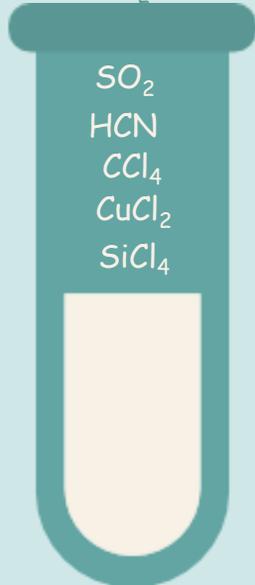
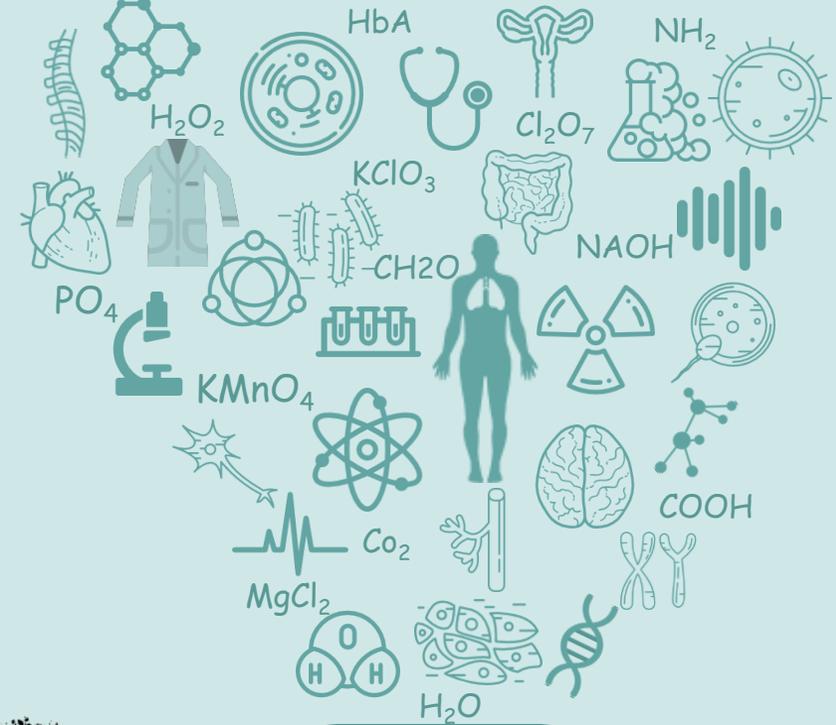




Important Doctors slides
Extra Information **Doctors notes**



Biochemistry

Vitamins B6 and B12

[Editing file](#)

OBJECTIVES

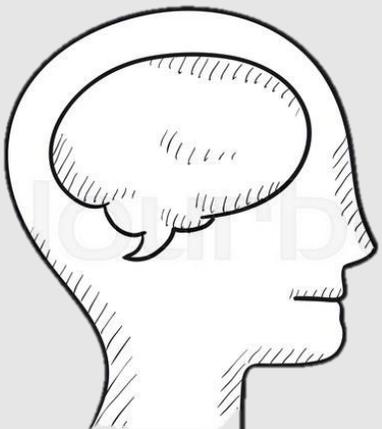
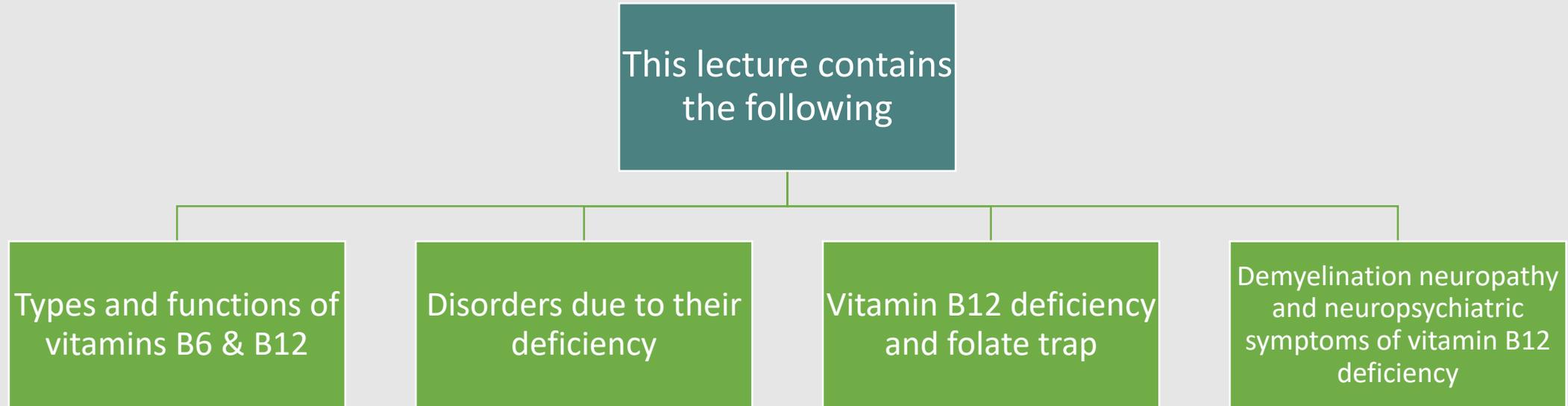
Upon completion of this lecture, the students should be able to:

