatty acids is unstable and degraded causing neuropathy.

Neuropsychiatric symptoms of Vitamin B_{12} Deficiency

1-Neurological symptoms
*Paraesthesia (abnormal sensation) of hands and feet (both sensory and motor tracts 'compined degeneration').
*Reduced perception of vibration and position.
*Absence of reflexes.
*Unsteady gait and balance (ataxia).
Babenski sign is positive
2-Psychiatric symptoms
*Confusion and memory loss.
*Depression.
*Unstable mood.

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Summary

Thank you shroog alharbi

Vitamins	B_6	B_{12}
forms	Pyridoxine Pyridoxal Pyridoxamine	Cyanocobalamin Hydroxycobalamin Adenosylcobalamin Methylcobalamin
Active form	pyridoxal phosphate (PLP)	Adenosylcobalamin and Methylcobalamin
Functions	coenzyme for 1- Transamination 2- Deamination 3- Decarboxylation 4- Condensation reactions	1- Conversion of propionyl-CoA to succinyl-CoA 2- Conversion of homocysteine to methionine
Dietary deficiency was observed in	1- Newborn infants fed on formulas low in B6 2- Women on oral contraceptives 3- Alcoholics 4- Isoniazid treatment for tuberculosis can lead to vitamin B_6 deficiency by forming inactive derivative with PLP	observed in patients with IF deficiency due to autoimmunity or by partial or total gastrectomy
Deficiency diseases	1- Deficient amino acid metabolism 2- Deficient lipid metabolism 3- demyelination of nerves 3- consequent peripheral neuritis 4- Deficient neurotransmitter synthesis	1- Pernicious anemia 2- Demyelination 3- Neuropathy

Questions

1-Pyridoxine functions as a coenzyme for ..... To produce neurotransmitters.

- a) Transamination
- b) Deamination
- c) Decarboxylation
- d) Condensation reactions

2-Pyridoxine deficiency, albeit rare, has been observed in the following condition:

- a) Newborn infants
- b) Women on OCPs
- c) Alcoholics
- d)All of the above

3-Which of the following statements is true of cobalamin

- a) Synthesized in the body
- b) Intrinsic factor is important for its absorption
- c) Not stored in the body
- d) Fat soluble

4-Vitamin B_{12} deficiency signs and symptoms include...

- a) Megaloblastic anemia
- b) Convulsions
- c) Memory loss
- d) A+C

5- Which one is the only water soluble vit. which stored in body & where it`s stored?

a) B6. In the Muscles
b) B6. In the liver
c) B12. In the Muscles
d) B12. In the liver

Answers: 1-c , 2-d , 3-b , 4-d, 5-d

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If you find any mistake, please contact us:)

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