VITAMINS

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Overview of Vitamins

- Define vitamins, classify them according to their solubility.
- Describe the role of water soluble vitamins in metabolism.
- Disuss sources and manifestation of water soluble vitamin deficiency.

Definition: Vitamins are organic compounds that characterized by:

1. They are essential for normal health and growth where they are not synthesized in human body. So, they must be supplied in the diet.

2- Their deficiency in the body leading to various diseases.

3. They do not enter in the structure of the tissues or oxidized by them.

4. They are needed in very small amounts.

N.B.:

Provitamins: These are precursors of vitamins that converted into vitamins inside the body e.g. Carotenes are provitamin A.

Vitamers: These are different forms of one vitamin e.g. Vitamin D has 2 vitamers; D2, & D3.

Classification:

Vitamins can be classified according to their solubility into two main categories:

A. Fat soluble vitamins: they include A, D, E and K vitamins.

Characters:

1. They are soluble in fat solvents.

2. They need bile salts for absorption.

3. They can be stored in the body.

B. Water soluble vitamins: they include vitamin C and B complex group (12 vitamins).

Characters:

1. They are soluble in water

2. Most of them are not stored in the body.

Water SOLUBLE VITAMINS

Vitamin C

Vitamin B complex

1. Vitamin C = L-Ascorbic Acid (Antiscorbutic vitamin)

Sources:

1- Fruits especially citrus fruits (lemon, orange), melon and strawberry. Guava is very rich in vitamin C.

2- Vegetables especially green leafy vegetables as lettuce, tomatoes, potatoes, raw cabbage and green peppers.

3- Liver and adrenals are animal sources of vitamin C are useless due to destruction of vitamin C by cooking.

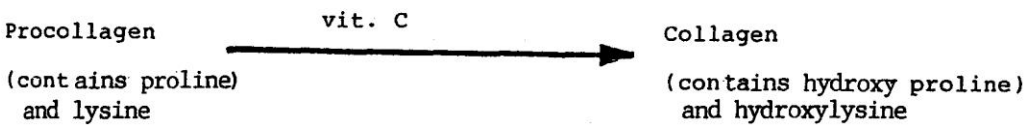
Functions

A- Formation of collagen protein

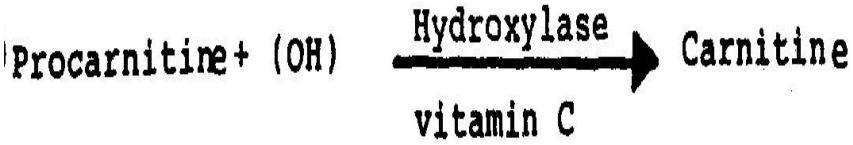
Ascorbic acid is essential for the conversion of the procollagen (immature collagen) into collagen. Procollagen is a protein containing proline and lysine. Hydroxylation of both amino acids is helped by Vit. C .

B- A potent reducing agent

1- Ascorbic acid is capable of giving electrons to ferric ions, cupric ions and metal ions bound to various cytochrome and oxygen:



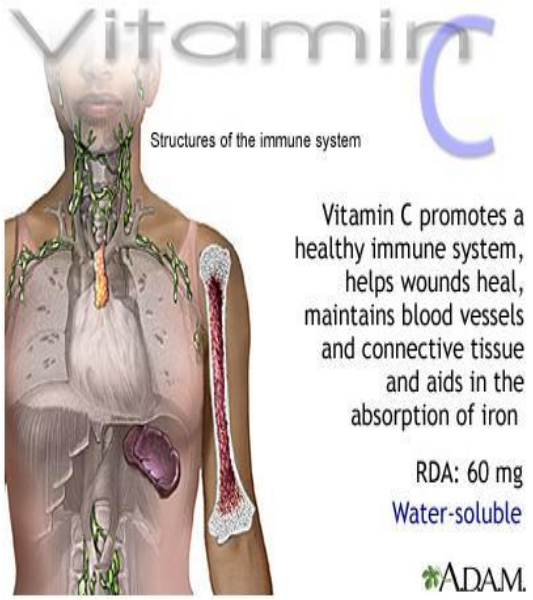
2- Ascorbic acid acts as a specific reducing agent for a number of hydroxylase enzymes:



3- Vitamin C may have a role in oxidation-reduction reactions acting as a hydrogen transport agent

C- Anti-Cancer: In large doses, vitamin C may inhibit the formation of carcinogenic N-nitrosocompound during cooking and digestion and lowered the risk for gastric and esophogeal cancers.

D- Defense Mechanism: The use of vitamin C in large doses relieve the symptoms of the common cold and increases the resistance of the body, as vit. C is required for normal leukocyte function and for the synthesis and release of histamine during stress situations.