- 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

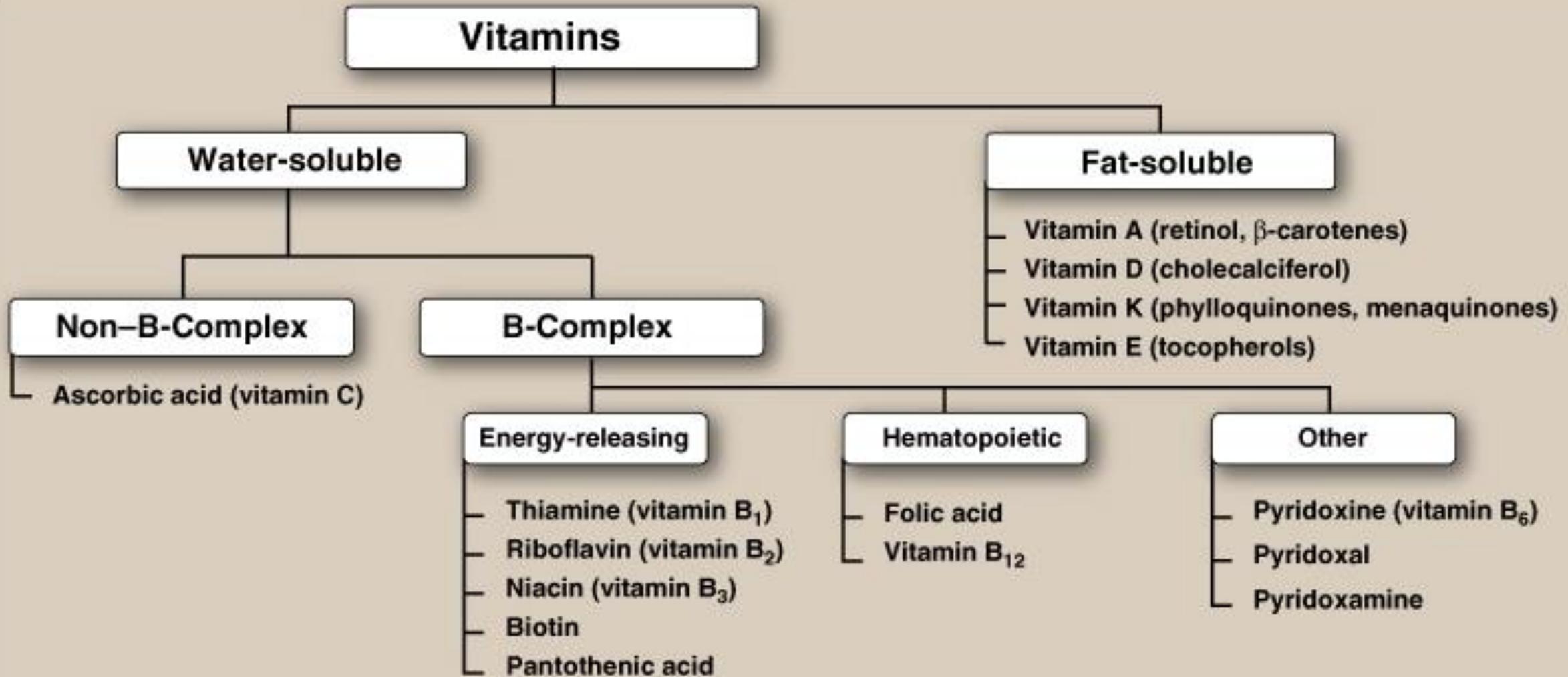


Overview

The lecture contains a lot of notes but as long as you focus while you are reading them, you will understand the lecture rapidly



Classification of vitamins



Water Soluble Vitamins:

Types of Vitamin B :

- Thiamine (B1)
- riboflavin (B2)
- niacin (B3)
- pantothenic acid (B5)
- pyridoxine (B6)
- biotin (B7)
- cobalamin (B12) can be stored in the body.
- Folate.
- The eight vitamins B types together (with folic acid) are called : B complex.
- **They function as coenzymes.**

Most Vitamins in vitamin B complex act as precursors for coenzymes (involved with enzymes that catalyse the reactions involved in energy synthesis).

-There are two types of enzymes: holoenzyme and apoenzyme.

-What are coenzymes?
Holoenzyme: some enzymes require a non protein part to become active, this part can either be a cofactor or a coenzyme.

-The coenzyme is bound transiently (not permanent) with the enzyme.

Characteristics of B complex:

Must be supplied regularly in the diet.

Not significantly stored in the body.

Excess excreted

Present in small quantities in different types of food

Help in various biochemical processes in cell

Important for growth and good health

Vitamin B6:

Functions:

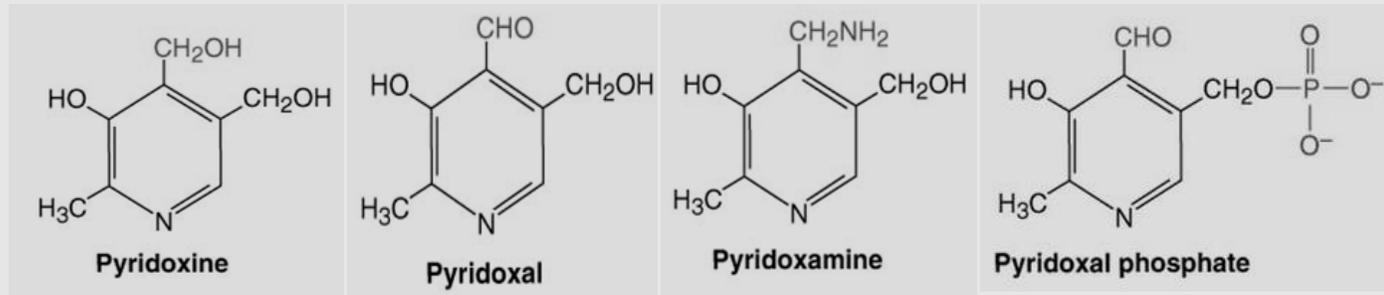
Three Forms:

- Pyridoxine: From plants.
- Pyridoxal: From animal proteins such as eggs and meat.
- Pyridoxamine: Same source as pyridoxal.

Active Form:

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

- As coenzyme for: Transamination, Deamination, Decarboxylation and Condensation reactions



Transamination :the amino group is being transported from one molecule to another.

Deamination is the removal of the amino group from a molecule.

Decarboxylation :is the removal of CO2 from a molecule.

Condensation reactions of two molecules combining together to form a third molecule.

these 4 forms differ only in the nature of the functional group attached to the ring and they are derivatives of pyridine

Metabolic roles of pyridoxal phosphate:

In this image we find some of the important roles which pyridoxal plays in metabolic reactions:

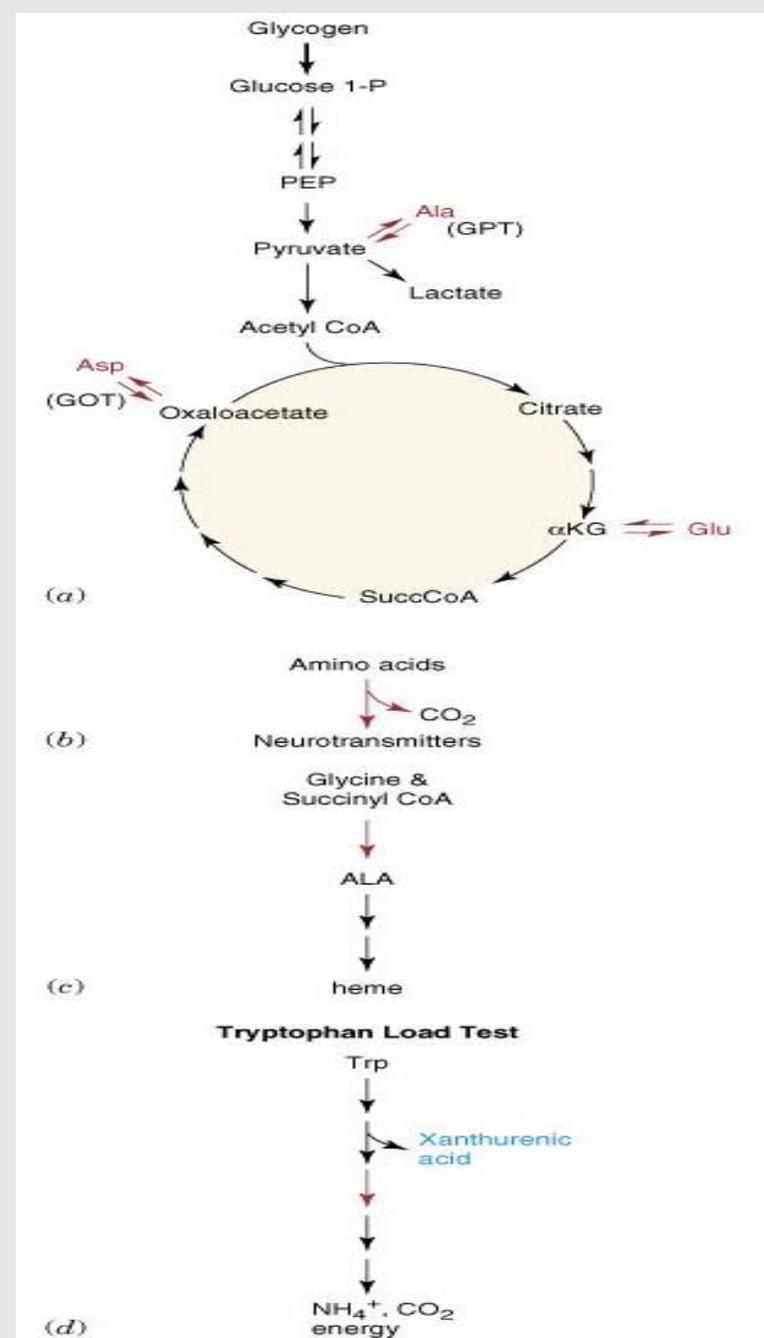
glycogen is giving you glucose phosphate and then finally giving you pyruvate .
So glycogenolysis and finally entering Krebs cycle.

The transamination reactions are involved in both the synthesis and breakdown of amino acids because they are reversible reactions, these reactions are also involved in energy synthesis because the resulting molecules enter Krebs. In order to form neurotransmitters ,decarboxylation must occur. Glycine and succinyl coA join to form aminoluvilinic acid which then forms heme.

What is the principle concept for the test used to diagnose for B6 deficiency ?

When tryptophan is degraded it gives you ammonium and carbon dioxide and energy, but **this reaction needs vitamin B6 to occur**. This reaction actually makes the basis of the test used to check for vitamin B6 deficiency.

So if vitamin B6 is deficient you will have a build up of a molecule called xanthurenic acid, this molecule is found (accumulated) in the blood of the patients who have vitamin B6 deficiency. Note that at the beginning of the test you give the patient tryptophan (to check if xanthurenic acid will accumulate or not).

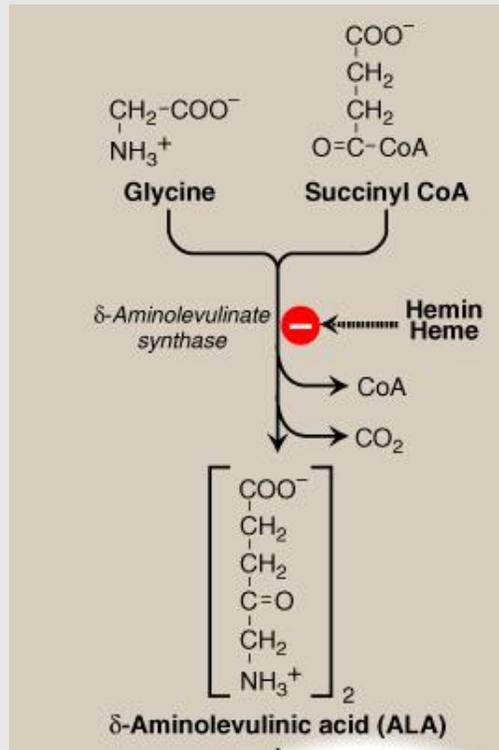


Reactions of Vitamin B6

decrease B6 may lead to depression

Condensation Reaction :

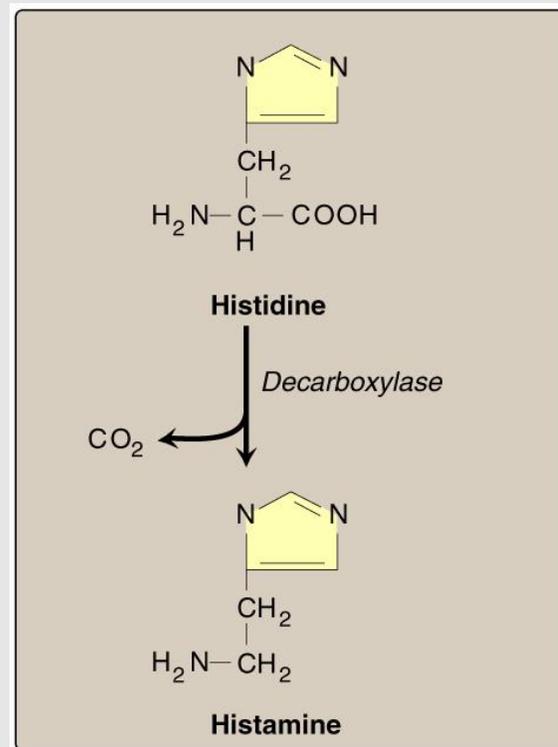
Formation of ALA by ALA synthase, The regulatory step in haemoglobin synthesis



Note that this reaction requires glycine and succinyl CoA to join together.

Decarboxylation Reaction:

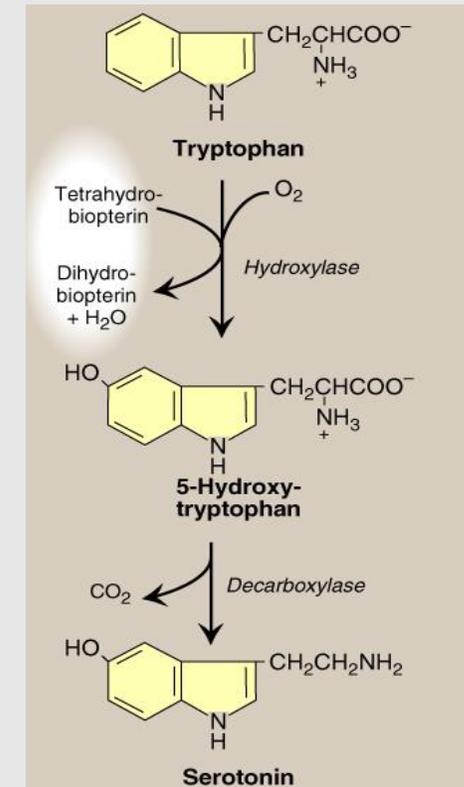
Formation of Histamine



The decarboxylation of histidine yields histamine.

