Vitamins

Classification

- Vitamins are classified into two major groups:
  - **Fat-soluble** (4 fat soluble) Vitamin A, D, E, K.
  - **Water-soluble** (9 water soluble)

    B_1 (thiamine)

    B_2 (riboflavin)

    B_3 or Vitamin P or Vitamin PP (niacin)

    B_5 (panthotenic acid)

    B_6 (pyridoxine and pyridoxamine)

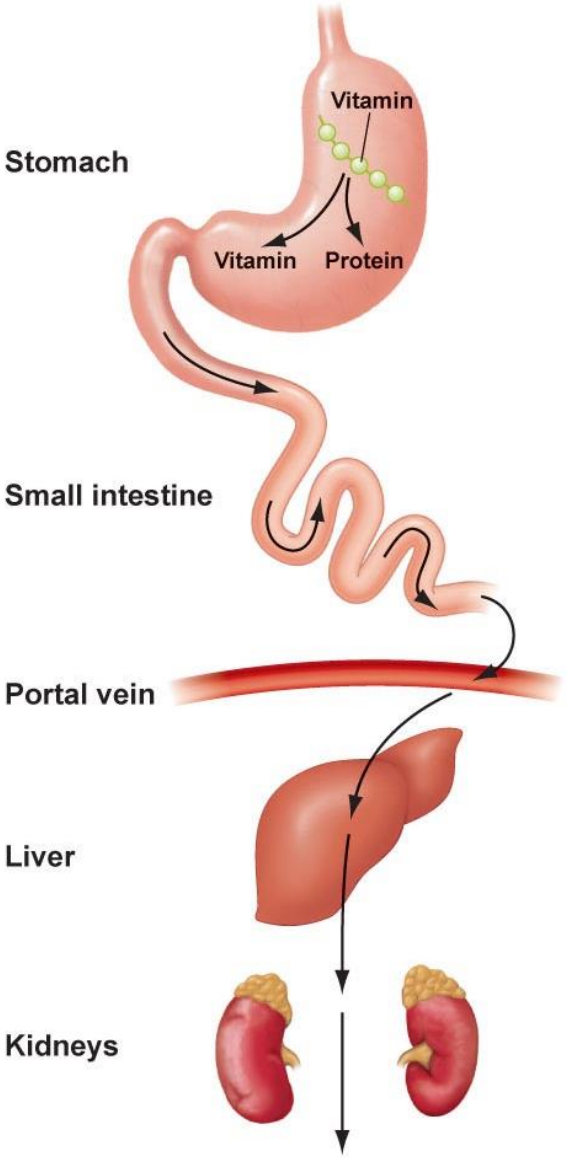
    B_7 or Vitamin H (biotin)

    B_9 or Vitamin M (folic acid)

    B_{12} (cobalamin)

    Vitamin C

Digesting and absorbing water-soluble vitamins



a Vitamins are hydrolyzed in the stomach from the protein complexes found in food.

b Most of the water-soluble vitamins are absorbed in the upper small intestine with the exception of vitamin B_{12}, which is absorbed in the ileum.

c The water-soluble vitamins are absorbed directly into the portal vein and transported to the liver, where they are either stored (B_{12}) or sent out into circulation.

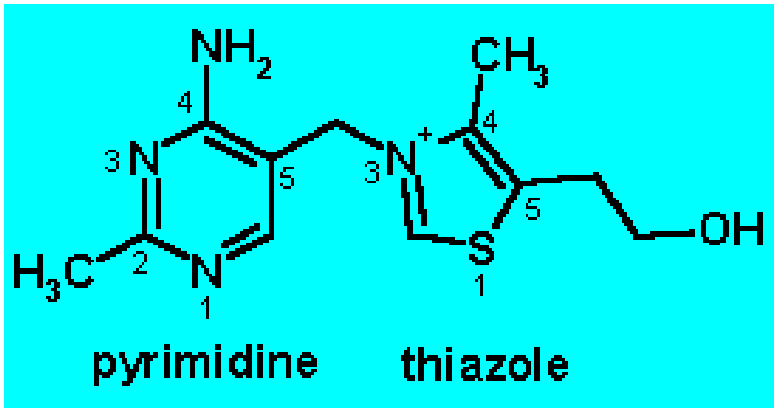
d Excess water-soluble vitamins are excreted through the kidneys in the urine.

Thiamin (B 1)

Chemistry:

- A substituted **pyrimidine** joined by a methylene bridge to a substituted **thiazole.**

Requirements: 1-1.5 mg/day for adults**.**
(Higher needs in pregnancy, high CHO diet)



Sources:

- **Plant sources:** whole grains (unrefined cereal grains), beans, peas, nuts and bran.
- **Animal sources:** liver, heart, kidney and milk.
- **Yeast**

Activation (Co-enzyme):

- Conversion of thiamin to its active form **thiamin pyrophosphate (TPP)**

Absorption

- Thiamine is released by the action of pyrophosphatase
- At low concentrations, the process is **carrier-mediated.**
- At higher concentrations, absorption also occurs via **passive diffusion.**
- It can be inhibited by **alcohol consumption**.
- On serosal side of the intestine, its transport is **Na^+-dependent ATPase**.
- The majority of thiamine in **serum** is bound to proteins, mainly **albumin**.
- Approximately 90% of total thiamine in blood is in **RBCs.**

Cellular uptake

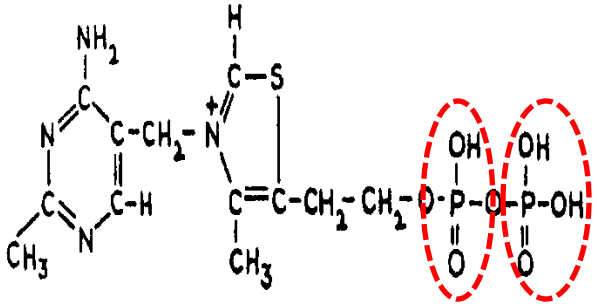
- Thiamine uptake and secretion appears to be mediated by a soluble thiamine transporter that is **dependent on Na^+ [Thiamin transporter-1 & 2 (**human THTR-1 & 2)].

Storage: of thiamine occurs in muscle, heart, brain, liver, and kidneys.

Excretion: Thiamine and its metabolites are excreted in **urine.**

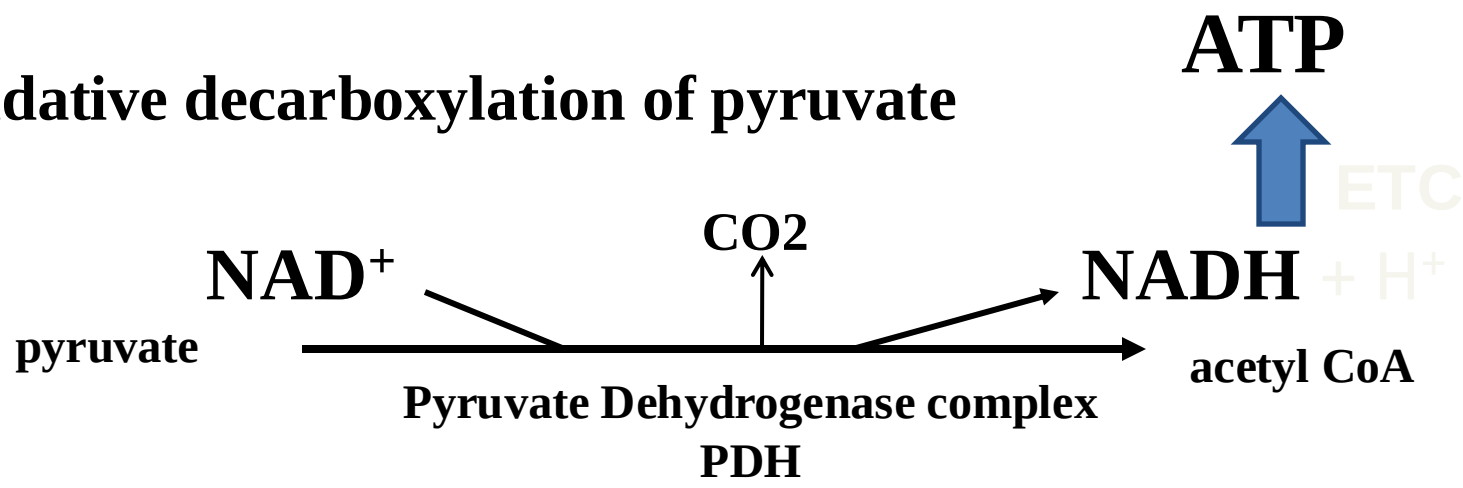
Thiamin: activation

Thiamin → (ATP-dependent thiamin diphosphotransferase; Brain, liver) → **TPP**



Thiamine + ATP → TPP + AMP (EC 2.7.6.2).

