

L2

Neuropsychiatry
Block

Vitamins B6 & B12



Editing File

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- Extra notes

Objectives

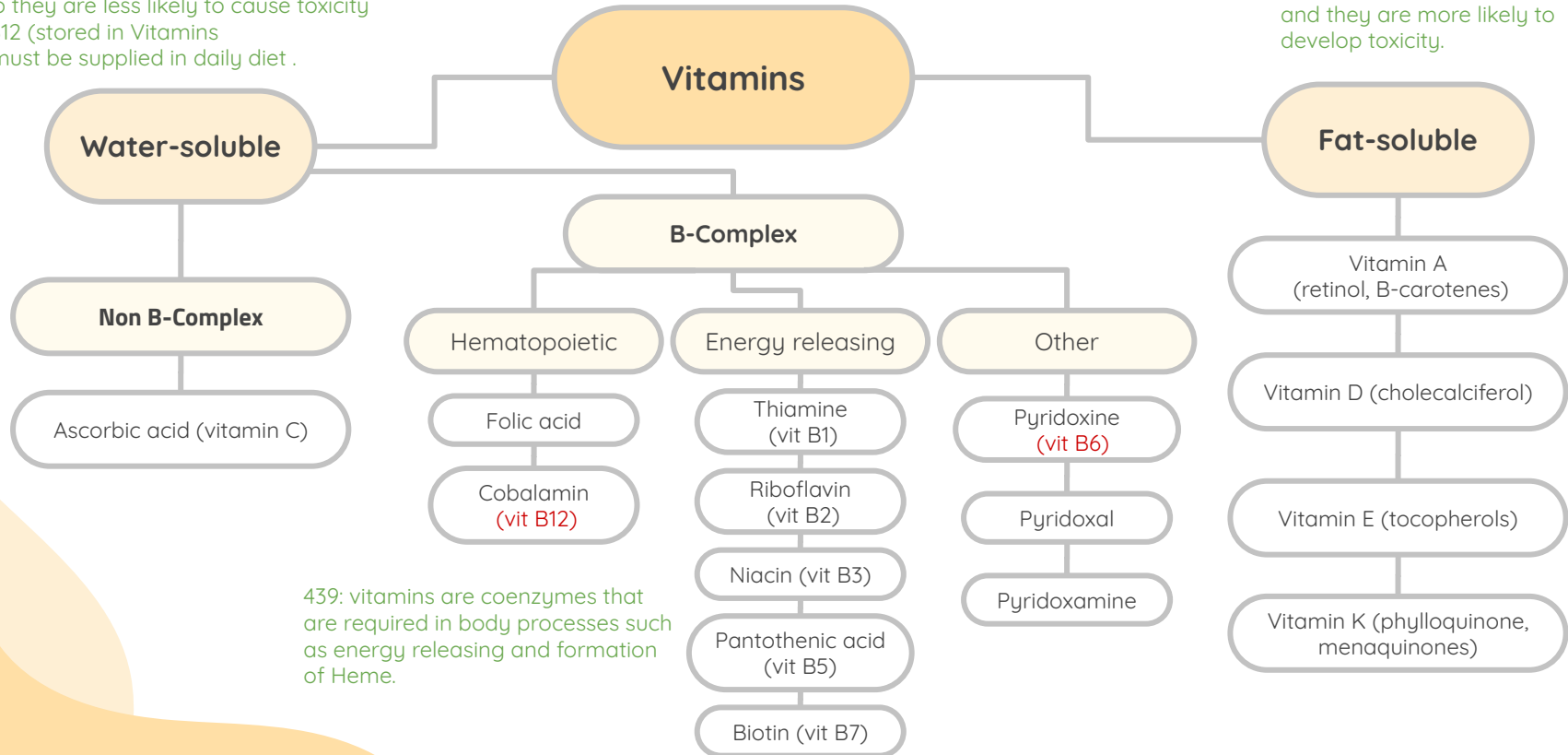


- 1 Understand the types and functions of vitamins B6 and B12.
- 2 Recognize the role of these vitamins in maintaining the myelin sheath of nerves and their function.
- 3 Discuss the consequences of vitamin B6 and B12 deficiency that can lead to nerve degeneration and irreversible neurological damage.

Classification of Vitamins

439: Water soluble vitamins aren't stored and absorbed so they are less likely to cause toxicity except for B12 (stored in Vitamins liver), they must be supplied in daily diet .

439: Fat soluble vitamins require fat to be transported and absorbed in the body , it cross the membrane so it's stored in the (liver and adipose tissue), and they are more likely to develop toxicity.