Decarboxylation Reaction:

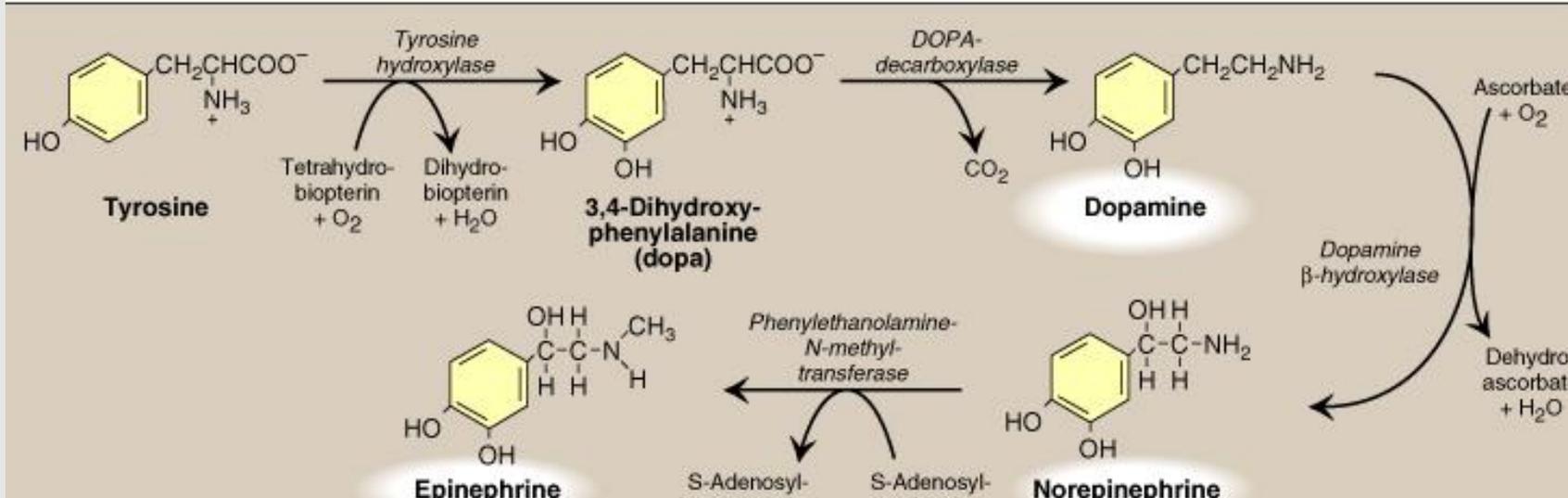
Formation of Serotonin



The decarboxylation of tryptophan yields serotonin.

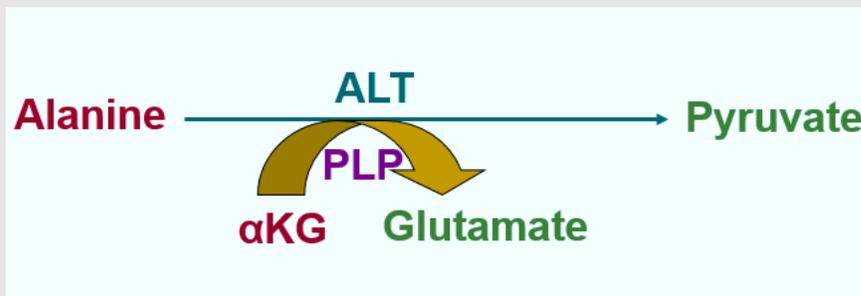
Reactions of Vitamin B6

Decarboxylation Reaction: Formation of Catecholamine
 “Dopamine, norepinephrine and epinephrine” .



Tyrosine is the parent compound here, then it gets decarboxylated into dopamine which is then converted into epinephrine and norepinephrine. So if there is a deficiency in vitamin B6, the catecholamine synthesis will decrease or stop.

Transamination Reaction



Alanine transfers its amino group to alpha keto glutarate which then turns into glutamate (catalyzed by alanine transaminase which needs PLP). What is left from alanine? Pyruvate

The transfer of amino groups is important when a nonessential amino acid (alanine) is converted into an essential amino acid (pyruvate). *Essential Amino Acids: are those that can't be synthesized by the body so we must get it in the diet.

Disorders of Vitamin B6 deficiency

Disorders Of Vit B6 Deficiency

Dietary deficiency

Medication side effect

poor activity of PLP-dependent enzymes

Demyelination

It is rare , but it is observed in :

- 1- Newborn infants fed on **formulas low** in **B6**.
- 2- Women on oral contraceptives (حبوب منع الحمل).
- 3- Alcoholics.

*Alcohol and oral contraceptives will interfere with absorption of Vitamin B6.

Isoniazid treatment for tuberculosis (by pyridoxine) can lead to vitamin B6 deficiency by forming **inactive derivative** with PLP.

Basically isoniazid forms a complex with pyridoxal phosphate (this complex is an inactive derivative).

Which leads to depleted levels of B6(PLP) in the blood.

Hence vitamin B6 is given to patients being treated for TB with isoniazid.

Disorders of Vitamin B6 deficiency

Disorders Of Vit B6 Deficiency

Dietary deficiency

Medication side effect

poor activity of PLP-dependent enzymes

Demyelination & neurogenic symptoms

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, norepinephrine and gamma amino butyric acid "GABA".

* PLP is involved in the synthesis of **sphingolipids** so its deficiency leads to **demyelination** of nerves and consequent peripheral neuritis .

Pyridoxine is the only water-soluble vitamin with significant toxicity.