Deficiency (scurvy)

Vitamin C store is sufficient for 3 months. If this store is depleted a disease called scurvy will result. It is characterized by :

I- Manifestations due to decrease neurotuanomitters:

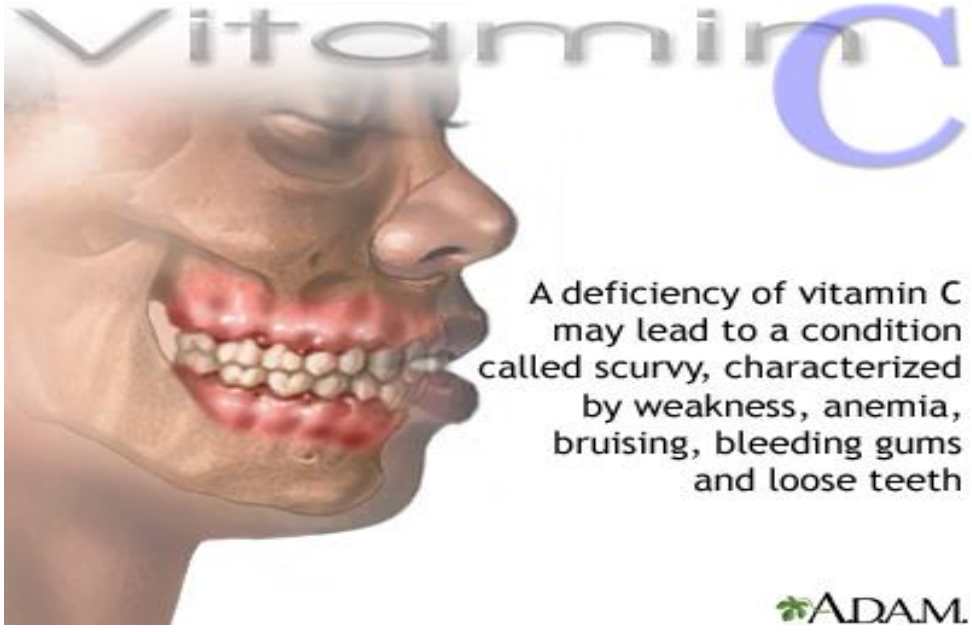
1- Behavioral changes 2- Severe emotional disturbances

II- Manifestations due to decrease carnitine and fatty acids oxidation:

General weakness

III- Manifestations due to decrease collagen formation :

1- Bleeding into gum, muscles, joints, kidneys, gastrointestinal tract and pericardium.
2- Bone lesions.
3- Necrosis of gums and loss of teeth .
4- Delayed wound healing
5- Easy bruising and haemorrhages under the skin due to increased capillary fragility.



B. Vitamin B Complex

Definition: These are groups of vitamin B complex that put together in one group of different chemical molecules. They include the following members:

1- Thiamin (vit. B1).
2- Riboflavin (Vitamin B2).
3- Niacin (P.P.F.).
4- Pyridoxine (Vitamin B6.)
5- Pantothenic acid.
6- Biotin (Vitamin H.).
7- Vitamin B12
8- Folic acid.
9- Choline .
10- Inositol
11- Lipoic acid
12- P-amino benzoic acid (PABA)

1- Thiamin = Vitamin B1

(Aneurine or Antiberiberi)

Structure

Thiamin is a sulphur containing vitamin and it consists of a substituted pyrimidine ring binds to a substituted thiazole ring through a methylene bridge (CH2(

Sources

Plants: Seeds as peas, beans, whole cereal grains, bran and yeast .

Animals: Liver, eggs and milk

The alcoholic, OH group on thiazole ring forms ester with phosphoric acid to give thiamin pyrophosphate (TPP, the active form of Vitamin B1). This reaction is catalyzed by an enzyme called thiamin pyrophosphokinas that present in the liver, erythrocytes and cells of cerebral cortex and requires ATP as phosphate donor.

1 -TPP is essential coenzyme for decarboxylation reactions of alpha -keto acids which includes:

a) Simple decarboxylation: These reactions that needs TPP only as a coenzyme. Conversion of pyruvate to acetyldehide.

b) Oxidative decarboxylation: These reactions that needs TPP and other coenzymes, FAD, NAD, COA-SH and lipoic acid. Conversion of pyruvate to acetyl COA.

2 -TPP is also required for transketolation reaction (i.e. transfer of ketol group) of HMP shunt in RBCs. The transketolase is the enzyme most commonly used for measuring thiamin status in the body.

3- TPP is necessary for optimal growth of infants and children.

4-TPP increases the activity of acetyl choline at nerve endings by inhibiting acetyl choline esterase enzyme. So, is also essential for the process of nerve conduction and structure of nerve membrane

Deficiency: Causes a disease called Beriberi.

Biochemical Changes

1-Accumulation of pyruvic acid in blood due to decreased activity of oxidative decarboxylation, and increase of lactic acid in blood.

2-Appearance of methyl glyoxal in urine due to decreased activity of glyoxalse enzyme that catalyze the conversion of methyl glyoxal to lactic acid in the liver.

3- Accumulation of pentose sugars in RBCs as a result of decreased transketolase reaction.

Manifestations:

There are two forms of beriberi.

a- Wet Beriberi: Affects mainly the cardiovascular system and it is characterized by:

1- Extensive edema.

2- Congestive heart failure.

b- Dry beriberi: Affects mainly the nervous system and it is associated with:

1- Polyneuritis: inflammation of pripheral nerves.
2- Hyperesthesia.
3- Muscle wasting and loss of weight.

Extreme thiamin deficiency may lead to neuronal degeneration and development of :

a-Wernicke's disease (Ver'ne–Keh): It is characterized by :

Occular disturbance.