Oxidative decarboxylation of pyruvate



Vitamins (thiamin, lipoic, riboflavin, Niacin, pantothenic acid)

Co enzymes (TPP, Lipoamide, FAD, NAD+, CoASH)

Functions

- TPP serves as a coenzyme transferring an **activated aldehyde unit** in the following enzymatic reactions:

1. **Oxidative decarboxylation** of α-keto acids.
2. **Transketolase reaction** (pentose phosphate pathway; PPP). It is used for the biosynthesis of pentose sugars deoxyribose and ribose.
3. **Acetylcholine synthesis** which is one of neurotransmitters and for myelin synthesis.

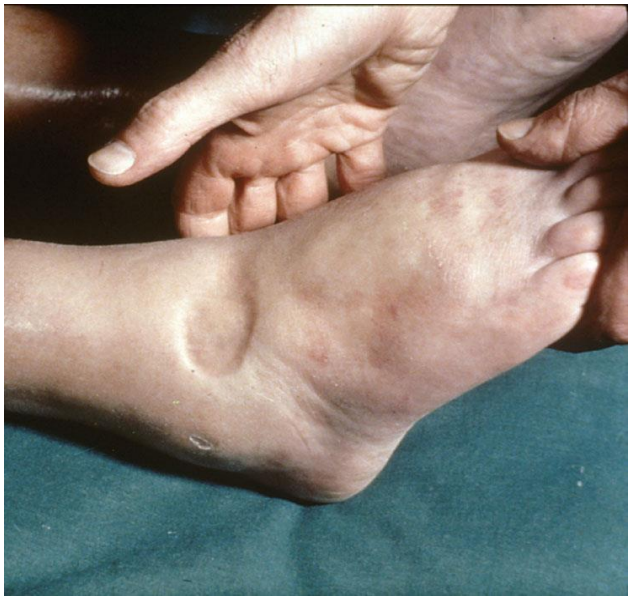
- **Important in:**
  - Producing **energy from carbohydrates**
  - **Nerve function**
  - **Muscle function**
  - **Appetite**
  - **Growth**
- **Therapy:** It can be used for treatment of Heart failure & Alzheimer disease.

Deficiency

Causes:

- **Low intake, malabsorption , and/ or defective phosphorylation** to TPP.
- **Antithiamine factors :** These are enzymes present in the viscera of shell fish and many microorganisms . They cause cleavage of thiamin producing pyrimidine and thiazole rings so they are called **thiaminases.** These antithiamine factors cause an isolated thiamine deficiency. **Plant** thiamine antagonists are heat-stable; for examples **caffeic acid**, and **tannic acid**. These compounds interact with the thiamine to oxidize the thiazole ring, thus rendering it unable to be absorbed.
- **Alcoholism :** Chronic alcoholism gives the manifestation of moderate thiamine deficiency. This is called **Wernike korsacoff ، syndrome.** Alcohol interferes with absorption
- **Excessive loss** (diuretics).

Manifestations of thiamine deficiency



1. **Mild deficiency:** leads to
   - Gastrointestinal complaints
   - Weakness.

2. Moderate deficiency:

Wernike korsacoff , syndrome

- Peripheral neuropathy.
- Mental abnormalities.

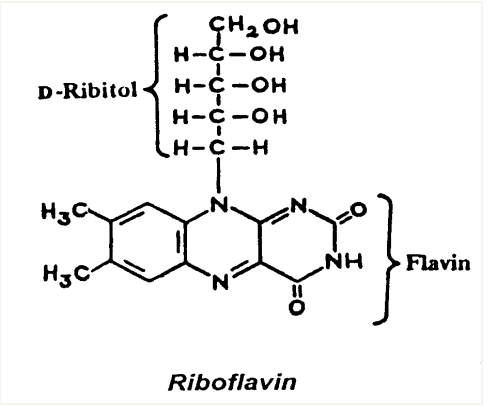
3. Severe thiamin deficiency

A. Beriberi

- **Dry beriberi** is characterized by advanced neuromuscular symptoms:
  - Atrophy and weakness of the muscles
  - Peripheral neuropathy
  - Memory loss.
- **Wet beriberi:** the previous symptoms (dry beriberi) are coupled with oedema.

B. Wernike korsacoff , syndrome

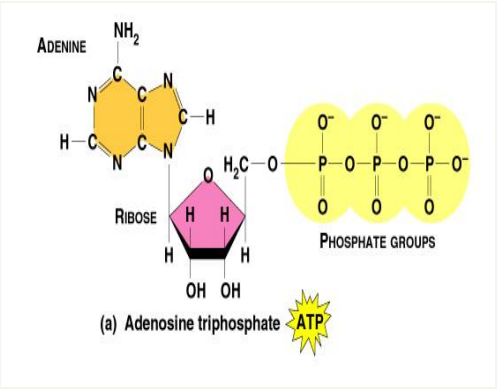
Riboflavin (B 2)

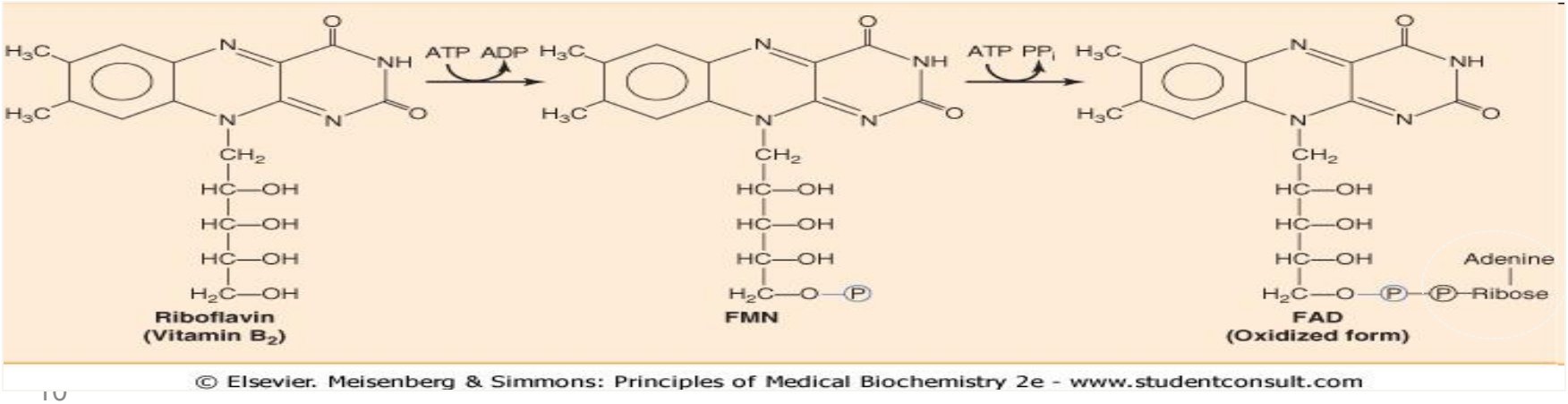


Chemistry: It consists of a **flavin ring** attached to the sugar alcohol **D- ribitol.**