* **Mild deficiency leads to:**

- 1- Irritability
- 2- Nervousness
- 3- Depression

* **Severe deficiency leads to:**

- 1- Peripheral neuropathy (sensory neuropathy), occurs at intakes above 500 mg/day.
- 2- Convulsions

Vitamin B12

Doctor mentioned this

Forms of Vitamin B12

*Note that cobalamin is the only hydrophilic vitamin stored in the body while other hydrophilic vitamins are NOT! Only lipid soluble are stored.
- What is the circulatory form of cobalamin? methylcobalamin

Cyanocobalamin

Hydroxycobalamin

Adenosylcobalamin
(major storage form in the liver)

Methylcobalamin
(mostly found in blood circulation)

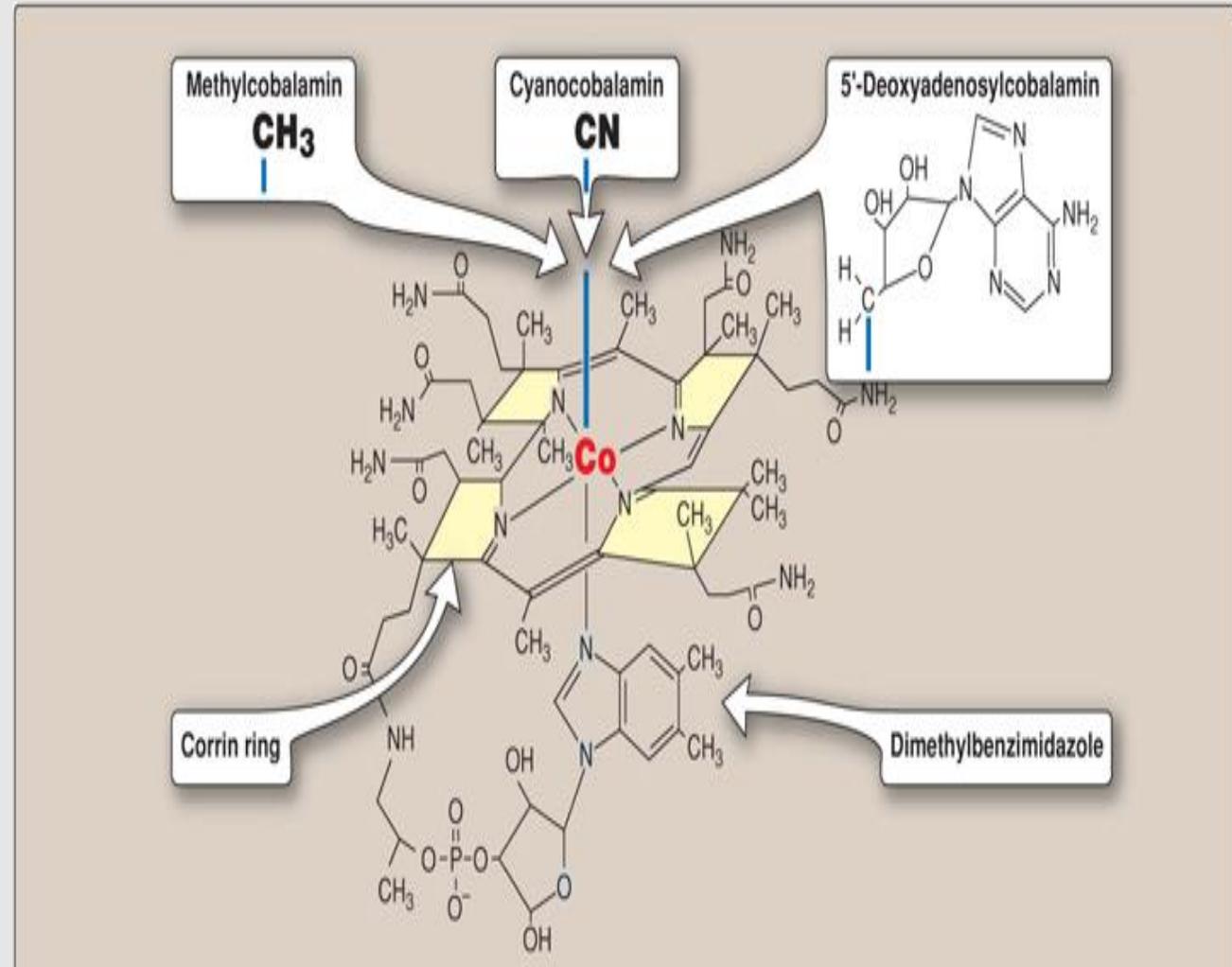
Commercial form made in factories (factories use bacteria to synthesize hydroxycobalamin and cyanocobalamin forms of vitamin B12).

These two are coenzymes for **metabolic reactions**. (the body can convert other cobalamins into active coenzymes).

Vitamin B12

In the centre of the Corrin ring, we have cobalt. And cobalt can make six bonds. Four of these bonds can attach to the nitrogen found in the Corrin ring, and one is attached to the dimethylbenzimidazole, and the sixth bond : If it is made with cyanide it is called cyanocobalamin.

If a methyl group is attached, its methylcobalamin. Or if adenosyl group is attached it is called adenosylcobalamin. So the form of cobalamin changes according to the change in the sixth group while the other 5 bonds remain the same



Vitamin B12 (Cobalamine)

Mainly found in animal liver bound to protein as: “ Methylcobalamin” or “ 5'-deoxyadenosylcobalamin”

✓ Essential for:

1. **Normal nervous system function .**
2. **Red blood cell maturation .**

* Note that folic acid and vitamin B 12 are both required in haematopoiesis .
Deficiency in B12 leads to megaloblastic macrocytic anemia.

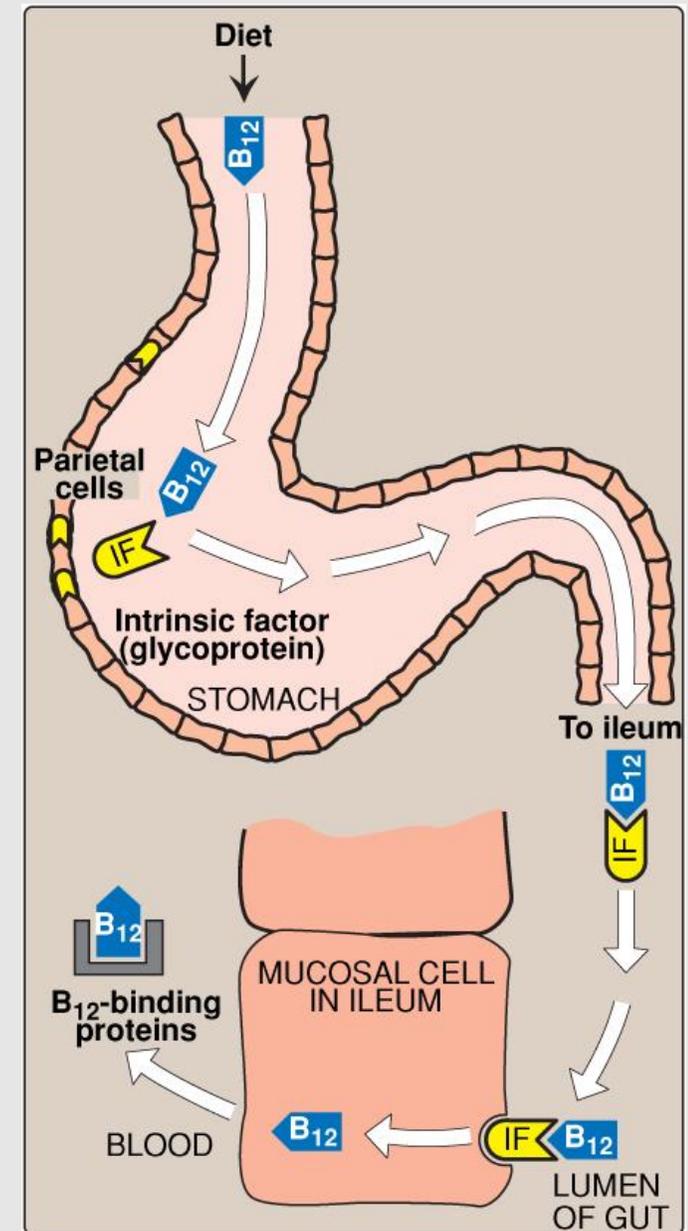
✓ Not synthesized in the body and must be supplied in the diet.