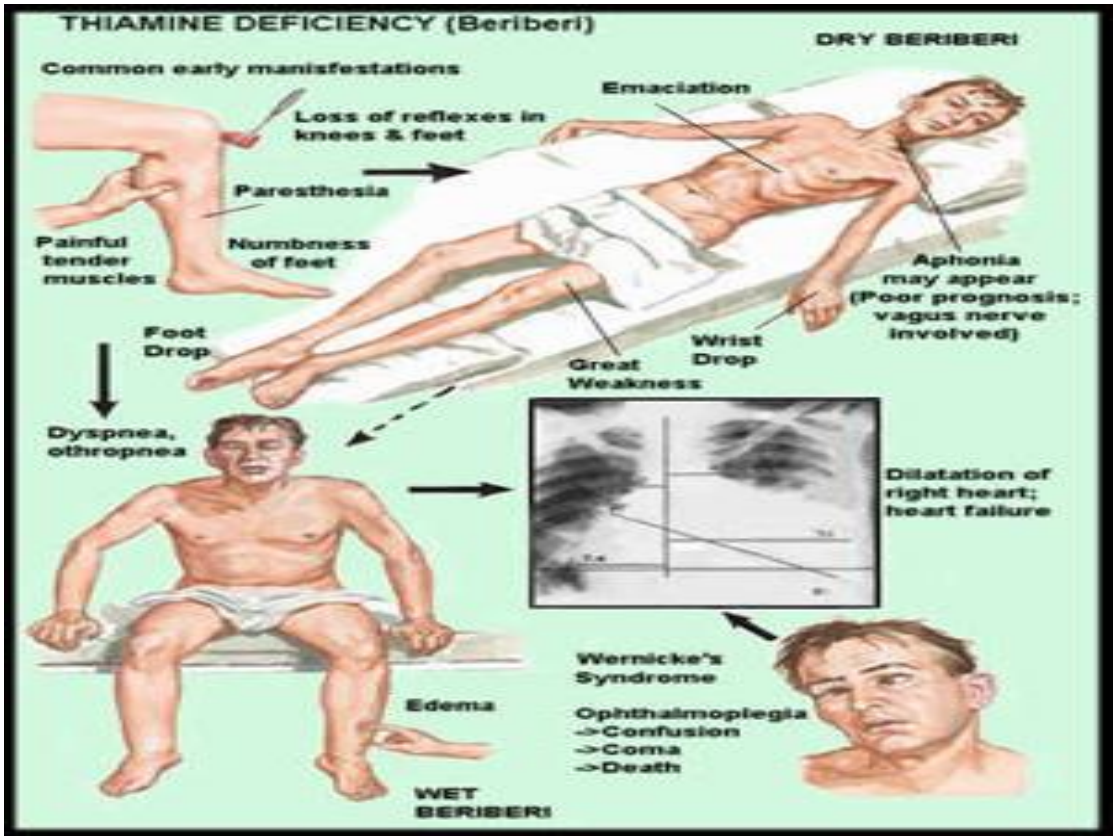
Ataxia = loss of muscular coordination .

b- Korsakoff's syndrome

It is characterized by :

1- Defective memory.

2- Impaired learning ability.

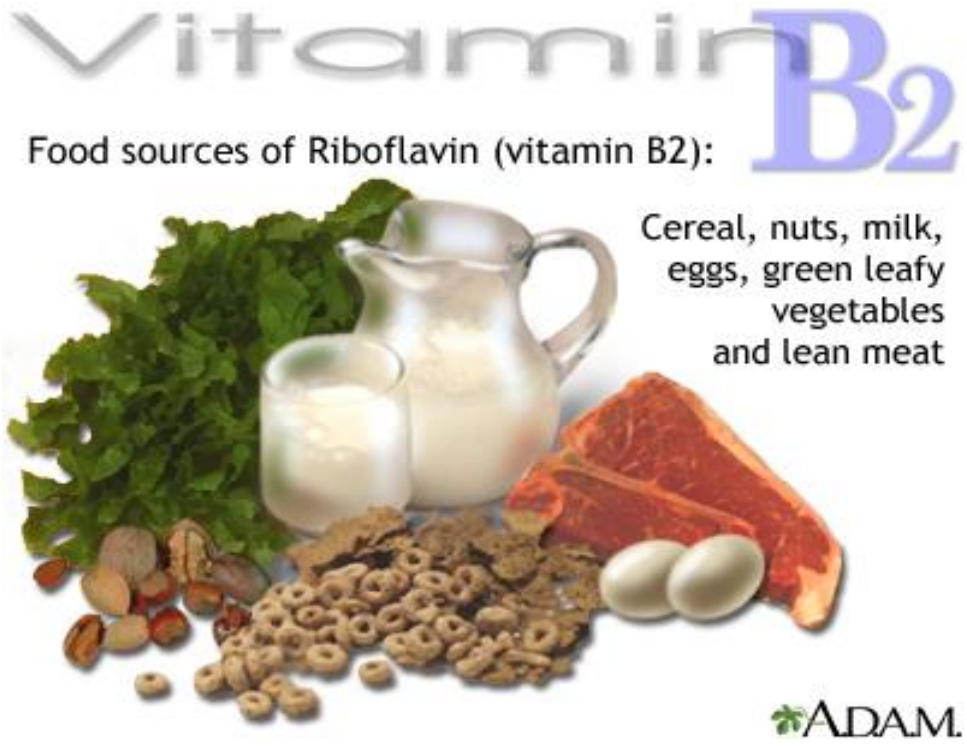


2- Riboflavin = Vitamin B2

Sources: It is abundant in liver, yeast, whole grain and milk.