Co enzyme forms

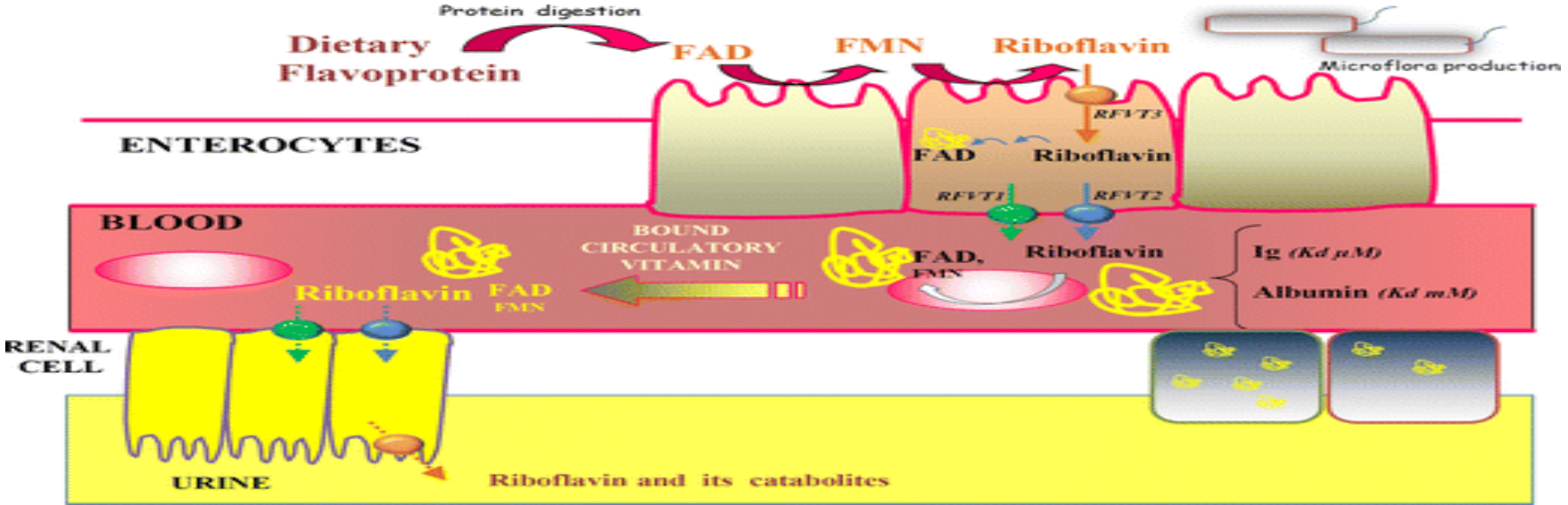
- Flavin mononucleotide (**FMN**) is formed by ATP-dependent phosphorylation of riboflavin.
- Flavin adenine dinucleotide (**FAD**) is synthesized by a further reaction with ATP in which the AMP moiety of ATP is transferred to FMN. Biosynthesis of FMN and FAD occurs in most tissues.





Absorption

- In diet, riboflavin (RF) exists in the free and FMN and FAD forms. They are **hydrolyzed to free Rf** by intestinal phosphatases.
- RF absorption in the **intestines** involve a **specific carrier-mediated mechanism for Rf uptake** located at the apical membrane & across the BLM.
- Both **RFT-1** (RF transporter1) and **RFT-2** are expressed in **intestine.**
- **RFT-3** is more **brain-** specific.
- Riboflavin in **blood** associates with **albumin or globulins.**



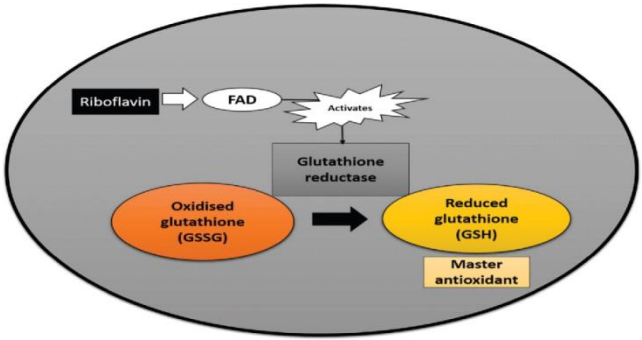
Sources

- **Animal origin:** liver and beef, milk, dairy products, fish, eggs, nuts
- **Yeast**
- **Plant origin:** Green leafy vegetables, nuts, of smaller quantities in cereals.

Function:

- **Involved in energy metabolism (ATP production):** Participate in
  - Oxidative decarboxylation
  - Citric acid cycle
  - Beta-oxidation of fatty acids
  - Electron transport
- **Associated with antioxidant glutathione reductase** (utilizes an **FAD** prosthetic group and **NADPH** to reduce GSSG to two GSH.)

$GS–SG + NADPH + H^+ \rightarrow 2\ GSH + NADP^+$



1. Chemical **structure** of vitamin B2 is ……..

[flavin + ribitol], fluorescent, light sensitive, heat stable.

2. Active form **(Co-enzyme)** of vitamin B2 is ……..

[FMN & FAD]

3. Its **function** is to act as ……

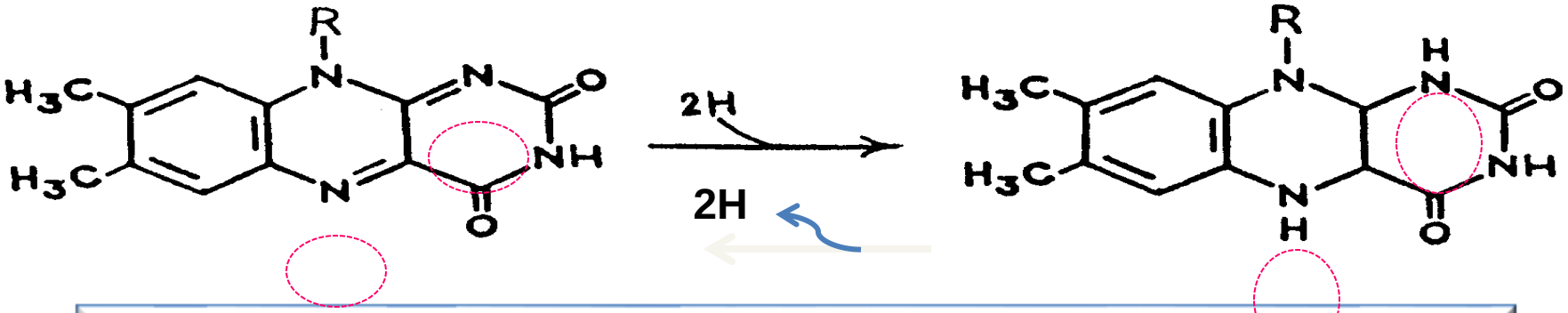
[prosthetic groups of oxidoreductases]

4. **Reactions** requiring **FAD** are:

a- **[oxidative decarboxylation of a keto acids as PDH → Energy (ATP)**

b- **[C.A.C.] → Energy (ATP)**

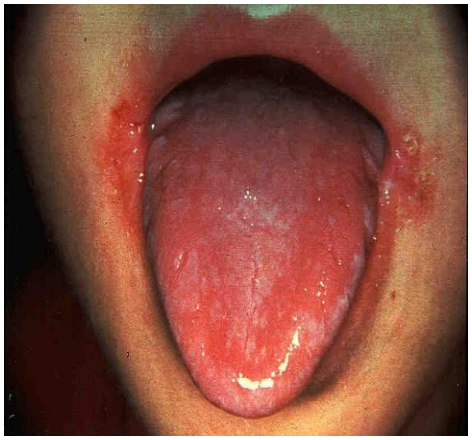
c- **[β -oxidation of F.A.] → Energy (ATP)**



FMN **FMNH2**

FAD **FADH2**

symptoms of deficiency



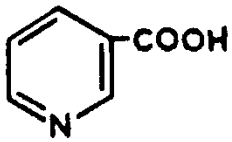
Related to Energy production (skin & mucous membrane inflammation).