439: vitamins are coenzymes that are required in body processes such as energy releasing and formation of Heme.

Water Soluble Vitamins

B Vitamins

- Thiamine (B1)
- Riboflavin (B2)
- Niacin (B3)
- Pantothenic acid (B5)
- Pyridoxine (B6)
- Biotin (B7)
- Folate (B9)
- Cobalamin (B12)

1

Must be supplied by diet

439: Your body can't synthesize all of these vitamins so you have to obtain them from the diet.

2

Not significantly stored in the body (except B12)

3

Excess secreted

Vitamin B Complex

1

Help in various biochemical processes in cell

2

Present in small quantities in different types of food

3

Important for growth and good health

4

Function as coenzymes (non-protein compound necessary for the function of an enzyme)

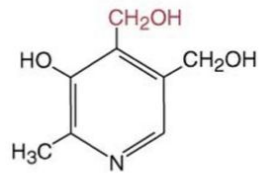


Video!

439: B6 could be obtained from plant sources like pyridoxine, or it could be obtained from animal sources like pyridoxal & pyridoxamine. Vitamin B6 comes from different sources so it has 3 forms differ in the group

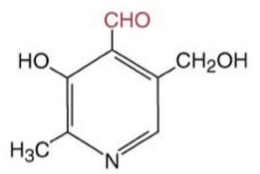
Three forms of Vitamin B6

Pyridoxine



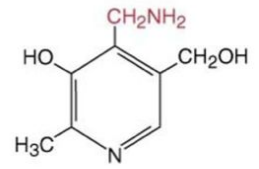
Pyridoxine

Pyridoxal



Pyridoxal

Pyridoxamine

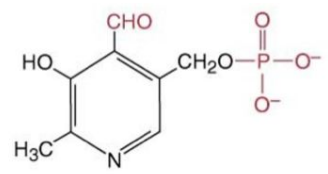


Pyridoxamine

All three forms converted to Active form

439: All forms of B6 has to be converted to pyridoxal first then phosphorylated to pyridoxal phosphate (the active form).

Pyridoxal phosphate (PLP)