Activation:

-Both flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) are active forms of vitamin B2 .



Functions:

FMN and FAD are coenzymes act as hydrogen carriers for certain enzymes called flavoproteins that are wide spread and involved in the oxidation-reduction reactions in:

1- Carbohydrate metabolism.

2- Lipid metabolism.

3- Sterol biosynthesis.

4- Intermediary metabolism of amino acids, purine and pyrimidine.

Deficiency

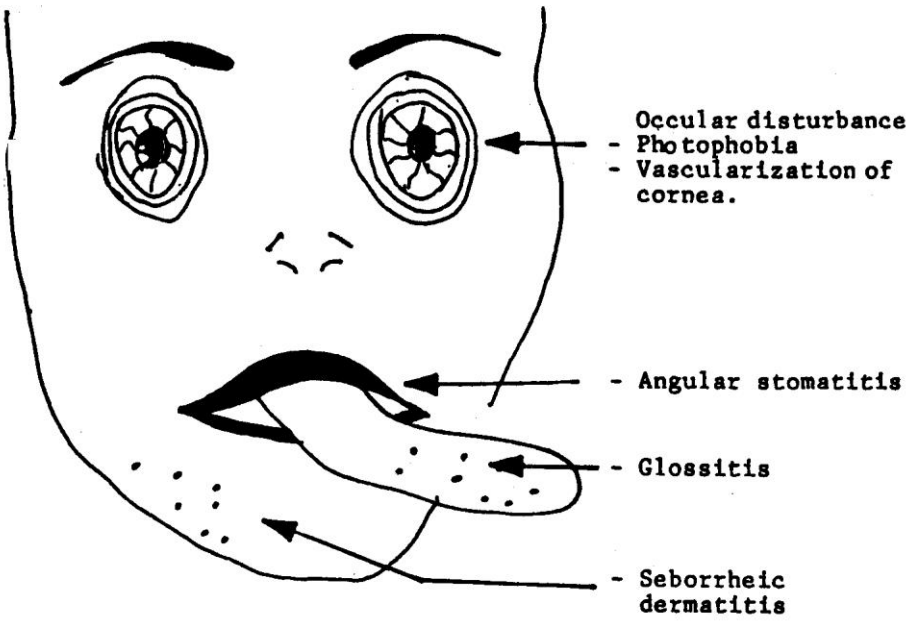
1- Eyes: Occular disturbances including:

a- Photophobia b-Vascularization of cornea.

2- Mouth: Red lips and shiny-Angular stomatitis (inflammation of angles of mouth). Glossitis (inflammation of tongue.(

3-Skin: Seborrheic dermatitis i.e. inflammation of sebaceous glands of skin.

4- Synthesis of proteins is impaired in severe riboflavin deficiency



3. Niacin

(Nicotinic acid or Pellagra Preventing Factor, PPF)

Sources:

1- Whole grain cereals, yeast, milk, leafy green vegetables and meat.

2- Niacin can be made endogenously from the amino acid tryptophan. Each 60 mg tryptophan can be converted to 1 mg niacin. This conversion requires vitamin B6, pyridoxine as a coenzyme.

N.B.: - Meat is rich in tryptophan.

-Corn is poor in both niacin and tryptophan .

Food sources of Niacin (vitamin B3) include dairy, poultry, fish, lean meat, nuts and eggs

A.D.A.M.

Functions:

Niacin is essential for the formation of the coenzymes NAD+ (Also called Coenzyme I), NADP+ (Also called Coenzyme II) and NMN (Also called Coenzyme III.(

a) NAD+ and NADP+ Coenzymes act as hydrogen carrier and they are essential for many biochemical oxidation-reduction reactionThese reactions are important in carbohydrate, protein and lipid metabolism.

Reduction of NAD+ or NADP+ yields NADH + H+ or NADPH+ H+.

Deficiency:

It leads to a disease called: Pellagra .

Causes of Pellagra:

Pellagra is usually associated with deficiency of niacin, tryptophan or pyridoxine.

Manifestations of Pellagra:

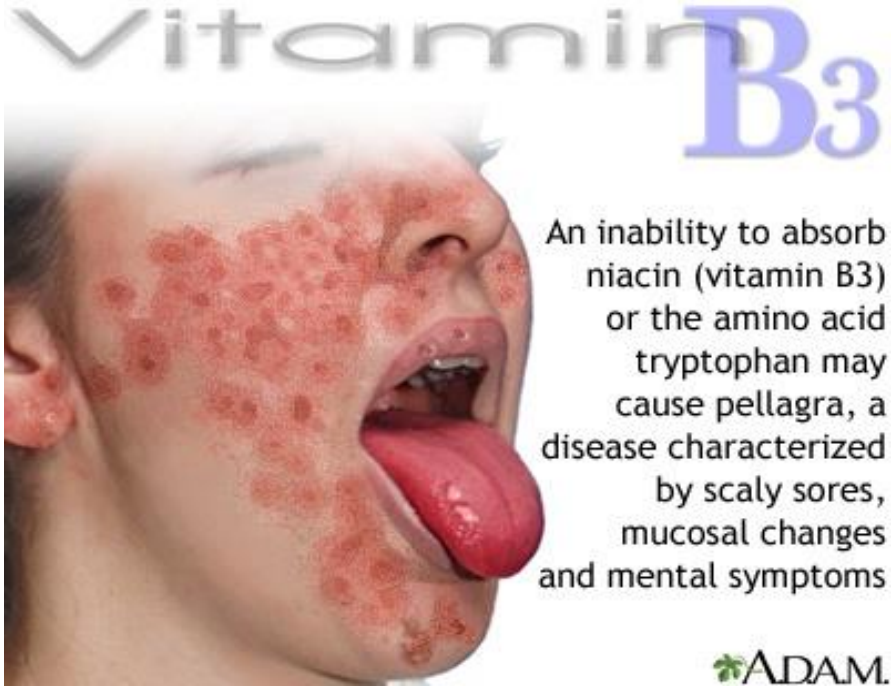
is called a disease of (4 Ds) including :