- **Glossitis & angular stomatitis (**Inflammation of the lining of mouth and tongue).
- Keratitis , dermatitis (Dry and scaling skin).
- **Cheilosis** (cracked and red lips).
- **Ocular manifestations (vascularization of cornea)**

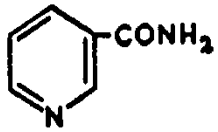
N.B. :

- Deficiency occurs in **newborn infants with hyperbilirubinemia** who are treated by phototherapy.

Niacin (B 3)



Niacin (nicotinic acid)



Niacinamid (nicotinamide)

Chemistry:

- Nicotinic acid is a carboxylic acid derivative of pyridine.

Synthesis: **PLP (vit. B6)**

- **Tryptophan** →→ → →→→→ **Niacin (vit. B3)** (insufficient)
- most people require dietary sources of both tryptophan and niacin.

Sources:

- Food stuffs containing nicotinic acid: as B_1
- Tryptophan containing proteins

Functions: niacin required for the synthesis of NAD^+ (nicotinamide adenine dinucleotide) and $NADP^+$ (nicotinamide adenine di-nucleotide phosphate)

- NAD^+ and $NADP^+$ are coenzymes of many oxidoreductase enzymes.
- Generally, NAD^+-linked dehydrogenases catalyze oxidoreduction reactions in **oxidative pathways**, e.g. the citric acid cycle.
- Whereas $NADP^+$-linked dehydrogenases are often found in pathways concerned with **reductive synthesis** e.g. the pentose phosphate pathway.
- $NAD^+ + AH_2 \longrightarrow NADH + H^+ + A$

- **Reactions** requiring **NAD+** are:

a- [oxidative decarboxylation of a keto acids as PDH]⟶ Energy (ATP)

b- [C.A.C.] ⟶ Energy (ATP)

c- [β oxidation of F.A.] ⟶ Energy (ATP)

- **Reactions** requiring co-enzyme **NADP+** as:

- Glucose-6-phosphate dehydrogenase (NADP+)
- Folate reductase (NADPH+H+)

intestinal niacin absorption process: intracellular **protein-tyrosine-kinase-mediated pathway** regulates vitamin uptake.

Deficiency

Causes of deficiency:

- in elderly on very restricted diet.
- malabsorption.
- in maize-dependant population.
- in vit. B6 def.
- Hartnup disease (decreased tryptophan absorption)
- Malignant carcinoid syndrome (increased tryptophan metabolism to serotonin)
- INH (anti-TB) (decreased B6)

Clinical use: Treatment of hyperlipidemia

- Deficiencies found in southeast if subsisting on diet of corn ; niacin is bound by protein. Pelagra is very rare now
- **Deficiency:**
- **Milder deficiencies of niacin** cause:

➢ Poor appetite, fatigue.

➢ Dermatitis, Diarrhea.

- **Severe deficiencies** lead to **pellagra** which is characterized by "the four D_S": dermatitis, diarrhea, dementia (lack of concentration) and death.
- Dermatitis is usually seen in skin areas exposed to sun light and is symmetric.
- The neurologic symptoms start by nervous disorders and mental disturbances.

Pantothenic acid (B 5)

Absorption

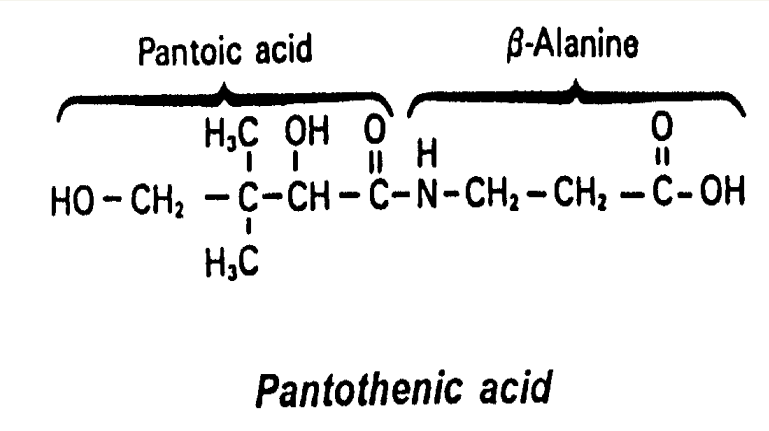
- For the intestinal cells to absorb pantothenic vitamin, it must be converted into free pantothenic acid.
- Free **Pantothenic acid** and **Biotin** are absorbed into intestinal cells via a saturable, sodium-dependent active transport system. **[Sodium-dependent multivitamin transporter (SMVT)]**

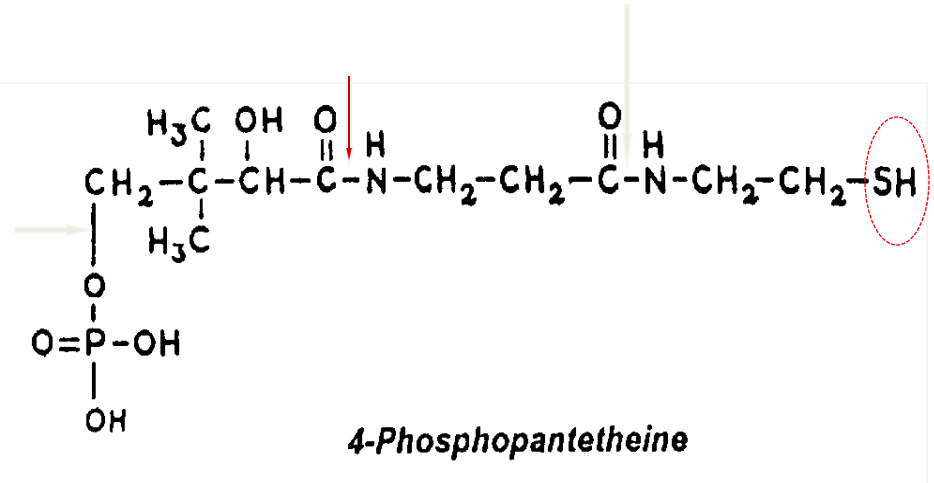
- At high levels of intake, when this mechanism is saturated, some pantothenic acid may also be absorbed via passive diffusion. As intake increases 10-fold, however, absorption rate decreases to 10%.

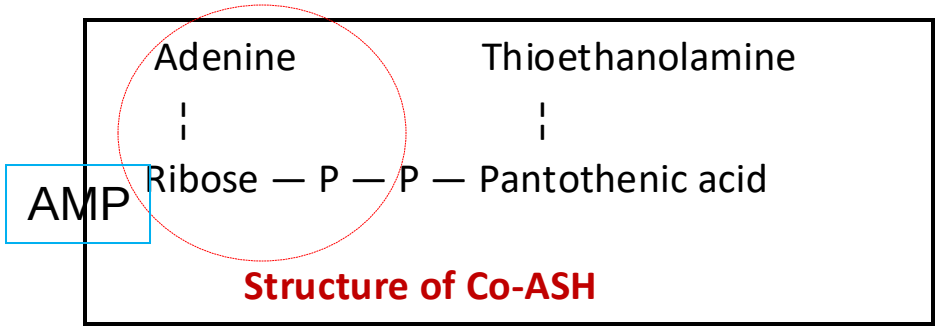
1. Chemical **structure** is …….. **[Pantoic & β- Alanine]**
2. **Active pantothenic** acid is …….. **[4-phosphopantotheine]**
3. Active form enters in the structure of ……

- **CoASH** = 4-phosphopantotheine + AMP
- **ACP**; acyl carrier protein

4. Its **active** group is: ……. **[Thiol group]**
5. Its **function as is: [Carrier of acyl radicals].** coenzyme A used in energy metabolism







6- Sources are: **[as B1]**

7- Reactions requiring **CoASH:**

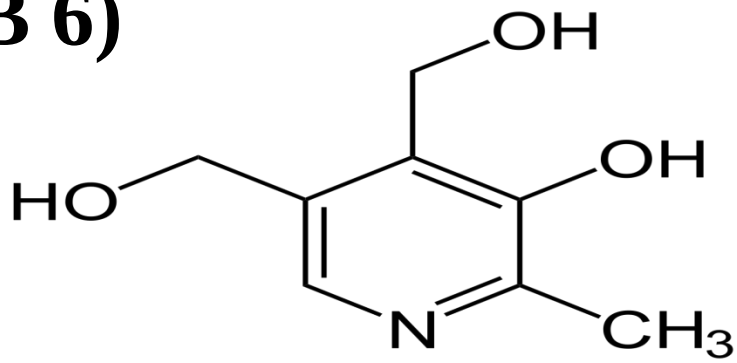
a- oxidative decarboxylation of a keto acids ⟶ Energy.
b- oxidation of Fatty acid
e- acetylating reactions as acetyl choline.