✓ Binds to intrinsic factor “a protein secreted by cells in the stomach “ and absorbed by the ileum.

* If a condition in which GIT flora are decreased such as in people taking antibiotics, vitamin B12 deficiency may occur .

* It may also occur in older people because their stomach acidity is decreased which impairs the absorption of vitamin B12 [Further information in the next slide]

synthesized by parietal cells of stomach, then it get attached to intrinsic factors in intestine, then it binds to ileum mucosal cells , then it get absorbed in the ileum as trans-cobalamin protein, deficiency in intrinsic factors due to autoimmune destructions or undergoing sleeve gastrectomy will reduce absorption of B12



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Vitamin B12: **IMPORTANT**

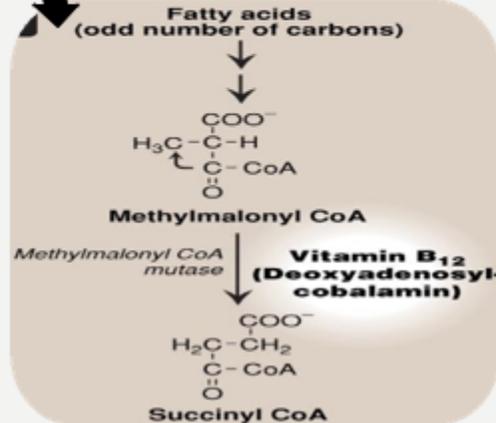
Storage

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

Functions

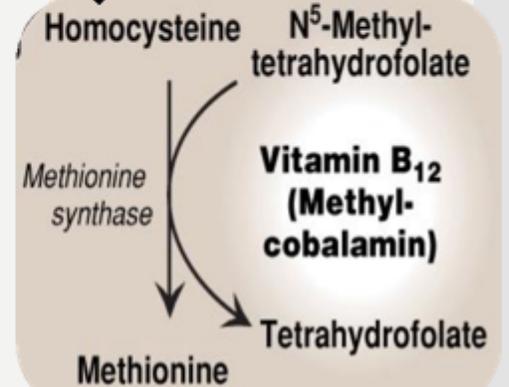
1. Conversion of methylmalonyl-CoA to succinyl-CoA.

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



2. Conversion of homocysteine to methionine.

Methionine synthase requires B₁₂ in converting homocysteine to methionine



Note that this reaction requires vitamin B12 in the form of methyl cobalamin. If deficiency occurs there will be accumulation of homocysteine which may lead to spina bifida or heart defects

Vitamin b12 is used in the breakdown of fatty acids methyl-malonyl CoA is converted into succinyl CoA by methyl malonyl CoA mutase which is actually vitamin B12 in the form of deoxy adenosyl cobalamin

-note that all of these points are important!!!!

-if there is a deficiency in vitamin B12 this will lead to accumulation of methylmalonyl coA

B12 Deficiency And Folate Trap “IMPORTANT”

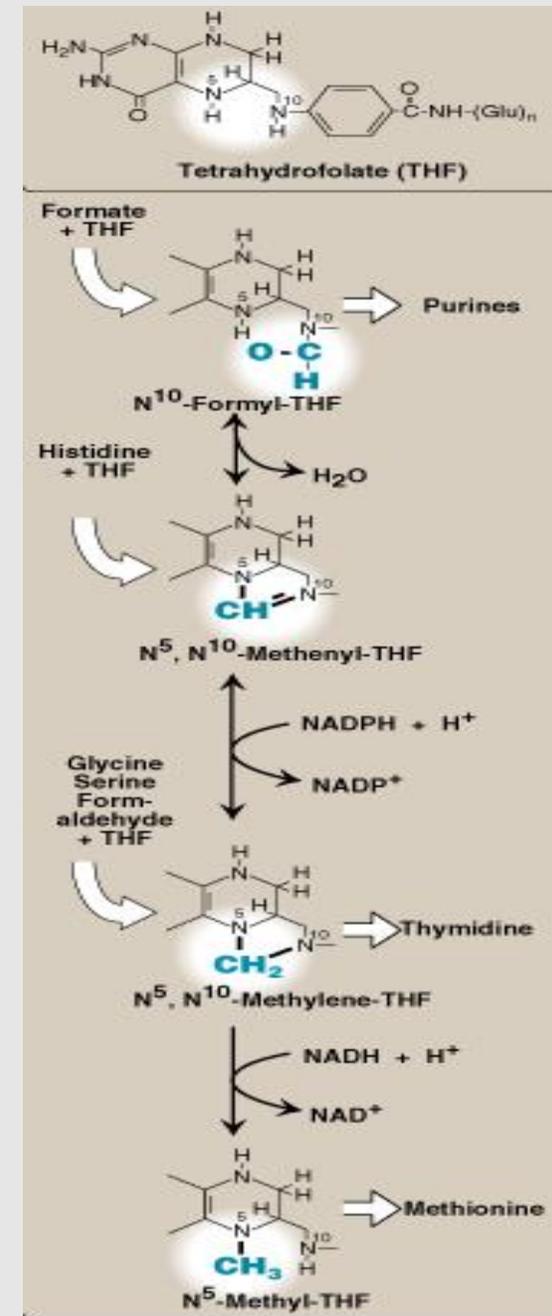
✓ **Homocysteine re-methylation reaction** is the only pathway where N₅-methyl TH₄ can be returned back to tetrahydrofolate pool

➤ 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

- Due to trapping of TH₄ all of these reactions can't go on.



-The functional form of folate is tetrahydrofolate.

Folate is trapped because it can not be converted to the active form while it exists as inactive form

B12 deficiency can be determined by the level of methylmalonic acid in blood, Which is elevated in individuals with low intake or decreased absorption of the vitamin

liver disease leads to elevation of vitamin B12 levels , its required for synthesis of proper red blood cell.
Fatty acid degradation also requires B12 , homocysteine > methionine reaction also requires B12 as a co-factor .
Deficiency of folic acid can lead to anemia since it's requires for RBC's maturation .