Dermatitis: The exposed skin becomes dry, rough and scaly with brown discoloration, glossitis and stomatitis are seen.

Diarrhea.

Dementia.

Death (if not treated)/



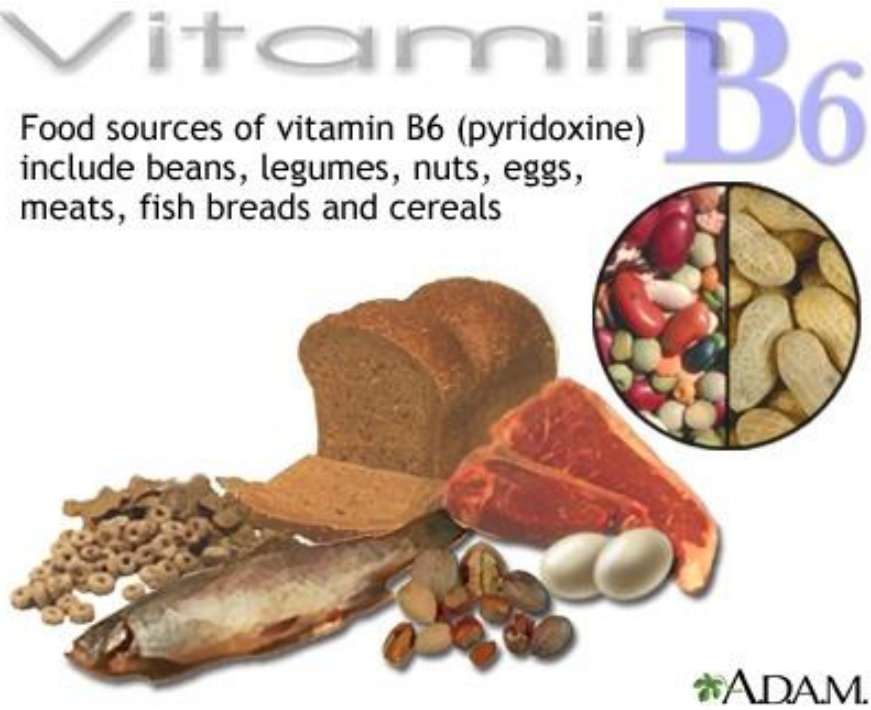
4. Pyridoxine “Vitamin B6”

Structure:

Vitamin B6 consists of 3 closely related pyridine derivatives: Pyridoxine, pyridoxal and pyridoxamine and their corresponding phosphates. All three have equal vitamin activity.

Sources:

1. Plants: Yeast, rice polishing, germinal portionof various seeds.
2. Animals: Egg Yolk.
3. Royal Jelly of bees (very rich in vitamin B6)



Physiological Function:

In the body, Pyridoxal can be phosphorylated by pyridoxal kinase enzyme to pyridoxal phosphate that acts as a coenzyme. This coenzyme (PLP) has the following functions :

A- It has a role in amino acid absorption from the intestine.

B- It acts as coenzyme for amino acid metabolism in the following reactions:

1- Transamination :

Examples of transaminases which use PLP as coenzyme are GOT and GPT

Decarboxylation

a) Synthesis of GABA, which act as an inhibitory transmitter in brain.

b) Decarboxylation of DOPA (produced from tyrosine) to dopamine, which act as neurotransmitter.

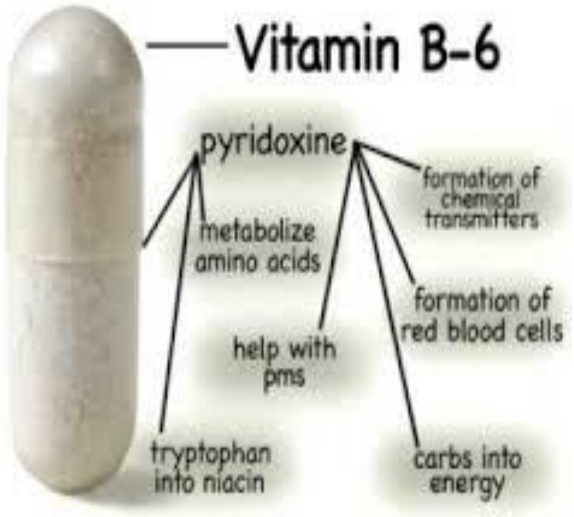
c) Synthesis of delta-aminolevulinic acid, which act as precursor of heme.

3 Non oxidative deamination: It is the removal of NH2 group of hydroxy amino acids in the form of ammonia (NH3)

4- PLP helps the formation of niacin from tryptophan

5- Pyridoxal phosphate activate glycogen phosphorylase (catalyses the breakdown of glycogen.