8- Reaction requiring **ACP is : [Fatty acids synthesis]**

- **Destruction:** Easily destroyed by food processing.
- **Functions:** Part of **coenzyme A** used in **energy metabolism.**
- **Deficiency: rare** because it is very widespread in natural food.

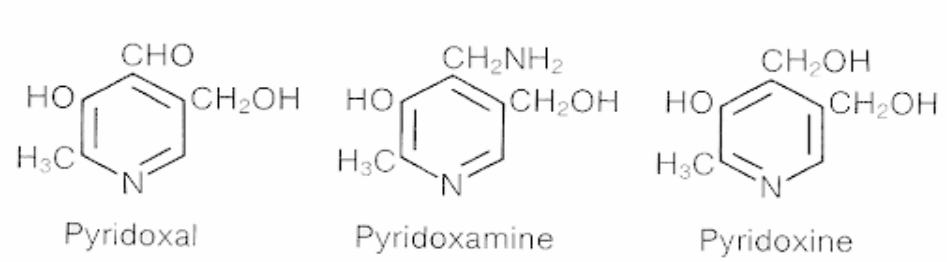
- Nausea, vomiting. -Easy fatigability. -Dermatitis.
- Depression, neurological symptoms (disorders of the synthesis of acetylcholine). Numbness, muscle cramps, inability to walk.
- **Burning foot syndrome** (severe burning and excessive sweating).

Pyridoxine (B 6)

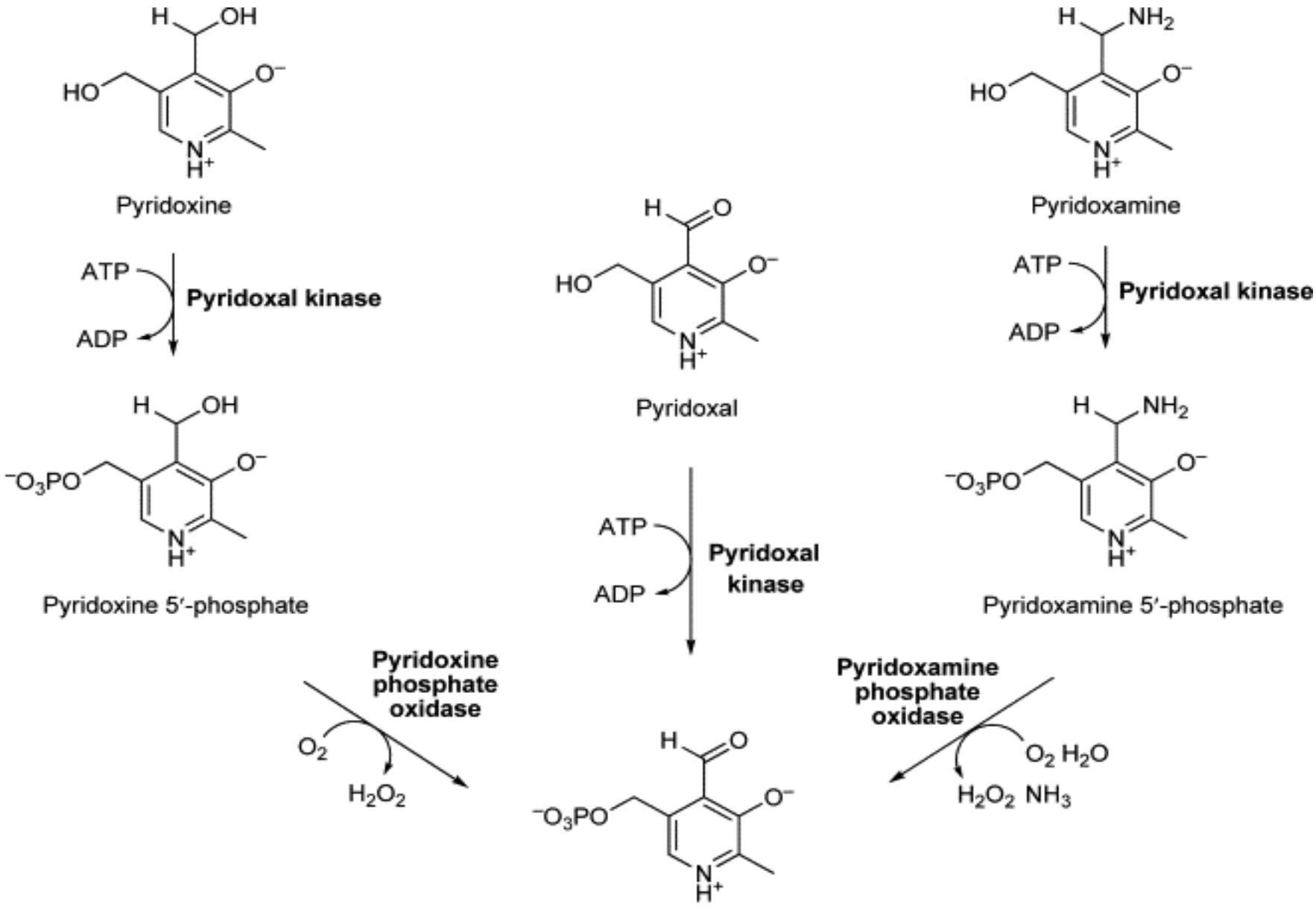


Chemistry:

- It is a water soluble vitamin
- A pyridoxine derivative
- Consists of 3 closely related compounds equally effective as precursors of its coenzyme PLP (pyridoxal phosphate)
    - Pyridoxine (alcohol)
    - Pyridoxal (aldehyde)
    - Pyridoxamine (amine)



- Pyridoxamine is mostly present in plants
- Pyridoxal & pyridoxine is present in animal foods
- Pyridoxine can be converted into pyridoxal & pyridoxamine
- Pyridoxal phosphate (PLP) is the active form of Pyridoxine
- PLP is synthesized by pyridoxal kinase, utilizing ATP


Pyridoxine
ATP
ADP
Pyridoxal kinase
Pyridoxine 5′-phosphate
Pyridoxal
Pyridoxamine
Pyridoxal kinase
Pyridoxamine 5′-phosphate
Pyridoxal kinase
Pyridoxine phosphate oxidase
Pyridoxamine phosphate oxidase
Pyridoxal 5′-phosphate

Metabolism

Absorption: It occurs in proximal jejunum by passive diffusion

- In the mucosal cells, all forms of pyridoxine is converted into pyridoxal
- Transport: It transported in the circulation bound to albumin
- Storage: It is stored in the tissues as its coenzyme form, PLP
- Mainly stored in liver, brain, kidney & muscle
- Excretion: 4 – pyridoxic acid excreted in urine

Biochemical functions

- PLP is the coenzyme of B6 is found attached to ε –amino group of lysine in the enzyme
- PLP is associated with Amino acid metabolism
- PLP is involved in:

1- Transamination 2- Decarboxylation 3- Deamination

4- Transsulfuration 5- Condensation

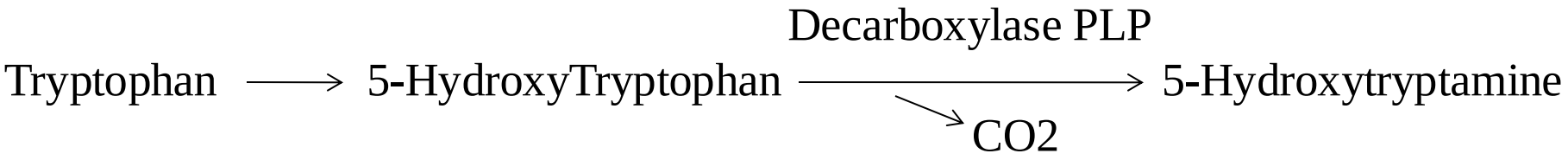
Transamination

- PLP is involved in transamination reaction converting amino acids to keto acids
- Keto acids enter the TCA cycle and get oxidized to generate energy
- During transamination, PLP interacts with amino acids to form Schiff base
- The amino group is handed over to PLP to form Pyridoxamine phosphate and ketoacid is liberated.