Disorders of Vitamin B12 Deficiency

Pernicious anemia

Megaloblastic anemia (RBC can't divide because of no DNA synthesis so it keeps on growing).

Vitamin B₁₂ deficiency is mainly due to the deficiency of intrinsic factor.

Can be corrected with b12 supplements .

Demyelination

Myelin sheath of neurons is chemically unstable and damaged.

Causes Neuropathy.

Neuropathy

Peripheral nerve damage.

Why demyelination occurs?

If there is deficiency there will be accumulation of methyl malonyl coA then - when the myeline sheath is being synthesized- lots of fatty acids instead of getting methyl coA ,they will get methylmalonyl coA in their structure which will lead to an unstable form of myelin thus demyelination occurs.

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

Symptoms of B12 deficiency FOCUS ON THE SYMPTOMS IT CAN PRESENT AS CLINICAL CASE

Neurological symptoms

Unsteady gait and balance (ataxia)

Neurological symptoms of B12 deficiency

Absence of reflexes

Paresthesia
(abnormal sensation of hands and feet)

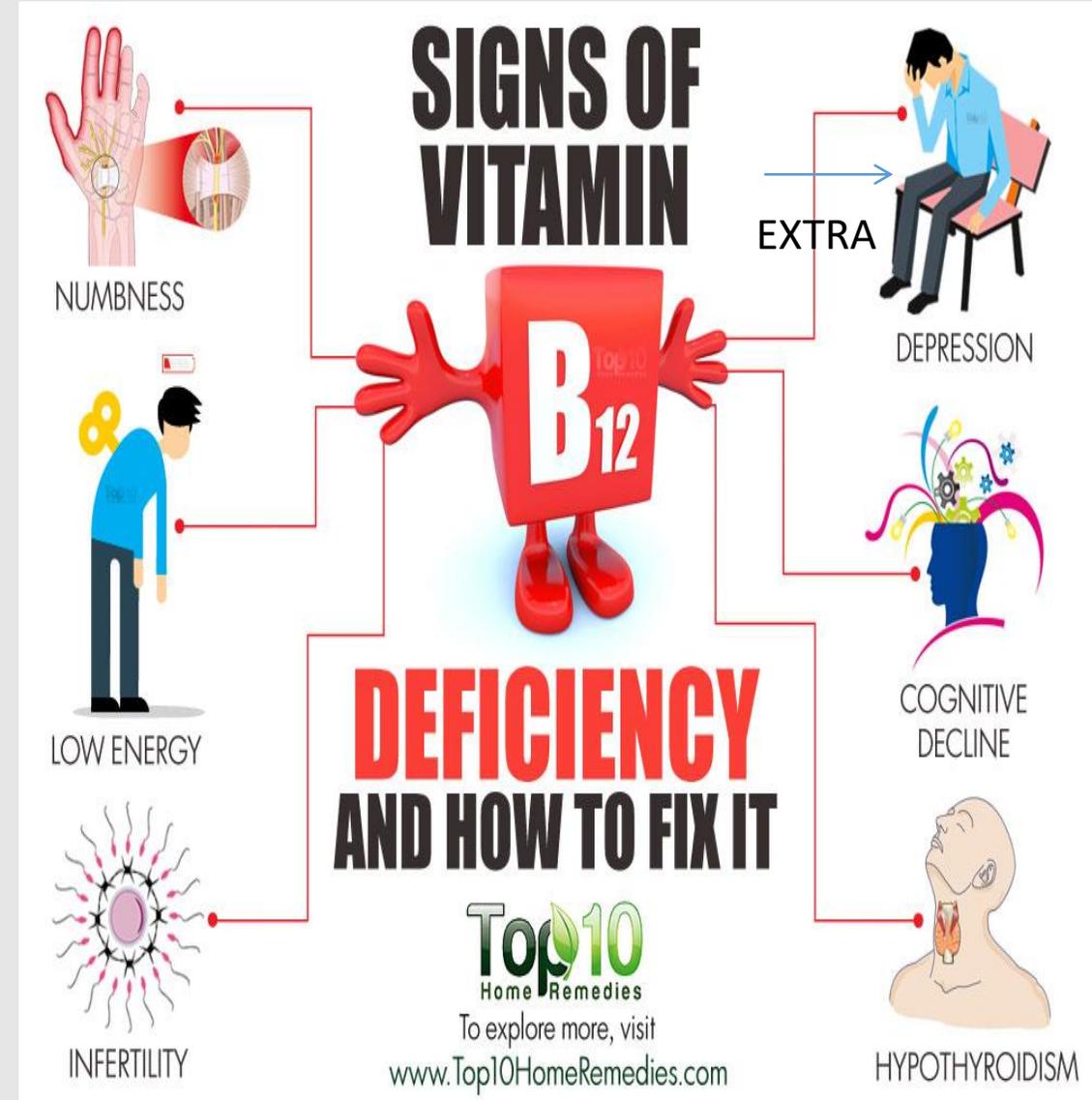
Reduced perception of vibration and position