6- Pyridoxal phosphate is also required for the synthesis of sphingosine of the sphingolipids necessary for myelin formation.



Deficiency:

1- Pellagra may result, because pyridoxal phosphate is needed for the conversion of tryptophan to niacin.
2- Disturbance in amino acids metabolism. This leads to growth retardation and may be mental retardation.
3- Convulsions in young infants due to deficinet formation of GABA.
4- Microcytic, hypochromic anaemia due to deficient formation of haem and haemoglobin.
5- Demyelination of the peripheral nerves and axons.
6- Nausea and vomiting of early pregnancy as a result of depletion of vitamin B6 from its excessive use in amino acid metabolism to synthesize the new proteins of the embryo.

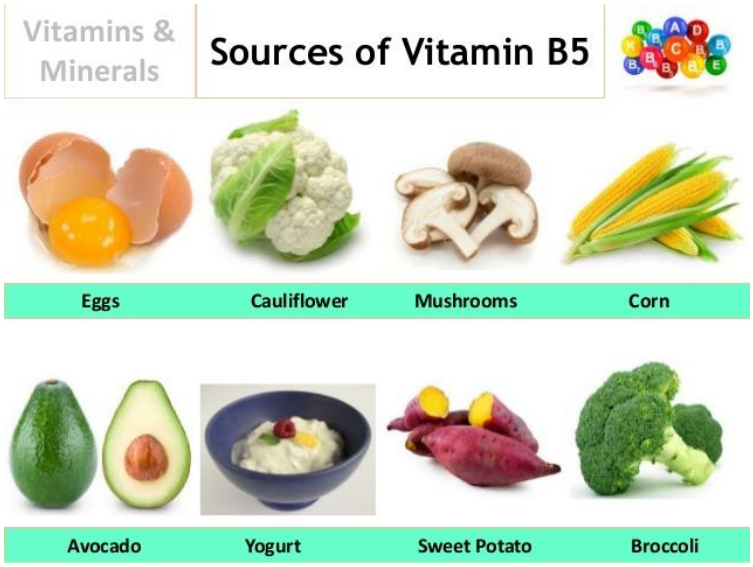
N.B. Patients with tuberculous taking high doses isoniazid drug inactivates the vitamin.

5. Pantothenic Acid

Sources:

Animal: Meat, liver, kidney. but the richest known source of pantothenic acid is the royal jelly of bees.

Plant: Legumes , wheat and rice.



Function

A) Coenzyme A (COASH) acts as acid carrier e.g. acetic acid, succinic acid, fatty acids and other carboxylic acids.

E.X. Acetic Acid to form Acetyl COA

B) Acyl carrier protein (ACP):

acts as acyl carrier during the reactions of extra-mitochondrial pathway for fatty acid synthesis.

6- Biotin

(Vitamin H or Coenzyme R)

Structure: Biotin is sulpher containing vitamin

Sources :

-The intestinal bacteria synthesize most of the human requirements of biotin

-Egg yolk, animal tissues, tomatoes and yeast are excellent sources of biotin.

Activation:

Biotin is attached to a lysine residue of carboxylase enzyme by the help of holocarboxylase synthetase enzyme forming biocytin which is active and acts as coenzyme.

Physiological Functions:

* Biotin functions as coenzyme of the carboxylase enzyme that catalyz carboxylation reactions.
* ***Important carboxylation reactions include:***
- functions as coenzyme of the carboxylase enzyme that catalyz carboxylation reactions.

1-Fixation of pyruvate to form oxaloacetate

2- Carboxylation of propinyl COA to give succinyl COA.

Deficiency:

* Deficiency of biotin does not occur in man because the intestinal bacteria supply all the human needs but, biotin deficiency may result from:

1) Ingestion of large amounts of avidin which is a protein present in raw egg white.

2) Deficiency of holocarboxylase synthetase enzyme in children. The enzyme is responsible for the attachement of biotin to carboxylase enzyme

The manifestations of biotin deficiency include:

1- Dermatitis of the extremities, muscle pain and loss of muscular control.

2- Pallor of the skin and Alopecia (loss of hair)

3- Hallucination and depression.

4- Immune deficiency disease (in some cases).

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5- Growth retardation.

7. Vitamin B12 = Cyanocobalamin

(Anti-pernicious anemia or extrinsic factor)

Structure:

- Vitamin B12 or cobalamin consists of:

a- A corin ring formed of 4 pyrrol rings all the them are linked together through a methylene bridge except rings I and IV which are directly linked together (similar to the porphyrins). These corin ring includes a cobalt ion at its center. The cobalt is red in colour. This is the cause of the red colour of vitamin B12.

b- A cyano group (CN) attached to cobalt ion.

c- A nucleotide side chain.

N.B.: The cyano group may be replaced by:

- Hydroxy group (OH) → hydroxy cobalamin
- Methyl group (CH3) ⟶ methylcobalamin
- 5 deoxyadenosine ⟶ adenosyl—cobalamin.
- The cyanocobalamine is the most stable form.