Decarboxylation

- α - Amino acids undergo decarboxylation to form respective amines
- The reaction is carried out by decarboxylases which require PLP

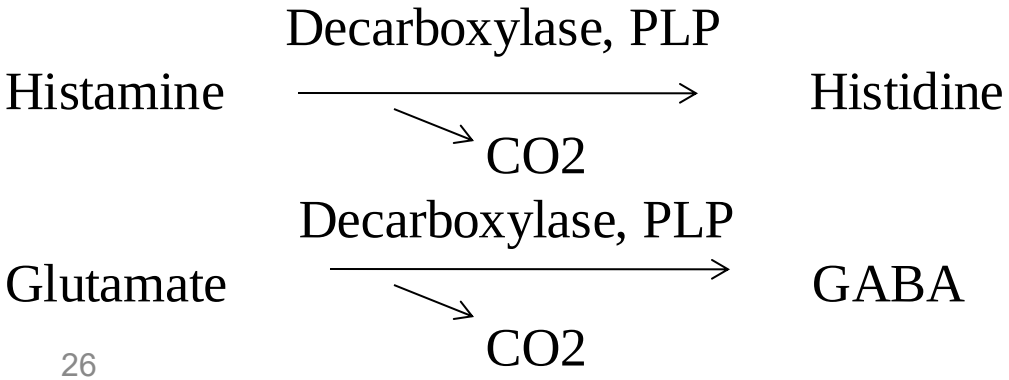
1- Serotonin produced from tryptophan is important in nerve impulse transmission. It regulates sleep, behavior, blood pressure.



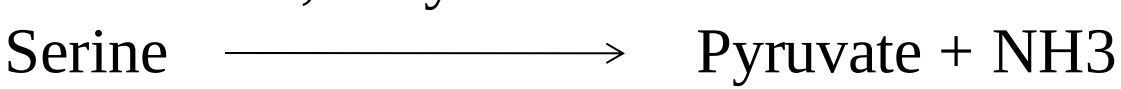
2- Histamine is vasodilator lowering blood pressure

- It stimulates gastric HCl secretion and is involved in inflammation and allergic reactions

3- Glutamate on decarboxylation gives GABA which inhibits transmission of nerve impulses



- PLP Plays an important role in metabolism of sulfur containing A.A.s
- Transsulfuration from homocysteine to serine occurs in the synthesis of cysteine
- PLP dependent enzyme cystathionine synthase
- Deamination of hydroxyl group containing A.A.s requires PLP



- Synthesis of serine from glycine require PLP.
- Glycogen phosphorylase contains PLP for converting glycogen to glucose 1-phosphate
- PLP is needed for the absorption of amino acids from intestine
- B6 is useful to prevent urinary stone formation

RDA (Recommended Dietary allowance) of vitamin B 6

- Adult men – 2 - 2.2 mg/day
- Adult women - 2.0 mg/day
- Pregnancy and lactation - 2.5 mg/day

Dietary sources:

- Animal sources: egg yolk, fish, milk, meat
- Vegetable sources: wheat, corn, cabbage, roots & tubers

Deficiency

- Decreased dietary intake
- Alcoholism
- Impaired absorption
- Antivitamins: chronic administration of drugs such as isoniazid and penicillamine

Clinical features

- Neurological manifestations due to B6 deficiency, serotonin, epinephrine, norepinephrine and GABA are not produced properly

- The synthesis of niacin from tryptophan is impaired
- Xanthurenic acid, produced in high quantities is excreted in urine and can be used as reliable index of B6 deficiency
- Decreased Hb levels, associated with hypochromic microytic anemia seen in B6 deficiency

Toxicity of B6

- Excess use of B6 (2.5 g/day) may lead to sensory neuropathy
- It is manifested by imbalance, numbness, muscle weakness and nerve damage

Biotin (B 7)

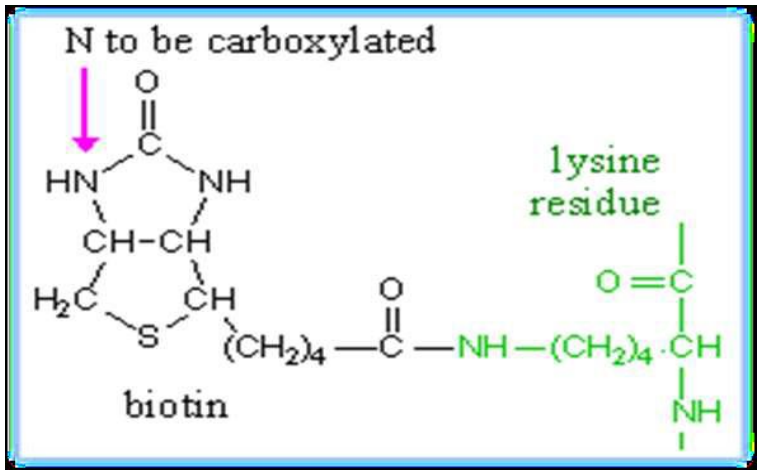
- It is formerly known as anti-egg white injury factor or vitamin H
- It is water soluble sulfur containing B-complex vitamin
- Biotin mainly participates in the carboxylation reactions

Chemistry

- It is a heterocyclic sulfur containing monocarboxylic acid
- Biotin is imidazole derivative formed by fusion of imidazole and thiophene rings with a valeric acid side chain
- Biotin covalently bound to ε – amino group of lysine to form biocytin

Coenzyme form

- Biocytin is the coenzyme form of Biotin
- Biotin is a prosthetic group of carboxylase



Biochemical functions

- Biotin is required for carboxylation reactions
- Biotin is required for the enzymes
    - Pyruvate carboxylase
    - Acetyl CoA carboxylase
    - Propionyl carboxylase
    - β - Methyl crotonyl CoA carboxylase

- Pyruvate carboxylase catalyzes conversion of pyruvate to oxaloacetate

$$\text{Pyruvate} \xrightarrow[\text{ADP+Pi Biotin, Mg++/Mn}]{\text{CO2, ATP, pyruvate carboxylase}} \text{Oxaloacetate}$$

- Acetyl CoA carboxylase catalyzes the formation of malonyl CoA from acetyl CoA, the reaction provides acetate molecule for fatty acid synthesis

$$\text{Acetyl CoA} \xrightarrow[\text{ADP+Pi Biotin, Mg++/Mn}]{\text{CO2, ATP, Acetyl CoA carboxylase}} \text{Malonyl CoA}$$

- Propionyl CoA carboxylase catalyzes the formation of D – Methyl malonyl CoA from propionyl CoA(from odd chain FA & methionine)
- It required for entry of Propionyl CoA to TCA cycle via succinyl CoA

$$\text{Propionyl CoA} \xrightarrow[\text{ADP+Pi Biotin, Mg++/Mn}]{\text{CO2, ATP, propionyl CoA carboxylase}} \text{D – Methyl malonyl CoA}$$

- β - Methyl crotonyl CoA carboxylase catalyzes the formation of β – Methylglutaconyl CoA from β - Methyl crotonyl CoA
- It is essential for leucine catabolism

$$\text{β - Methyl crotonyl CoA} \xrightarrow[\text{ADP+Pi Biotin, Mg++/Mn}]{\text{CO2, ATP, β - Methyl crotonyl CoA carboxylase}} \text{β – Methylglutaconyl CoA}$$