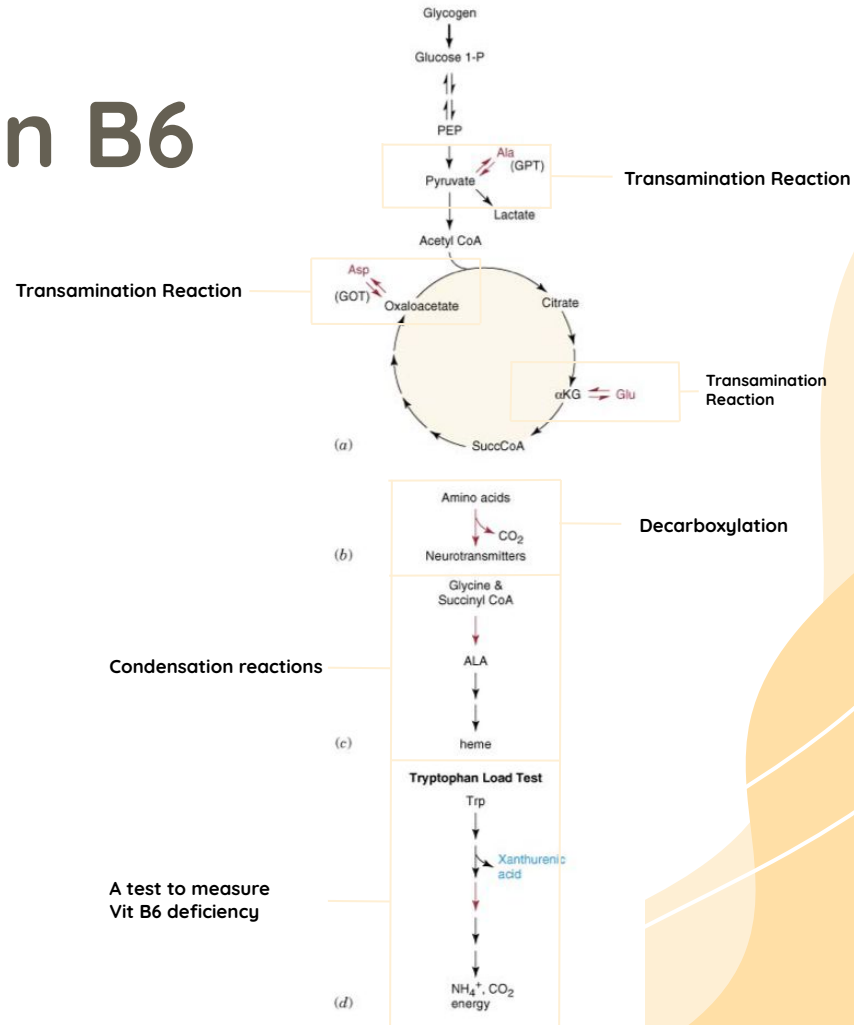
Pyridoxal phosphate

Functions of Vitamin B6

As a coenzyme for

1. Transamination
2. Deamination
3. Decarboxylation
4. Condensation reactions

439: From all the reactions you need to know three things: (substrate, final product, type of reaction).



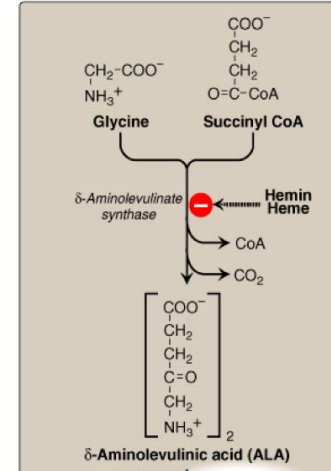
439: Delta aminolevulinic acid is the first step in the synthesis of heme.

1. Condensation Reactions

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

ALA = AminoLevulinic Acid

Condensation reaction: A reaction in which two or more molecules combine to form a larger molecule, with the simultaneous loss of a small molecule



2. Transamination Reaction



442: Alanine is converted to pyruvate with the help of ALT and Pyridoxal phosphate.

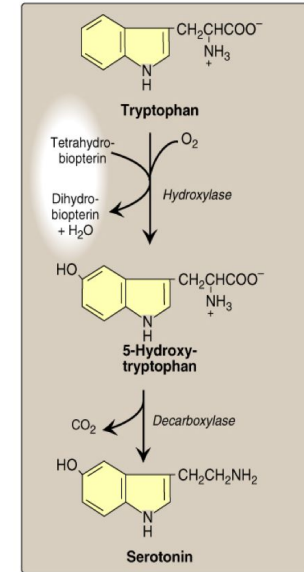
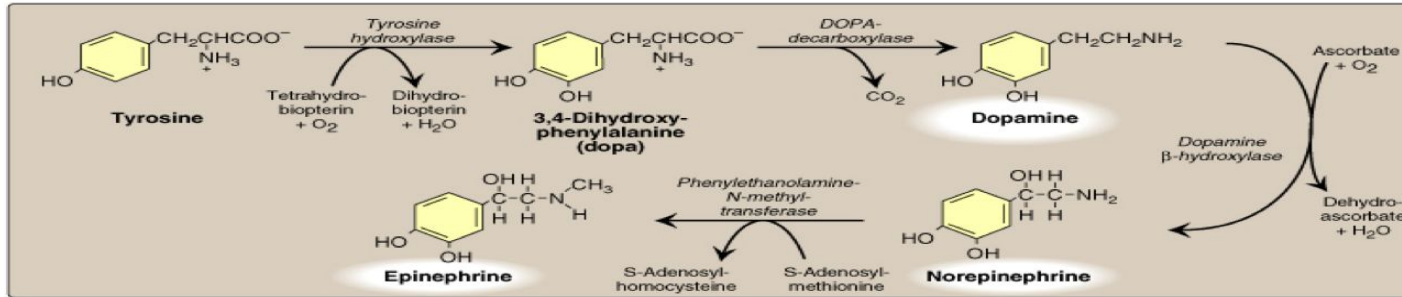
439: Alanine is converted to pyruvate with the help of ALT and Pyridoxal

- Alanine transfers its amino group to alpha ketoglutarate which then turns alpha ketoglutarate into glutamate, and alanine to pyruvate.
- Pyruvate then is converted to acetyl CoA and it enters TCA cycle (Krebs cycle).
- This reaction is catalyzed by ALT "alanine transaminase" which needs PLP.

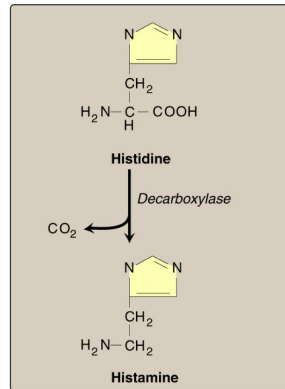
3. Decarboxylation Reactions

Formation of Catecholamines:
Dopamine, norepinephrine and epinephrine

439: Pyridoxal phosphate is a coenzyme for dopa decarboxylase which is essential for catecholamines synthesis.