Sources

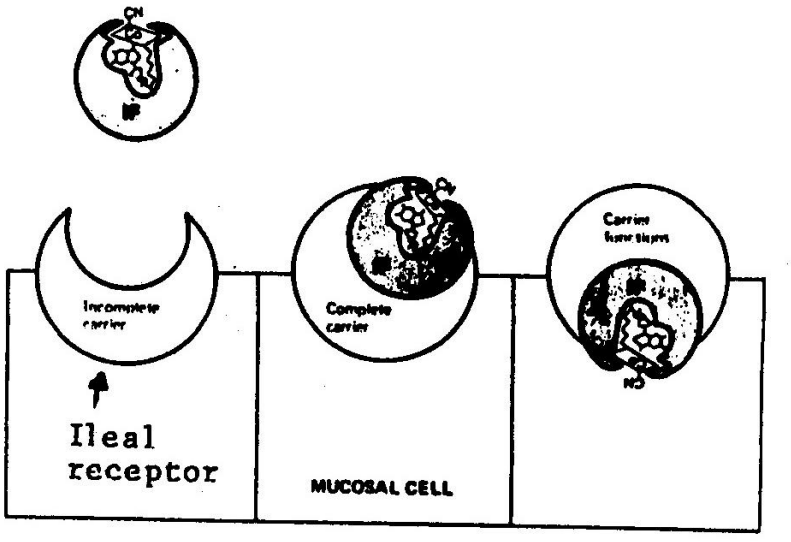
1- Meat, egg, milk and milk products.

2- Vitamin B12 is not present in vegetables.

3- Intestinal microorganisms synthesize B12 in human colon, but it is not absorbed through the mucosa in this region of the gastrointestinal tract.

Absorption and Transport in Blood:

For the absorption of vitamin B12 it combines with a glycoprotein secreted by the gastric parietal cell called intrinsic factor (IF). This IF–B12 complex binds with specific receptor in the ileum.



Physiological Functions

Cobalamin acts as a coenzyme for:

a- Methylation of homocysteine to methionine

b- Isomerization of L-methyl malonyl COA to succinyl COA.

Deficiency:

Causes:

1. Decrease vitamin B12 intake. This may occur among vegetarians. i.e. people who eat vegetables only.
2. Atrophy of gastric mucosa ⟶ lack of intrinsic factor. This gives rise to a condition known as pernicious anaemia (PA). PA is mostly common in those over 60 years of age.
3. Autoantibodies against gastric parietal cells.
4. Antibodies against intrinsic factors.
5. Defective absorption as in sprue or regional enteritis.
6. Drugs induced vitamin B12 deficiency

Manifestations of deficiency:

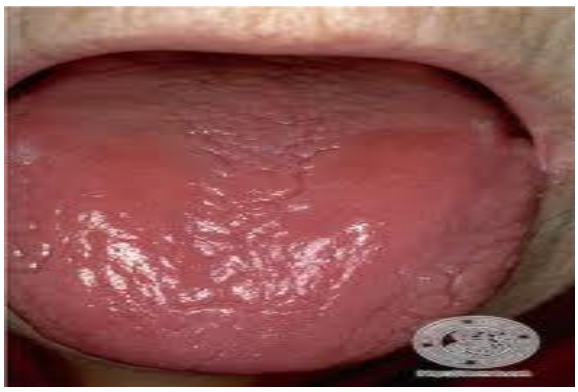
1- Megaloblastic anaemia

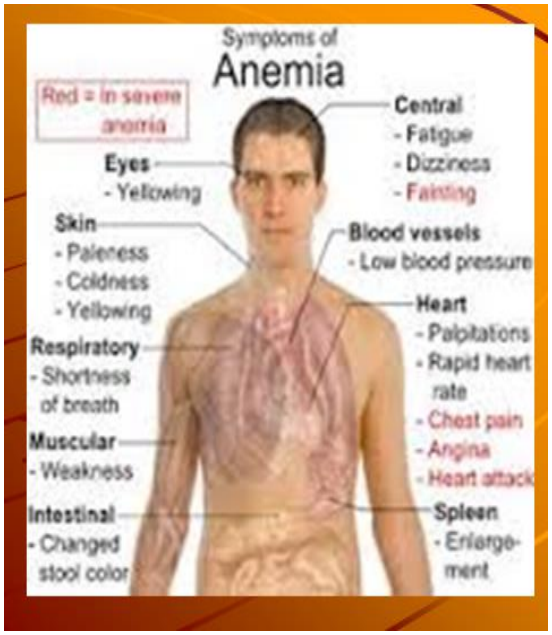
- It is a macrocytic hyperchromic anaemia.
- It is due to abnormal replication of DNA in hematopoietic tissue.

2- Neurological manifestations

- a- Subacute combined degeneration of the spinal cord of lateral (motor) and posterior (sensory) columns.

- b- Peripheral neuritis leads to numbness tingling and weakness of extrimities.
- ***Laboratory Findings:***
- Increased the excretion of methylmalonyl COA in urine.





8. Folic acid (Folacin = Peteroyl

Glutamic Acid)*:*

Folic acid, or folate, consists of the base pteridine attached to one molecule each of **P-aminobenzoic acid (PABA) and glutamic acid.**

Sources:

1-The major source is leafy vegatables.

2-Liver, kidney and yeast are also rich in folate.