- Not all carboxylation reactions in the biological system are biotin dependent, few carboxylation reactions which do not require biotin
- Formation of carbamoyl phosphate in urea cycle
- Incorporation of CO2 in purine synthesis

Dietary sources

- Rich sources are eggs, liver, kidney, & yeast, pulses, nuts, vegetables
- Poor sources are cereals & dairy products

RDA

- Adults - 200 – 300 mg/day

Deficiency

- Biotin deficiency is generally not seen in man because of

1- Its wide distribution in foods

2- Synthesis of vitamin by the bacterial flora in the gut

Clinical features

- Severe dermatitis, weakness, & nausea
- In animals muscle weakness, dermatitis & loss of hair around the eye

- Avidin-biotin system is commonly utilized for detection of pathogenesis in ELISA test
- DNA is generally labelled by radioactive nucleotides
- Recently, biotin labelling of DNA is becoming more popular
- Biotin is added to nucleotides, which will be incorporated into the newly synthesized DNA
- The fixed biotin can be identified by reaction with Avidin
- Intake of 20 raw eggs/day will produce Biotin deficiency in humans
- Prolonged use of antibacterial drugs such as sulfonamides

Biotin antagonists

- Avidin (Raw egg white injury factor)

- Raw egg white injury factor is a heat labile protein known as avidin and is present in raw egg white

- Avidin binds to biotin & makes its unavailable for absorption

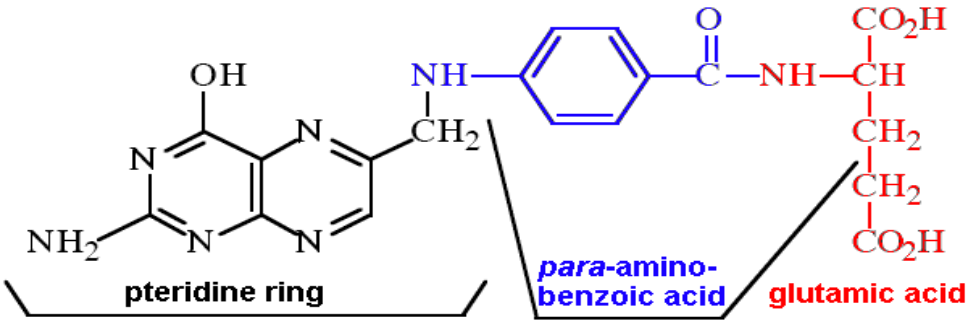
- Avidin is inactivated by boiling the eggs & biotin is readily absorbed when boiled eggs are used in the diet

- One molecule of avidin can combine with four molecules of biotin
- Egg white contains Avidin & egg yolk contains biotin

- The affinity of Avidin to biotin is greater than most of the usual antigen-antibody reactions

Vitamin B9 Folic acid (pteroylglutamic acid)

- Folic acid (dihydrofolate) is activated by reducing it to tetrahydrofolic acid by the enzyme dihydrofolate reductase



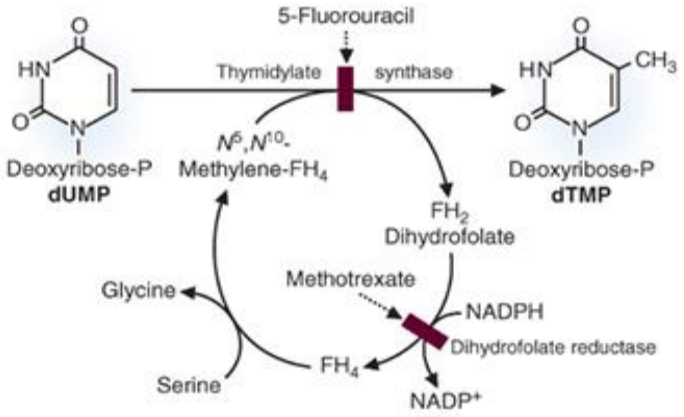
Health Functions

it helps the body as a coenzyme to:

- Utilize amino acids
- Produce nucleic acids
- Form blood cells in the bone marrow
- Ensure rapid cell growth in infancy, adolescence, and pregnancy
- Control (together with vitamin B6 and vitamin B12) blood levels of the amino acid homocysteine
- Associated with certain chronic conditions such as heart disease.
- Deficiency can lead to megaloblastic anemia
- Vitamin B12 plays a role in folate metabolism, therefore, the megaloblastic marrow of cobalamin deficiency is partly due to interference with folic acid utilization and can be partially reversed by folic acid

FH4 and one-carbon metabolism

- The sources of one-carbon group are serine, glycine, histidine, formaldehyde, and formate to be utilized in biosynthetic reactions
- The one-carbon group carried by FH4 is bound to N at position 5, or N at position 10, or linked to both by forming a bridge between N5 and N10



- For example
- The transfer methyl group to deoxyuridine monophosphate (dUMP) to form deoxythymidine monophosphate (dTMP). Therefore, FH4 is required for cell division thus compounds that inhibit formation of tetrahydrofolates will block purine synthesis and thus have been used in cancer chemotherapy.
- Also, transfer a one-carbon group to the amino acid glycine to form serine

Occurrence

- Folic acid is widely distributed particularly in green vegetables, fruits, yeast and liver
- Daily requirement 400 μg, for pregnant woman 400-1000 μg

Indications

- It is used for deficiency of folic acid which are either due to:
- Decreased supply (common in malnutrition, alcoholics, some slimming diets, elderly ...)
- Increased requirement e.g. pregnancy, hemolytic anemias
- Vigorous iron therapy in pregnancy may unmask folate deficiency
- Prevention of fetal neural tube defect if taken before conception and during early weeks of pregnancy can prevent the condition if occurred in a previous pregnancy
- Some antimalarial e.g. Pyrimethamine may interfere with conversion of folate to active tetrahydrofolate leading to macrocytic anemia
- Methotrexate another folate antagonist may cause a megaloblastic anemia

Folate deficiency

Causes:

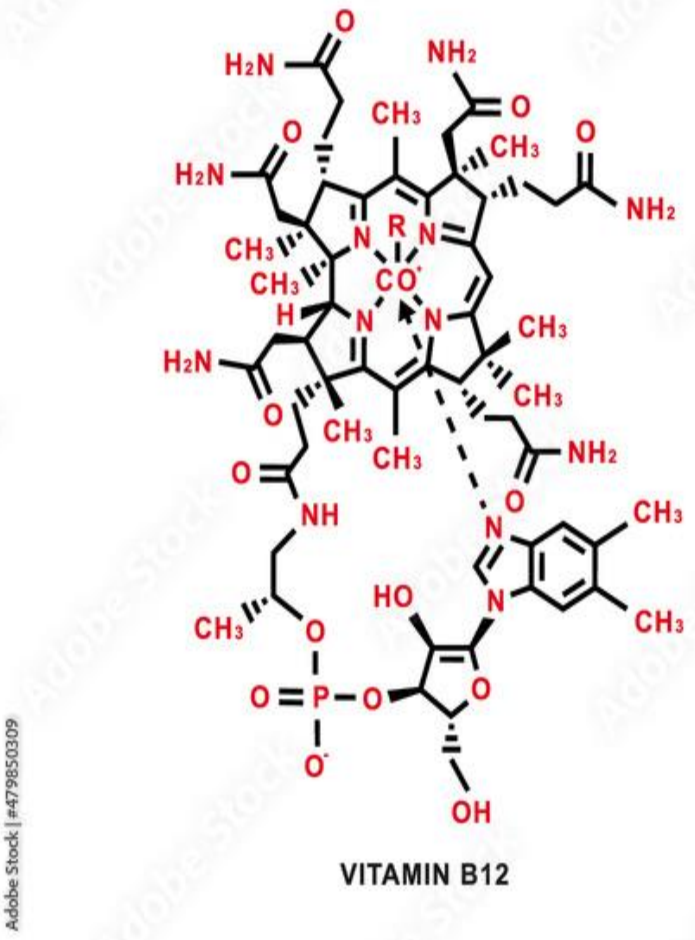
- Inadequate dietary intake of folate.
- Malabsorption of folate in jejunum due to intestinal diseases.
- Alcoholism.
- Pregnancy due to increased requirements.
- Some medications that can inhibit folate absorption or its conversion to the active form
- Deficiency of enzymes required in folate metabolism
- Vitamin B12 is required by methionine synthase for methyl group removal from N5-methyl FH4. Thus, when vitamin B12 is deficient N5-methyl FH4 will accumulate and the functional folate will be deficient results because the carbons cannot be removed from the folate.