Formation of **Histamine**



Formation of Serotonin

Disorders of Vitamin B6 Deficiency

439: Food is rich in B6 so deficiency is rare.

Dietary deficiency is rare but can be observed in:

- Newborn infants fed on formulas low on B6
- Alcoholics

(439: Newborn infants who drink formulas instead of breast milk might develop deficiency if the formula isn't rich in B6, or they don't have access to food.)

- Women on oral contraceptives

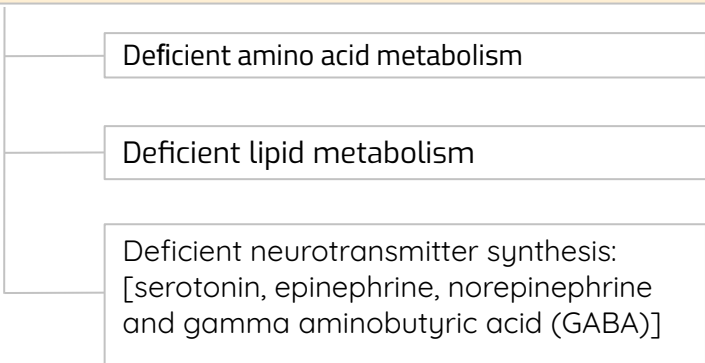
(Oral contraceptives (OCs) can increase excretion of B6 and poor absorption of the vitamin which leads to a deficiency in the vitamin among females using OCs)

Mild Deficiency	Severe Deficiency
Irritability	Peripheral neuropathy
Nervousness	Convulsions
Depression	

isoniazid treatment for tuberculosis can lead to vitamin B6 deficiency **by forming inactive derivative with PLP** (439: isoniazid can binds to pyridoxal phosphate and it becomes inactive.)
PLP = Pyridoxal phosphate

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

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



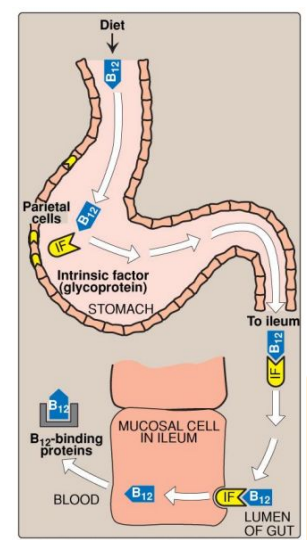


Video!

Vitamin B12 (cobalamin)

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

- Essential for:
 - Normal nervous system function
 - Red blood cell maturation
- Not synthesized in the body and must be supplied in the diet
- **Binds to intrinsic factor** (IF: is a protein secreted by cells in the stomach) and absorbed by the ileum people with IF deficiency we give them B12 injection