Physiological Functions:

Tetrahydrofolic acid (H4 folate) act as a carrier for one–

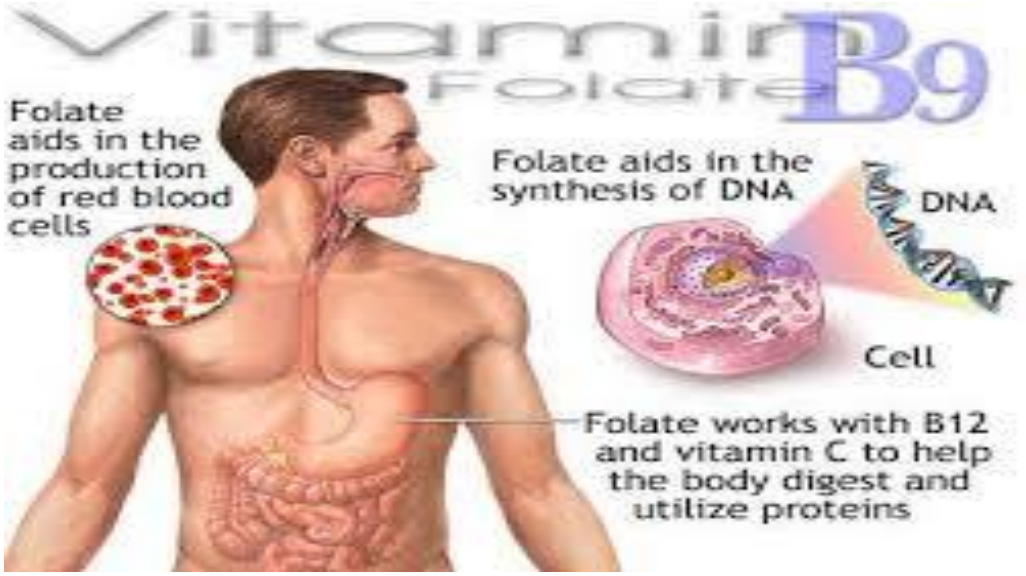
carbon groups.

Fate of one carbon groups:

1-formation of thymine. Thymine is important for DNA synthesis.

2-formation of methionin.

3-formation of purines



Deficiency:

1- Pancytopenia: i.e. all blood cells are affected

a) Megaloblastic anaemia (Marocytic, hyperchromic).

It is difficult to differentiate between megaloblastic anaemia resulting from folate deficiency and vitamin B deficiency. But a daily dose of 300–500 ug of folate will improve the blood picture in the first condition.

b) Leucopenia: ↓ W.B.Cs.

c) Thrombocytopnea: ↓ Platelets.

2- Impaired growth.

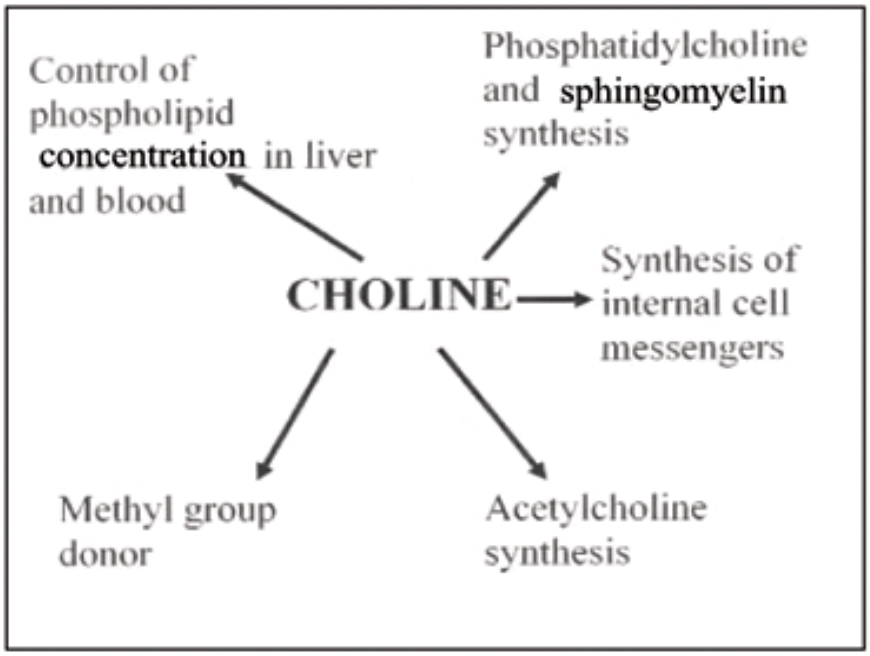
9. Choline

Function:

1. It enters in the formation of lecithin and sphingomyelin.
2. It has a lipotropic action. i.e. it prevents fatty liver.
3. It enters in the formation of acetyloholine.

Choline is sometimes not regarded as a vitamin because:

- It is needed in a relatively big amount.
- It can be formed in the body from serine.
- It enters in the structure of tissues.



10- Inositol

It has 12 isomers, myoinositol is the most biologically

important one.

Function

1-It enters in structure of certain phospholipids. It is a lipotropic factor that prevents

fatty liver disease.

2-Inositol can combines with 6 molecules of phosphoric to form phytic acid.

11- Lipoic Acid

Structure: It is sulpher-containing vitamin

***Function*:**

It acts as coenzyme in conversion of decarboxylation of α –keto acid e.g. pyruvic acid.

12. Para Amino Benzoic Acid "PABA"

Function:

- It enters in the structure of folic acid.

- It is a growth factor of certain pathogenic bacteria and is antagonized by the antibiotic sulphonamide which has a structural similarty with it.