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These reactions are mainly involved amino acids metabolism

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

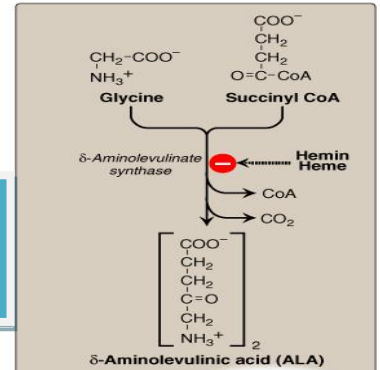
❖ **As coenzyme for**

- **Transamination** (interconversion of the amino acids) (amino acid-α ketoacids) it is a reversible reaction
- **Deamination** (removal of amino groups >> required in the degradation of the amino acids)
- **Decarboxylation** (removal of carbon dioxide) (involved in most neurotransmitters formation ) e.g. glutamate gets decarboxylated to GABA , histidine gets decarboxylated to histamine.
- **Condensation reactions** e.g. the main enzyme in glycogenolysis is glycogen phosphrylase which requires vitamin B6 as co-enzyme.

• **Condensation Reaction**

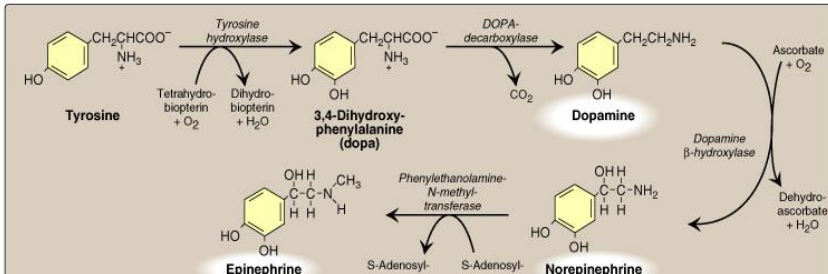
Formation of ALA by ALA synthase,  
The regulatory step in hemoglobin synthesis  
**glycogenolysis**

Glycine with succinyle coA involved in the heme synthesis.

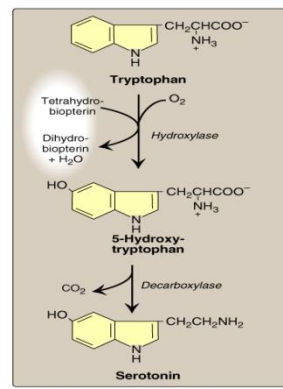


• **Decarboxylation Reaction:**

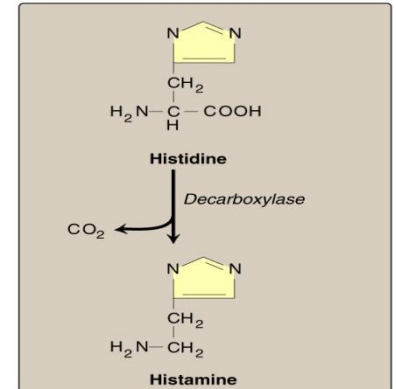
Formation of :  
Dopamine, norepinephrine, epinephrine, GABA, Histamine, and Serotonin



Chatecholamines formation



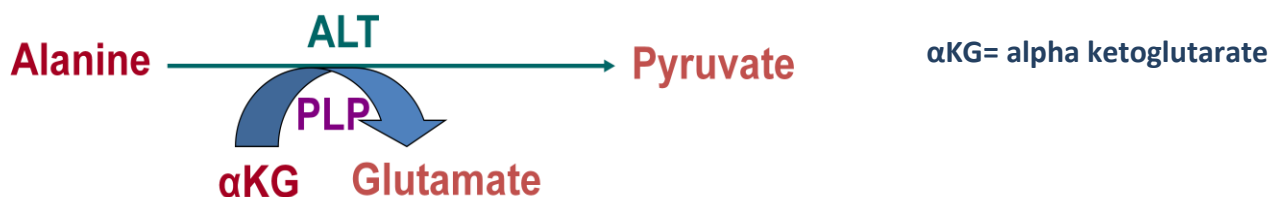
Formation of Serotonin



Formation of Histamine

The doctor said that the details of reactions are not required

• **Transamination Reaction**



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

❖ Dietary deficiency is rare, (widely present) but it was observed in:

- ❑ Newborn infants fed on formulas low in B6
- ❑ Women on oral contraceptives; because they will bind to vitamin B6 and get excreted. (Since vitamin B6 removes the hormone receptor complex from the DNA, terminating the action of the hormone).
- ❑ Alcoholics, due to low dietary intake and impaired vitamin metabolism.
- ❑ Isoniazid treatment for tuberculosis can lead to vitamin B6 deficiency by forming inactive derivative with PLP. (will bind to vitamin B6 and get excreted, so we give B6 supplementation)

❖ Deficiency leads to poor activity of PLP-dependent enzymes Causing:

- ❑ Deficient amino acid metabolism ( most important )
- ❑ Deficient lipid metabolism
- ❑ 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:

- Irritability
- Nervousness
- Depression

❑ Severe deficiency involves:

- Peripheral neuropathy
- Convulsions

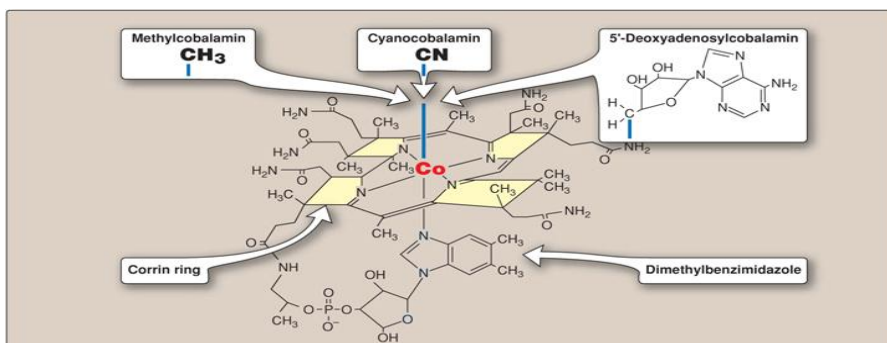
## • Forms of Vitamin B12

- Cyanocobalamin= Vit.B12( contains CN group)
- Hydroxycobalamin
- Adenosylcobalamin (major storage form in the liver)
- Methylcobalamin (mostly found in blood circulation)
- All of them contain cobalt Co

✓ Adenosylcobalamin and Methylcobalamin

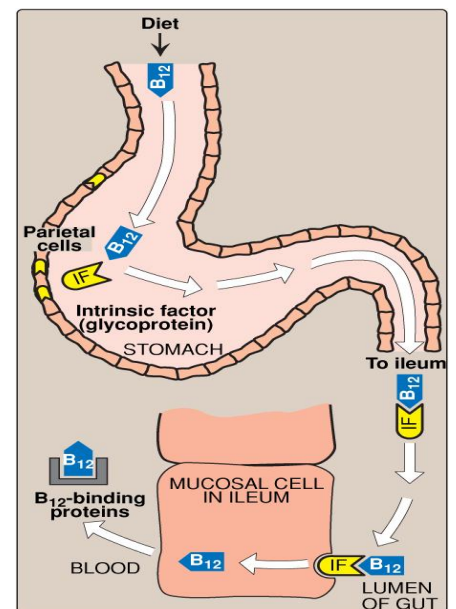
- Coenzymes for metabolic reactions

✓ Body can convert other cobalamins into active coenzymes



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The doctor said that these structures is not required



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(Synthesized only by the bacteria present as normal flora)

- **Vitamin B12 (Cobalamin)**

- Mainly found in animal liver bound to protein as
  - Methylcobalamin , or
  - 5'-deoxyadenosylcobalamin
- 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 (glycoprotein) and absorbed by the ileum
- Intrinsic factor is a protein secreted by (parietal) 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, because vitamin B12 is required in small amounts and there is some amount stored in the liver.

- **Functions of Vitamin B12**

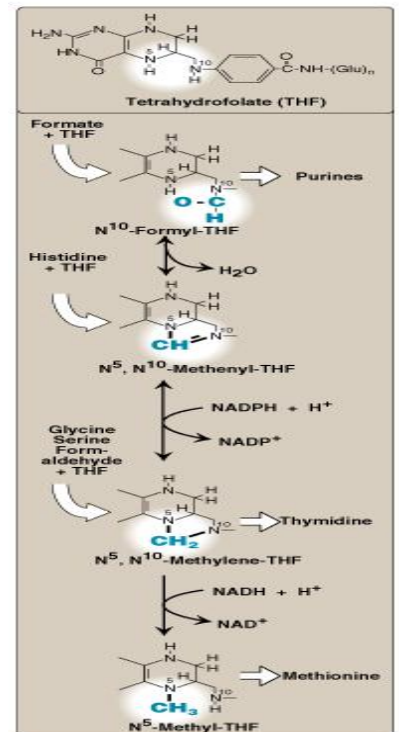
- Two reactions require B12 :-
  1. Conversion of propionyl-CoA to succinyl-CoA
    - The enzyme in this pathway, methyl-malonyl-CoA mutase
    - Succinyl-coA will join krebs cycle .
  2. Conversion of homocysteine to methionine (Methionine is an essential fatty acid)
    - Methionine synthase requires 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 = is the active form of folic acid.

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



Reduction to carbon

^ not required.

- ***Disorders of Vitamin B12 Deficiency***

- ❖ ***Deficiency occurs mainly due to loss of intrinsic factor .***

- **Pernicious anemia**
  - Megaloblastic anemia (large RBCs precursors)
  - Vitamin B12 deficiency is mainly due to the deficiency of intrinsic factor
- **Demyelination**
  - Myelin sheath of neurons is chemically unstable and damaged
- **Neuropathy**
  - Peripheral nerve damage
- **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

- ***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)
- **Psychiatric symptoms**
  - Confusion and memory loss
  - Depression
  - Unstable mood



### Questions:

**Q1. which one of the following statements concerning vitamin B12 is correct?**

- A. the cofactor form is vitamin B12 itself.
- B. it is involved in the transfer of amino groups.
- C. it requires a specific glycoprotein for its absorption.
- D. it is present in plant products.
- E. its deficiency is most often caused by a lack of vitamin in the diet.

**Q2. what is the active form of vitamin B6?**

- A. vitamin B6 itself.
- B. methylcobalamin.
- C. ascorbic acid.
- D. coenzyme A.
- E. pyridoxal phosphate.

**Q3. which one of the situations results in neuropathy?**

- A. Deficiency of methylmalonyl CoA.
- B. Using malonyl CoA for fatty acid synthesis.
- C. synthesis of abnormal fatty acids by methylmalonyl CoA
- D. Accumulation of Vitamin B12
- E. megaloblastic anemia

**Q4. what is decarboxylation required for?**

- A. For the degradation of the amino acids.
- B. For the formation of the neurotransmitters.
- C. The interconversion of amino acids.
- D. The process of glycogenolysis.
- E. In the Krebs cycle.

**Done by:**

**Saud Alawad and Osamah Al-Jarallah  
Reem AlMansour and Deema Jomar**

### **Answers:**

- 1- C / glycoprotein = intrinsic factor
- 2- E / pyridoxal phosphate = PLP
- 3- C
- 4- B