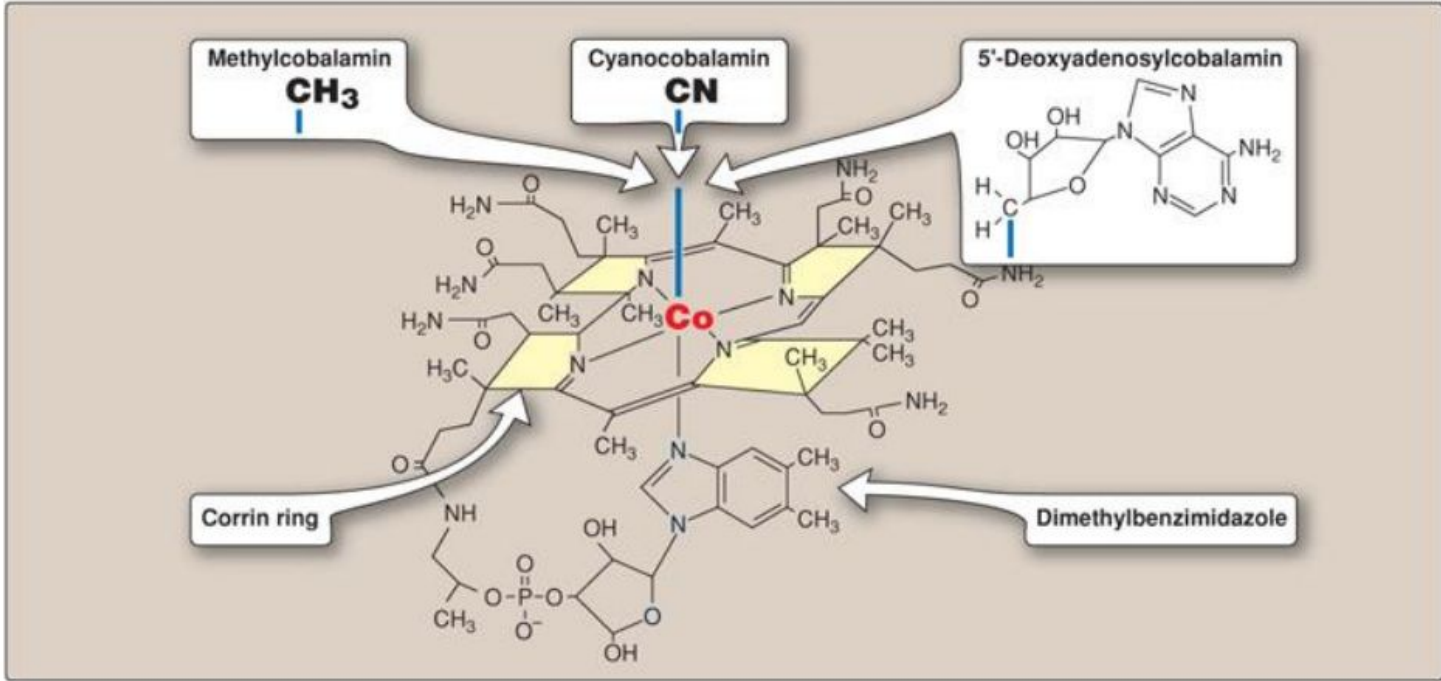


Forms of vitamin B12	Coenzyme forms of vitamin B12
Cyanocobalamin	Body can convert other cobalamins into active coenzymes
Hydroxocobalamin	
Adenosylcobalamin (major storage form in the liver)	Adenosylcobalamin and Methylcobalamin (coenzymes for metabolic reactions)
Methylcobalamin (mostly found in blood circulation)	



For more info!

Forms of Vitamin B12



[For more info!](#)

Vitamin B12 Storage

1 Liver stores vitamin B12 (4-5mg)

2 Other B vitamins are not stored in the body

3 Vitamin B12 Deficiency:

- Vitamin B12 deficiency is observed in patients with IF (intrinsic factor) deficiency due to:

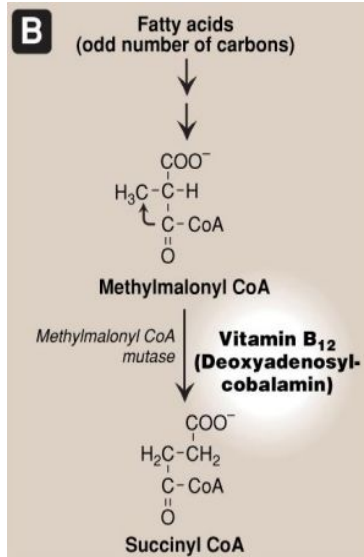
autoimmunity or by partial or **total gastrectomy**

- Clinical deficiency symptoms develop in several years

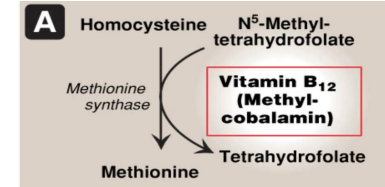
Functions of B12

Two reactions require B12

Conversion of **propionyl-CoA** to **methylmalonyl-CoA** to **succinyl-CoA**
The enzyme in this pathway, **methyl-malonyl CoA mutase**, requires B12



Conversion of homocysteine to methionine, Methionine synthase requires B12 in converting homocysteine to methionine



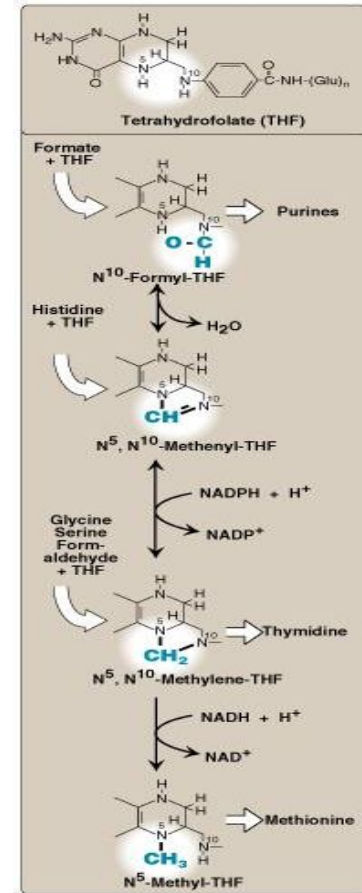
439: B12 involved in the degradation of fatty acids containing odd number of carbon to convert it into propionyl-CoA into methylmalonyl-CoA which's then converted into succinyl-CoA (the last step requires methylmalonyl-CoA mutase which requires B12), **without vit B12 there'll be methylmalonyl CoA accumulation and Succinyl CoA deficiency.**