Psychological symptoms

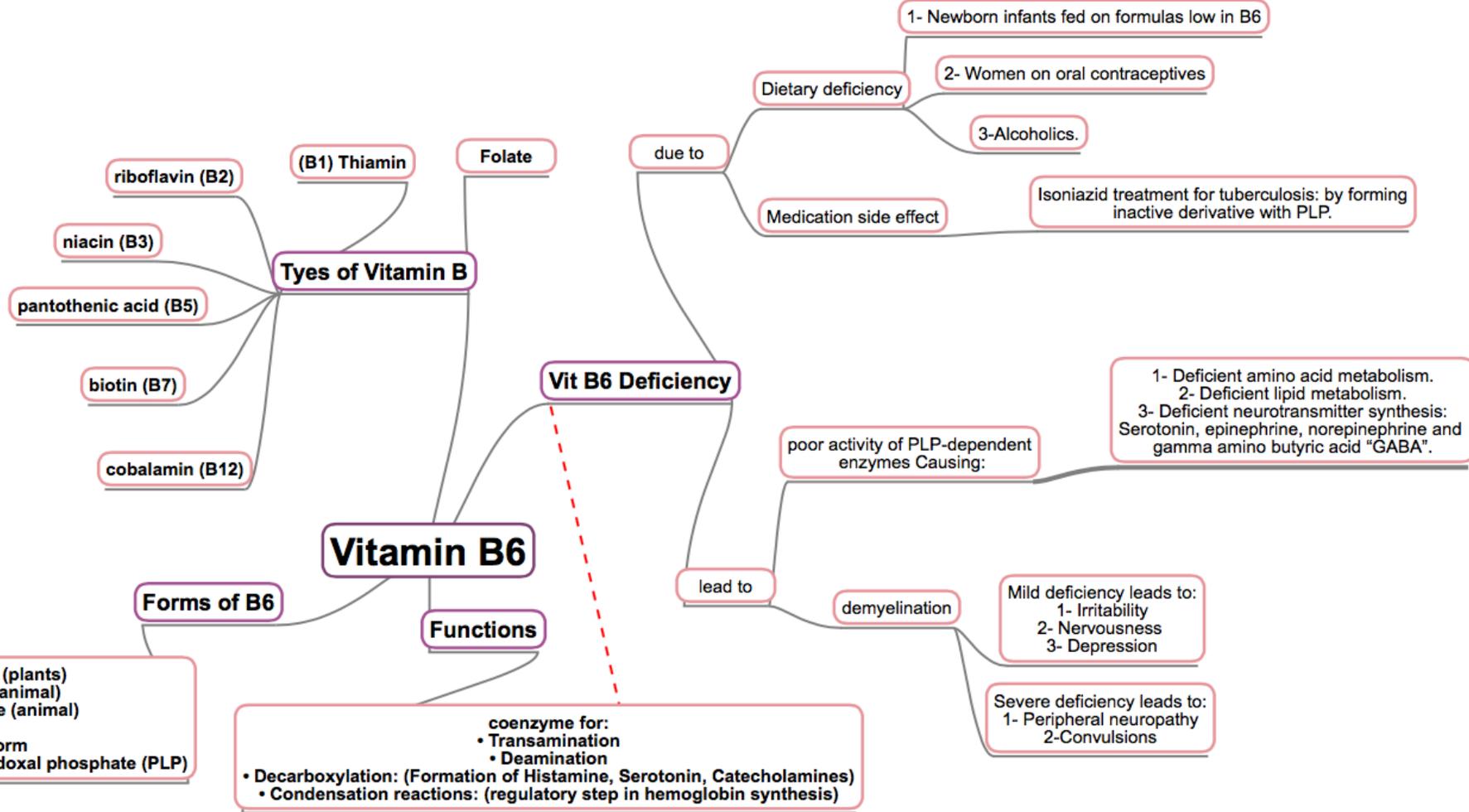
Depression

Unstable mood

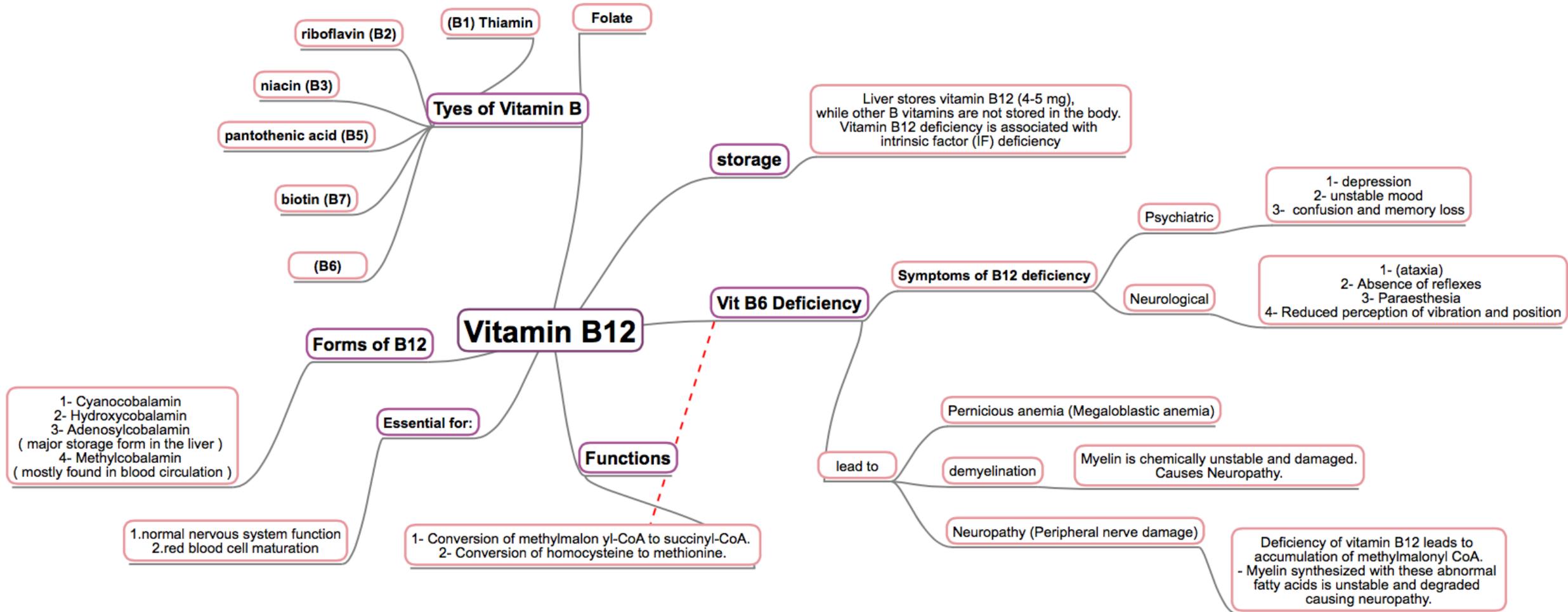
Confusion and memory loss



Summary



Summary



Quiz

1) The active form of vitamin B6 is:?

- a) Pyridoxine
- b) Pyridoxal
- c) Pyridoxamine
- d) PLP

2) Which one of the following is a psychiatric symptom of vitamin B12 deficiency?

- a) Paresthesia
- b) Reduced perception of vibration and position
- c) Confusion and memory loss
- d) Ataxia

3) Which one of the following symptoms is caused by severe deficiency of vitamin B6?

- a) Irritability
- b) Depression
- c) Convulsions
- d) Nervousness

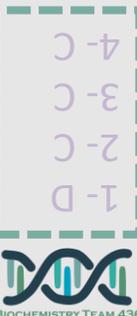
4) Which one of the following is the major storage form of vitamin B12 in the liver?

- a) Cyanocobalamin
- b) Hydroxycobalamin
- c) Adenosylcobalamin
- d) Methycobalamin

Q : Describe the process through which folate is trapped as N5–methyltetrahydrofolate causing vitamin B12 deficiency ?

Q : List the functions of vitamin B6 as a coenzyme ?

[Suggestions and recommendations](#)





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THANK YOU

FOR CHECKING OUR WORK



PLEASE CONTACT US IF YOU HAVE ANY ISSUE



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Don't forget to review the notes



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