Complications of folate-deficiency

1- Megaloblastic anemia
2- Impaired cognitive status
3- Neural tube defect such as spina bifida

Vitamin B12 (Cobalamin)

- The vitamin B12 synthesized in microorganisms (such as bacteria and algae) enters the human food chain through incorporation into food of animal origin.
- In many animals gastrointestinal fermentation supports the growth of these vitamin B12– synthesizing microorganisms, and subsequently the vitamin is absorbed and incorporated into the animal tissues.
- Vitamin B12 is only found in food of animal origin such as dietary meat, liver, eggs, dairy products, fish and seafood.



Vitamin B12 could be in the following forms:

1- 5-deoxyadenosylcobalamin
2- Methylcobalamin
3- Hydroxycobalamin
4- Cyanocobalamin

- The active forms of vitamin B12 are methylcobalamin and 5-deoxyadenosylcobalamin

Absorption of Vitamin B12

1. Free B12 binds directly to transcobalamin I of salivary and gastric mucosal cells within the stomach and will remain in the bound till reaching the duodenum in the small intestine
2. Bound B12 is released from the proteins by gastric and intestinal proteases, then, will bind also to the transcobalamin I.

- In the small intestine, the released B12 binds to intrinsic factor (a glycoprotein secreted by the gastric parietal cells).
- Intrinsic factor–B12 complex binds to receptors on the ileum to facilitate absorption of B12, then, binds to transcobalamin II to be transported to tissues (50% of the vitamin B12 will be uptaken by liver, and the remainder will be distributed to other tissues.

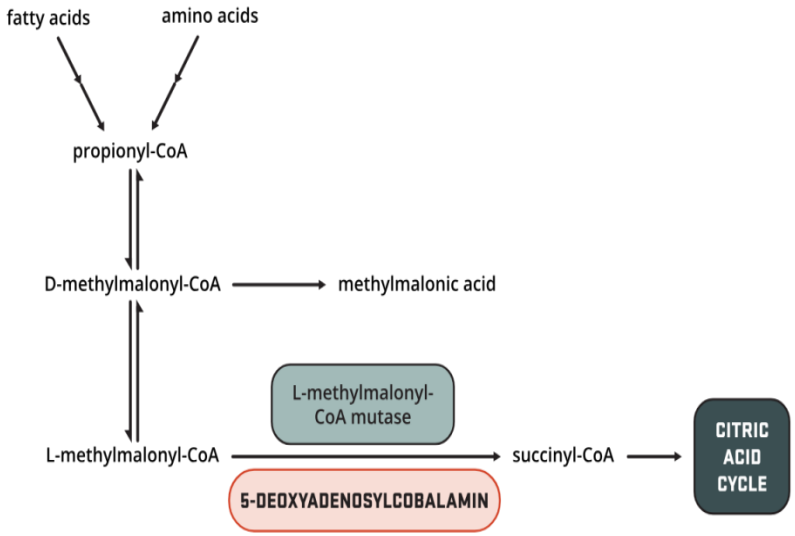
Vitamin B12 is participating as a cofactor in the following reactions:

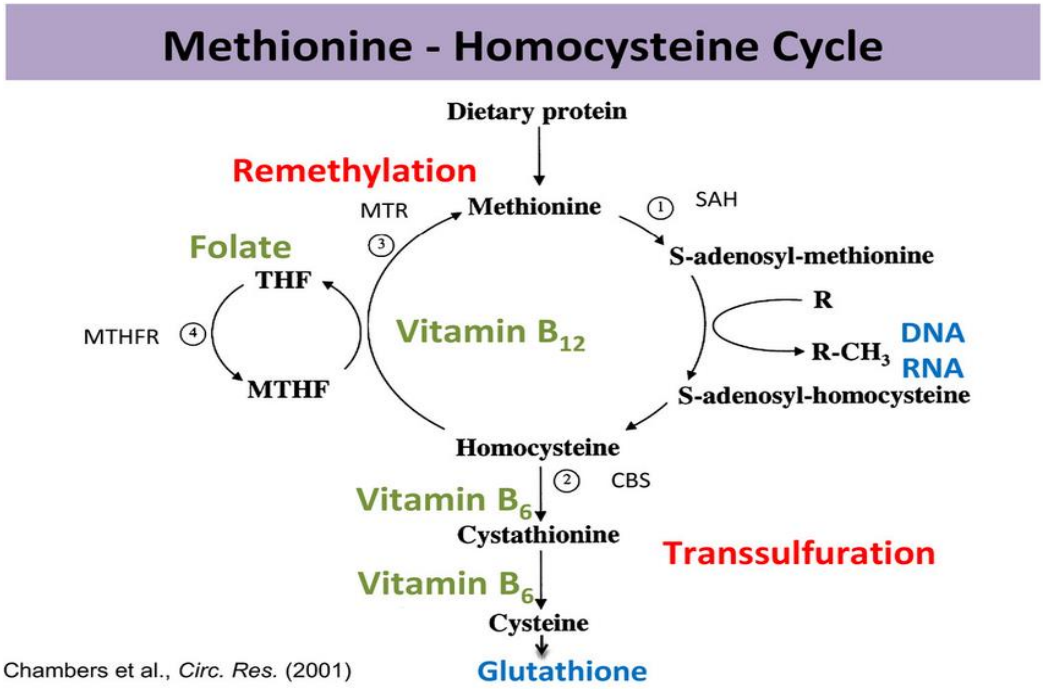
1- Methylation of homocysteine to methionine: this is important for DNA synthesis, myelin synthesis, neurotransmitters & brain metabolism and growth.

N.B. High homocysteine blood levels may be an indicator for vitamin deficiency, if not treatment, elevated homocysteine increases your risks for dementia, heart disease and stroke.

2- Conversion of L- methylmalonyl CoA to succinyl CoA to join TCA cycle for producing energy.

Figure 2. Metabolic Pathway Requiring 5-Deoxyadenosylcobalamin





CoA - coenzyme A

Causes of vitamin B12 deficiency

1- Pernicious anemia: is an autoimmune causing destruction of gastric parietal cells that are responsible for the synthesis of intrinsic factor thus the absorption of vitamin B12 will be interrupted leading to anemia.

- Surgery in the gastrointestinal tract such as gastric balloon, sleeve gastrectomy and gastric band
- Prolonged use of certain medications such as metformin, proton pump inhibitors (for treating GERD and peptic ulcers), histamine H2 blockers
- Dietary deficiency

- The amount of the vitamin stored in the liver is large enough that 3 to 6 years pass before symptoms of a dietary deficiency occur.

- Symptoms of vitamin B12 deficiency include tingling and numbness in the extremities, nerve damage, and memory loss.

Vitamin C (L-ascorbic acid)

- Its active form is ascorbate.
- Not synthesized by human cells
- Not stored
- The main functions of ascorbate are:

1. A reducing agent in many different reactions.
2. Biosynthesis of collagen (hydroxylysine and hydroxyproline).
3. Iron absorption
4. Regeneration of the reduced form of vitamin E
5- Antioxidant

- Vitamin C deficiency is associated with improper formation of connective tissue leading wound healing defect.
- The deficiency of ascorbic acid results in scurvy, a disease characterized by sores, spongy gums, loose teeth, fragile blood vessels, swollen joints, and anemia which are attributed to defective hydroxylation of collagen (hydroxylation of proline and lysine amino acids).