B12 Deficiency and Folate Trap

Homocysteine re-methylation reaction is the only pathway where **N5methyl TH4** can be returned back to tetrahydrofolate pool

Hence folate is trapped as **N5-methyltetrahydrofolate (N5 -methyl TH4)** (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



Interconversion between TH4 carrier of “one carbon units”

Disorders of Vitamin B12 Deficiency

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graph TD; A[Disorders of Vitamin B12 Deficiency] --- B[Pernicious anemia]; A --- C[Demyelination]; A --- D[Neuropathy]
```

Pernicious anemia

- **Megaloblastic Anemia**

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

Remember foundation physiology?

Demyelination

-Myelin sheath of neurons is chemically unstable and damaged

B12 helps with maintaining myelin sheaths

Neuropathy

-Peripheral nerve damage

Disorders of Vitamin B12 Deficiency

Causes of neuropathy	Neurological symptoms	Psychiatric symptoms
<ul style="list-style-type: none">• Deficiency of vitamin B12 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 (due to methylmalonyl CoA)	<ul style="list-style-type: none">• Paraesthesia (abnormal sensation) of hands and feet (tangling of hands and feet)• Reduced perception of vibration and position• Absence of reflexes• Unsteady gait and balance (ataxia)	<ul style="list-style-type: none">• Confusion and memory loss• Depression• Unstable mood

Take Home Messages



Vitamins B6 and B12 are essential in maintaining the nerve function and the central nervous system



Various neurological symptoms have been associated with their deficiency



Summary!



Q1: Which of the following is a fat-soluble vitamin?

- | | | | | | | | |
|----------|----------|----------|------------|----------|-----------------|----------|------------|
| A | Thiamine | B | Folic Acid | C | Cholecalciferol | D | Pyridoxine |
|----------|----------|----------|------------|----------|-----------------|----------|------------|

Q2: Formation of ALA by ALA synthase is the regulatory step in the synthesis of what?

- | | | | | | | | |
|----------|------------|----------|----------|----------|------|----------|---------------------|
| A | Hemoglobin | B | Pyruvate | C | GABA | D | Pyridoxal Phosphate |
|----------|------------|----------|----------|----------|------|----------|---------------------|

Q3: Which Vitamin B has 3 forms which all convert to the active form (Pyridoxal Phosphate)?

- | | | | | | | | |
|----------|---------|----------|--------|----------|--------|----------|--------|
| A | Vit B12 | B | Vit B3 | C | Vit B6 | D | Vit B7 |
|----------|---------|----------|--------|----------|--------|----------|--------|

Q4: The folate is trapped in form of?

- | | | | | | | | |
|----------|----------------|----------|----------------|----------|----------------------|----------|----------------|
| A | N10-formly TH4 | B | N5- Methyl TH4 | C | N5-N10-methylene TH4 | D | N5- formly TH4 |
|----------|----------------|----------|----------------|----------|----------------------|----------|----------------|

Q5: What's the enzyme is required for conversion of propionyl-CoA to succinyl-CoA?

- | | | | | | | | |
|----------|----------------------|----------|---------------------------|----------|---------|----------|--------------|
| A | Mythioninis synthase | B | methyl-malonyl CoA mutase | C | Amylase | D | None of them |
|----------|----------------------|----------|---------------------------|----------|---------|----------|--------------|



Q6: List the reactions that Vitamin B6 is a coenzyme for?

Answer:

- 1- Transamination
- 2- Demethylation
- 3- Decarboxylation
- 4- Condensation reactions

Q7: Vitamin B6 dietary deficiency can occur in?

Answer:

- Newborn infants fed on formulas low in B6
- Women on oral contraceptives
- Alcoholics

Q8: List 3 disorders of Vitamin B12 deficiency?

Answer:

- Neuropathy
- Pernicious anemia
- Demyelination

